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Stereoretentive Preparation and Reactions of Highly Optically Enriched Secondary Alkyllithium, Alkylmagnesium and Alkylzinc Reagents. Exploiting Coordination Effects for the Regioselective Zincation of Diazines

von

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aus

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Erklärung

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Eidesstattliche Versicherung

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(Alexander Kremsmair)

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A) Communications and Research Articles:

1. J. Skotnitzki†, **A. Kremsmair**†, D. Keefer, Y. Gong, R. de Vivie-Riedle, P. Knochel, "Stereoselective C*sp*^{3}-C*sp*^{2} Cross-Couplings of Chiral Secondary Alkylzinc Reagents with Alkenyl and Aryl Halides" *Angew. Chem. Int. Ed.* **2020**, *59*, 320–324.

2. **A. Kremsmair**†, H. R. Wilke†, Q. Schmidt, P. Knochel, "General Stereoretentive Preparation of Chiral Secondary Mixed Alkylmagnesium Reagents and Their Use for Enantioselective Electrophilic Aminations" *Chem. Sci*. **2022**, *13*, 44–49.

3. **A. Kremsmair**, A. S. Sunagatullina, L. J. Bole, P. Mastropierro, S. Graßl, H. R. Wilke, E. Godineau, E. Hevia, P. Knochel, "Exploiting Coordination Effects for the Regioselective Zincations of Diazines using TMPZnX·LiX (X = Cl, Br)" *Angew. Chem. Int. Ed*. **2022**, *e202210491*.

4. **A. Kremsmair**, H. R. Wilke, M. M. Simon, B. Bissinger, N. Alandini, K. Karaghiosoff, P. Knochel, „*In situ* Quench Reactions of Chiral Secondary Alkyllithium Reagents in Batch and Continuous Flow" *Angew. Chem. Int. Ed*. **2022**, *e202214377.*

† These Authors contributed equally

B) Reviews:

1. J. Skotnitzki, **A. Kremsmair**, P. Knochel, "Stereoselective Preparation and Reactions of Chiral Secondary Alkyllithiums" *Synthesis* **2020**, *52*, 189–196.

2. **A. Kremsmair**, J. H. Harenberg, K. Schwärzer, A. Hess, P. Knochel, "Preparation and Reactions of Polyfunctional Magnesium and Zinc Organometallics in Organic Synthesis" *Chem. Sci.* **2021**, 12, 6011–6019.

C) Poster Presentations:

1. **A. Kremsmair**, J. Skotnitzki, D. Keefer, Y. Gong, R. de Vivie-Riedle, P. Knochel "Stereoselective Csp^3-Csp^2 Cross-Couplings of Chiral Secondary Alkylzinc Reagents with Alkenyl and Aryl Halides", *OMCOS20 conference* **2019**, *Heidelberg (Germany).*

2. **A. Kremsmair**, H. R. Wilke, M. M. Simon, K. Kublik, Q. Schmidt, P. Knochel "Stereoretentive Preparation of Chiral Secondary Alkyllithiums and Their Use in Organic Synthesis", *Syngenta PhD Workshop for Talented Chemistry PhD Students* **2021**, *online*.

3. **A. Kremsmair**, H. R. Wilke, P. Knochel "General Stereoretentive Preparation of Chiral Secondary Mixed Alkylmagnesium Reagents and Their Use for Enantioselective Electrophilic Aminations" *CaRLa Winterschool **2022**, Heidelberg (Germany).*

4. **A. Kremsmair**, H. R. Wilke, P. Knochel "*In situ* Quench Reactions of Chiral Secondary Alkyllithium Reagents in Batch and Continuous Flow" *BOSS XVII **2022**, Namur (Belgium).*

Additional publications:

1. J. Skotnitzki, **A. Kremsmair**, B. Kicin, R. Saeb, V. Ruf, P. Knochel, "Stereoselective *anti*-S_N2'-Substitutions of Secondary Alkylcopper-Zinc Reagents with Allylic Epoxides. Total Synthesis of (3*S*,6*R*,7*S*)-Zingiberenol" *Synthesis* **2020**, *52*, 873–881.

2. J. Skotnitzki, **A. Kremsmair**, D. Keefer, F. Schueppel, B. Cacher de Bonneville, R. de Vivie-Riedle, P. Knochel, "Regio- and Diastereoselective Reactions of Chiral Secondary Alkylcopper Reagents with Propargylic Phosphates: Preparation of Chiral Allenes" *Chem. Sci.* **2020**, *11*, 5328–5332.

3. **A. Kremsmair**, J. Skotnitzki, P. Knochel, "Diastereo- and Enantioselective Cross-Couplings of Secondary Alkylcopper Reagents and 3-Halogeno-Unsaturated Carbonyl Derivatives" *Chem. Eur. J.* **2020**, 26, 11971–11973.

4. A. Hess, **A. Kremsmair**, P. Knochel, "Lithium Dichloro(2,2,6,6-tetramethylpiperidinato)-magnesiate", *Encyclopedia of Reagents for Organic Synthesis* **2021**, doi: 10.1002/047084289X.rn02373.

5. **A. Kremsmair**, S. Graßl, C. B. J. Seifert, E. Godineau, P. Knochel, "Cobalt-Catalyzed Preparation of *N*-Heterocycles from Heteroaryl Chlorides", *Synthesis* **2021**, *53*, 4068–4074.

6. **A. Kremsmair**, A. Hess, B. Heinz, P. Knochel, "Regioselective Magnesiations and Zincations of Aromatics and Heterocycles Triggered by Lewis Acids" *Chem. Eur. J.* **2022**, *28*, e2021032.

"*What we do in life echoes in eternity*"

-Maximus Decimus Meridius,

Gladiator

Abbreviations

Ac	acetyl
aq	aqueous
Ar	undefined aryl substituent
ATR	attenuated total reflection
Bn	benzyl
Bu	butyl
Bz	benzoyl
C	celsius
ca.	circa
calc.	calculated
CCDC	cambridge crystallographic data centre
CIPE	complex induced proximity effect
CFU	continuous flow unit
conc.	concentrated
Cy	cyclohexyl
d	doublet (NMR)
dba	dibenzylideneacetone
DCM	dichloromethane
DMF	dimethylformamide
DMG	directed metalation group
DMSO	dimethylsulfoxide
dppf	1,1'-bis(diphenylphosphino)ferrocene
E	electrophile
e.g.	for example (lat. *exempli gratia*)
EI	electron ionisation
equiv	equivalents
Et	ethyl
etc.	and so no (lat. *et cetera*)
g	gram
GC	gas chromatography
h	hour
Het	undefined heteroaryl substituent
h	hour
hex	hexyl
HMDS	hexamethyldisilazane

HPLC	high performance liquid chromatography
HRMS	high resolution mass spectroscopy
Hz	hertz
i	*iso*
i. d.	internal diameter
IR	infrared
J	coupling constant
LDA	lithium diisopropylamide
m	multiplet (NMR)
M	metal
m	*meta*
Me	methyl
Met	undefined metallic substituent
mL	milliliter
mm	millimeter
mmol	millimole
mol%	mole percent
m.p.	melting point
NaDA	sodium diisopropylamide
NMR	nuclear magnetic resonance
o	*ortho*
p	*para*
Ph	phenyl
PMDTA	pentamethyldiethylenetriamine
ppm	parts per milion
Pr	propyl
PTFE	polytetrafluoroethylene
q	quartet (NMR)
R	undefined organic substituent
s	singlet (NMR)
s	*sec*
s	second
sat.	saturated
SPhos	2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl
t	*tert*
t	triplet (NMR)

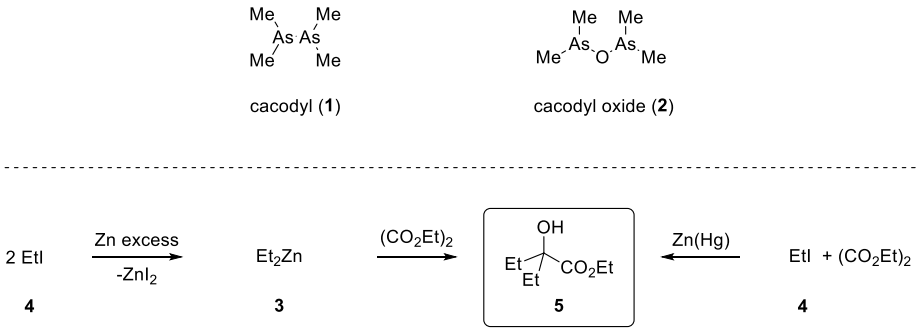
t	time
T	temperature
TBS	*tert*-butyldimethylsilyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMEDA	*N*,*N*,*N*´,*N*´-tetramethylethylenediamine
TMP	2,2,6,6-tetramethylpiperidyl
TMS	trimethylsilyl
TMU	tetramethylurea
TP	typical procedure
V	volume
vol%	volume percent

Contents

A. Introduction

1 Historical Background

Organometallic chemistry emerged at the end of the 18th century with the discovery of cacodyl (**1**) and cacodyl oxide (**2**) prepared by Louis Cadet de Gassicourt, a Parisian apothecary.[1] He obtained these organometallics by heating As_2O_3 with potassium acetate. At first, this discovery had little impact on synthetic organic chemistry. However, the good availability of zinc led English chemist Edward Frankland to the discovery of Et_2Zn (**3**) by heating metallic zinc with ethyl iodide (**4**).[2] In 1863 Frankland proved that this highly pyrophoric liquid, which reacts violently with air or oxygen, adds readily to diethyl oxalate producing the tertiary alcohol **5**.[3] This reaction has been extended to several organozinc reagents as well as carbonyl derivatives and may be considered as the birth of synthetic organometallic chemistry. Shortly after his initial discoveries, Frankland and Duppa[4] reported a modified procedure for the preparation of **4** by heating amalgamated zinc with ethyl iodide and ethyl oxalate (see Scheme 1).



Scheme 1. First reported organometallic reagents cacodyl (**1**) and cacodyl oxide (**2**) and synthesis of **5** *via* stepwise or one-pot procedure according to Frankland.

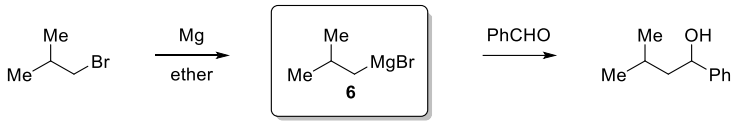
[1] a) L. C. Cadet de Gassicourt, *Memoires de Mathematique et de Physique. Presenté á l'Académie Royale des Sciences par diverse Savans et lûs dans ses Assemblées* **1760**, *13*, 62; b) D. Seyferth, *Organometallics* **2001**, *20*, 1488-1498.

[2] D. Seyferth, *Organometallics* **2001**, *20*, 14, 2940–2955.

[3] a) E. Frankland, *Proc. R. Soc. London* **1863**, *12*, 396; b) E. Frankland, *Ann.* **1863**, *126*, 109.

[4] a) E. Frankland, B. F. Duppa, *Ann.* **1864**, *130*, 104; b) E. Frankland, B. F. Duppa, *J. Chem. Soc.* **1864**, *17*, 29.

Due to the good availability of magnesium turnings and powder, the French chemist Philippe Barbier replaced zinc with magnesium. In 1899, he reported the first one-pot procedure for the preparation of organomagnesium nucleophiles in the presence of a carbonyl electrophile.[5] A year later, his co-worker Victor Grignard reported a similar procedure, but this time Grignard pre-formed the organometallic reagent of type **6** upon addition of the electrophile (see Scheme 2).[6] This heterogeneous reaction is nowadays widely applied in chemical laboratories and industries.



Scheme 2. Preparation of organomagnesium reagent **6** according to Grignard.

The use of organomagnesium halides as reactive intermediates developed rapidly due to their higher reactivity compared to organozinc compounds. Nevertheless, due to their moderate reactivity and inherently higher functional group tolerance, organozinc reagents proved to be a complementary tool for organic chemists, allowing the preparation of organometallic reagents, which are inaccessible using Grignards procedure. Furthermore, by adding a transition-metal catalyst, these organozincs can undergo a transmetalation producing a transition-metal species with extended reaction pathways.[7]

In general, the reactivity of a carbon-metal bond depends on the ionic character of the carbon-metal bond: the more ionic, the more reactive. Thus, the lower the electronegativity of the metal, the more reactive is this organometallic (see Figure 1).[8] Therefore, it becomes clear, that metals like B, Ni, Cu, Fe, In, Zn and Mn are predicted to display an excellent functional group tolerance, whereas organometallics of metals such as Ti, Zr, Mg will show a moderate functional group compatibility and metals like Li or Na will tolerate functional groups only at low temperatures or in special set-ups.

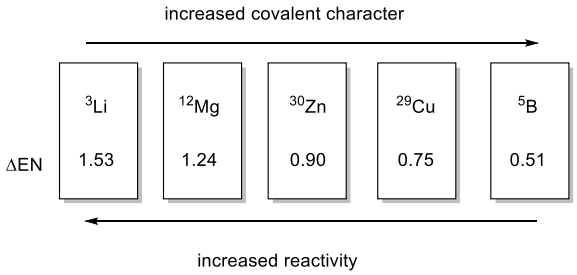


Figure 1. Difference in electronegativity of selected metals in comparison to carbon and their reactivity trends in the periodic table.

[5] P. Barbier, *Compt. Rend.* **1899**, *128*, 110–112.
[6] V. Grignard, *Compt. Rend. Acad. Sci.* ***1900***, *130*, 1322–1324.
[7] J. F. Hartwig, *Organotransition Metal Chemistry from Bonding to Catalysis* Wiley-VCH, Weinheim, **2010**.
[8] P. Knochel, *Handbook of Functionalized Organometallics Vol. 1 and 2*, Wiley-VCH, Weinheim, **2005**.

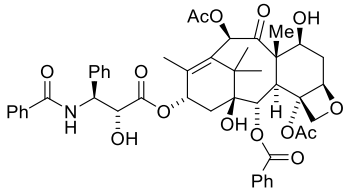
2 Access to Stereodefined Molecules

Isolation of natural products, chiral resolution and asymmetric synthesis represent main strategies to access stereodefined molecules. While the isolation of natural products from plants, microorganisms and other natural sources is attractive due to the unmatched range of chemical diversity provided, their isolation and separation is challenging and often can only be performed in insufficient yields.[9] Furthermore, isolation is often accompanied by the irreversible consumption of hundred years old evolutional feedstock. Thus, designing new reactions which would yield one enantiomer over the other, nowadays called asymmetric synthesis, and their application in the artificial total synthesis of natural products and APIs became one of the most emerging fields of organic chemistry.[10] These routes can often yield several hundred milligrams of a desired compound, enabling a range of biological activity tests. Furthermore, natural products can often be prepared in concise fashion and several related congeners can be easily prepared. This leads to a range of tuned natural products, offering new insights in drug discovery through structure-activity relationship explorations.[11]

Nevertheless, chiral resolution for the separation of racemic compounds is also a highly attractive solution for chemical industry to access stereodefined molecules due to their easy handling and scalability. The right choice of conditions facilitates the preparation of several multigrams of highly enantioenriched products.[12]

2.1 Isolation of Natural Products

Paclitaxel (**7**), commercially sold under the name Taxol, was first isolated from the bark extract of a pacific yew tree and soon approved as versatile chemotherapy candidate for the treatment of several cancer types (see Figure 2).[13]



7

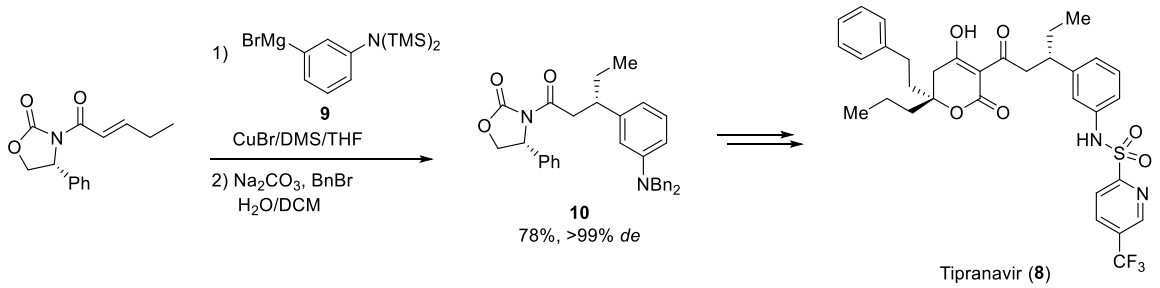
Figure 2. Structure of Paclitaxel (**7**), isolated from the pacific yew tree *Taxus Brefivolia*.

[9] a) S. D. Sarker, L. Nahar, *Natural Products Isolation*, Springer Protocol, Springer Science+Business Media LLC, Berlin, **2013**; b) F. Bucar, A. Wube, M. Schmid, *Nat. Prod. Rep.* **2013**, *30*, 525–545.
[10] V. Farina, J. T. Reeves, C. H. Senayake, J. J. Song, *Chem. Rev.* **2006**, *106*, 2734–2793.
[11] C. D. Selassie, *Burger's Medicinal Chemistry and Drug Discovery*, John Wiley&Sons, Inc, **2003**.
[12] a) William H. Porter, *Pure Appl. Chem.* **1991**, *63*, 1119–1122; b) Y. Fujima, M. Ikunaka, T. Inoue, J. Matsumoto, *Org. Process Res. Dev.* **2006**, *10*, 905–913.
[13] J. Gallego-Jara, G. Lozano-Terol, R. A. Sola-Martínez, M. Cánovas-Diaz, T. de Diego Puente *Molecules* **2020**, *25*, 5986.

While the isolation and separation of paclitaxel (**7**) was only achieved in low yields, the scarce plant material was constantly destroyed leading to problematic supply of the desired raw material. Soon, organic chemists found ways of artificially producing this highly complex natural product, however, accompanied by high stepcount and low overall yield.[14] Today, Taxol is produced completely independent from natural sources in a bioreactor by modified plant cell cultures.[15]

2.2 Asymmetric Synthesis

Synthesis of highly enantioenriched molecules using chiral ligands or auxiliaries represents a desirable tool for the highly enantioselective preparation of chiral molecules and several large-scale applications have been reported.[10,16] For example, the non-peptide HIV protease inhibitor Tipranivir (**8**), was prepared using a chiral auxiliary-controlled copper-catalyzed conjugate addition of Grignard reagent **9**. The obtained intermediate product **10** was recrystallized to give the desired stereoisomer in >99% diastereomeric excess (*de*) (see Scheme 3).[17]



Scheme 3. Use of asymmetric copper-catalyzed conjugate addition of organomagnesium reagent **9** in the synthesis of the non-peptide HIV protease inhibitor Tipranavir (**8**).

[14] a) K. C. Nicolaou, Z. Yang, J. J. Liu, H. Ueno, P. G. Nantermet, R. K. Guy, C. F. Claiborne, J. Renaud, E. A. Couladouros, K. Paulvannan, E. J. Sorensen, *Nature* **1994**, *367*, 630; b) R. A. Holton, C. Somoza, H. B. Kim, F. Liang, R. J. Biediger, P. D. Boatman, M. Shindo, C. C. Smith, S. Kim, *J. Am. Chem. Soc.* **1994**, *116*, 1597–1598; c) R. A. Holton, H. B. Kim, C. Somoza, F. Liang, R. J. Biediger, P. D. Boatman, M. Shindo, C. C. Smith, S. Kim, *J. Am. Chem. Soc.* **1994**, *116*, 1599–1600.

[15] S.-H. Pyo, M.-S. Kim, J.-S. Cho, B.-K. Song, B.-H. Han, H.-J. Choi, *J. Chem. Technol. Biotechnol.* **2004**, *79*, 1162–1168.

[16] G. Diaz-Muñoz, I. L. Miranda, S. K. Sarotir, D. C. Re Rezende, M. A. Nogueira Diaz *Chirality* **2019**, 31, 776–812.

[17] T. M. Judge, G. Phillips, J. K. Morris, K. D. Lovasz, K. R. Romines, G. P. Luke, J. Tulinsky, J. M. Tustin, R. A. Chrusciel, L. A. Dolak, S. A. Mizsak, W. Watt, J. Morris, S. L. Vander Velde, J. W. Strohbach, R. B. Gammill, *J. Am. Chem. Soc.* **1997**, *119*, 3627–3628.

While the use of chiral auxiliaries is desirable due to their cheap price, high selectivity and straightforward installation, the waste produced by their stepwise installation and de-installation is considerably high, especially in large scale reactions.[18] Therefore, the use of catalytic amounts of finely tuned chiral ligands is highly desirable in terms of a more sustainable synthesis.[19]

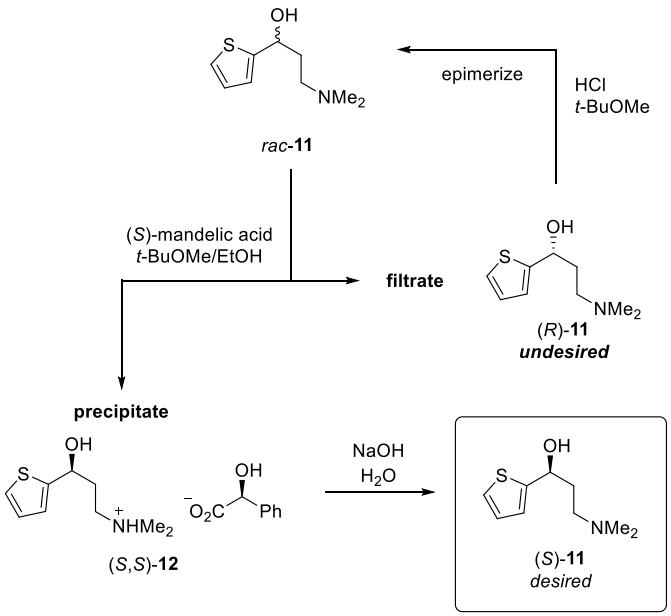
Prochiral double bonds can be asymmetrically hydrogenated using catalytic amounts of a chiral catalyst and molecular hydrogen.[20] This cost and atom efficient process has been largely applied in chemical laboratories and industry to access chiral alkanes, alcohols or amines from alkenes, ketones and imines.

[18] R. J. Sullivan, S. G. Newman, *Chem. Sci.* **2018**, *9*, 2130–2134.
[19] I. Ojima, *Catalytic Asymmetric Synthesis*, John Wiley & Sons, New York, **2010**.
[20] a) R. Noyori, M. Kitamura, T. Okuma, *PNAS* **2004**, *101*, 5356–5362; b) M. Yoshimura, S. Tanaka, M. Kitamura, *Tetrahedron Lett.* **2014**, *55*, 3635–3640.

2.3 Chiral Resolution

Chiral resolution was among the first known processes to access chiral molecules and discovered already in 1853 by French chemist Louis Pasteur.[21] He observed that the crystals of the double sodium-ammonium salt of tartaric acid looked different under a microscope and was even able to separate them by hand with a tweezer. To date, highly advanced chemical systems have been developed for the separation of enantiomers, which have, for example, found application in the synthesis of a precursor of the serotonin-norepinphrine reuptake inhibitor (SNRI) Duloxetine.[12b]

Thus, the racemic alcohol *rac*-**11** was treated with (*S*)-mandelic acid leading to the insoluble diastereomeric salt (*S*,*S*)-**12**, which was filtered off from the undesired (*R*)-**11**. Addition of sodium hydroxide liberated the free alcohol (*S*)-**11** again, while the remaining (*R*)-**11**, which stayed in the filtrate, was epimerized using HCl in toluene yielding *rac*-**11**, which was used in another resolution cycle (see Scheme 4).



Scheme 4. Resolution-Racemization-Recycle synthesis of Duloxetine precursor (*S*)-**11**.

In general, synthetically valuable (asymmetric) syntheses often rely on finely tuned organometallic reagents, which display high reactivity combined with high regio-, chemo- and stereoselectivity. In the following part, general methods for the preparation of functionalized organometallics will be discussed as well as their use in modern organic synthesis.

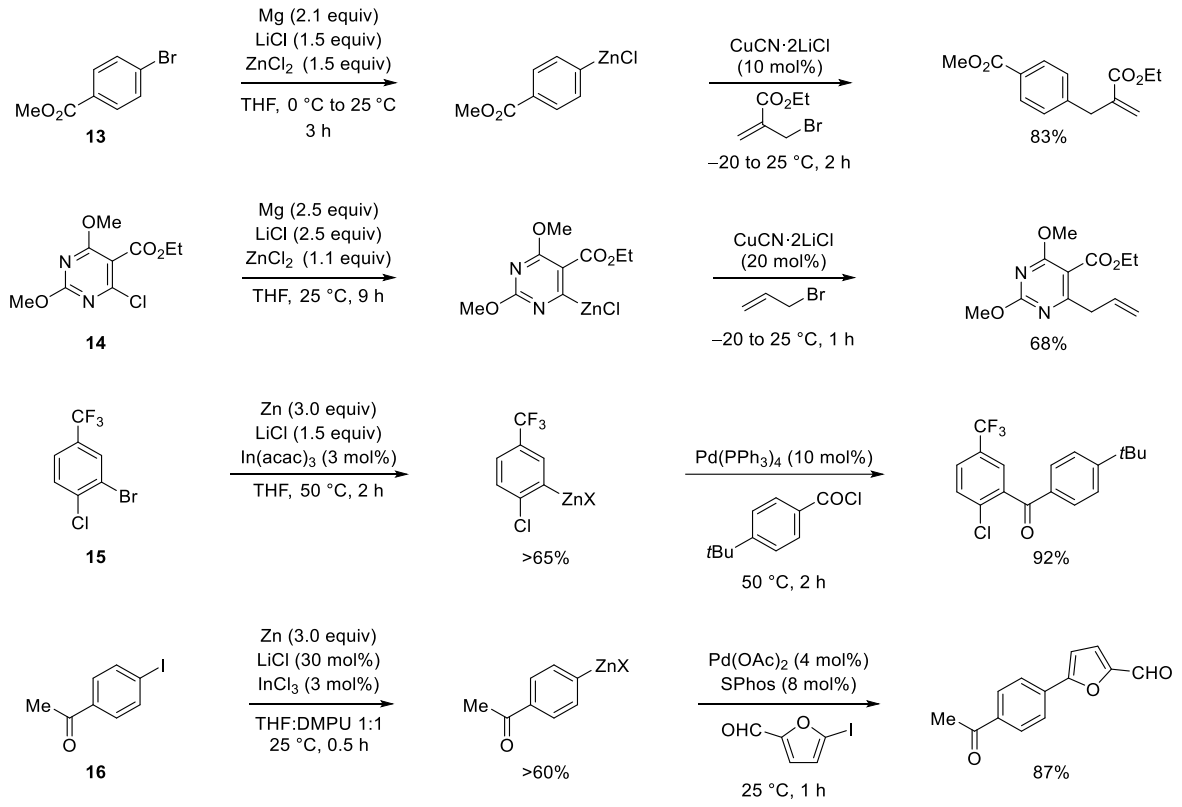
[21] L. Pasteur, *Compt. R. Acad. Sci.* **1848**, *26*, 535–538.

3 Preparation and Reactions of Polyfunctional Organomagnesium and Zinc reagents

The most common ways to access organometallic reagents (oxidative addition, halogen/metal exchange, directed metalation and transmetalation) have been well described in the literature. These methods offer advantages, but also drawbacks, especially in the preparation of chiral organometallics.

3.1 Direct Insertion of Magnesium or Zinc into Organic Halides

The carbon-zinc bond is a covalent carbon-metal bond with moderate intrinsic reactivity. Metallic zinc is a weaker reducing agent compared to magnesium, and therefore a mixed metal synthesis using magnesium dust in the presence of LiCl and $ZnCl_2$ is an advantageous procedure for the preparation of aryl and heteroaryl zinc reagents bearing sensitive functional groups.[22] Under these conditions, methyl 4-bromobenzoate (**13**) underwent a smooth conversion to the corresponding zinc reagent within 3 h at 25 °C (see Scheme 5).

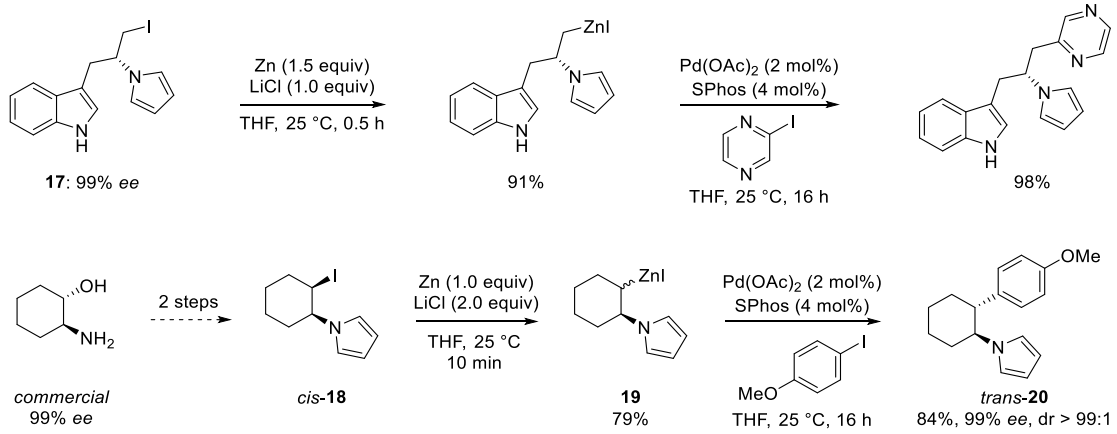


Scheme 5. Magnesium and zinc insertions into functionalized hetero(aryl) halides mediated by LiCl and indium salts.

[22] a) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040–6044; b) F. M. Piller, A. Metzger, M. A. Schade, B. A. Haag, A. Gavryushin, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 7192–7202.

The addition of LiCl was crucial for removing the organometallic species on the metal surface by forming a mixed magnesium-lithium complex of the type RMgX·LiCl.[23] Fast magnesium insertion rates were observed with electron-deficient substrates such as **14**.[22b] Direct zinc insertion may require the addition of a Lewis-acid catalyst whose role is to facilitate electron transfer steps from the metal surface to the organic halide. Thus, in the presence of $In(acac)_3$ (3 mol%), **15** was converted to the corresponding zinc reagent at 50 °C within 2 h.[24] The use of a polar co-solvent such as DMPU proved to be helpful.[25] Under these conditions, a sensitive functional group like an acetyl group which is prone to enolization, like in 4-iodoacetophenone (**16**), was perfectly tolerated.

The mild conditions required for these insertion reactions are also compatible with the presence of acidic NH-groups.[26] Thus, **17** was converted to the corresponding zinc reagent at 25 °C[27] and in the presence of a palladium catalyst cross-couplings with an *N*-heteroaryl iodide readily took place. Secondary alkyl iodides usually react faster in these direct insertion reactions. Thus, *cis*-iodo-pyrrole **18**, prepared from *trans*-2-aminocyclohexanol, underwent a zinc insertion within 10 min at 25 °C leading to a *cis,trans*-mixture of zinc reagent **19**. However, in the presence of a palladium catalyst, a diastereoselective cross-coupling[28] took place exclusively affording *trans*-**20** (84%; 99% ee; dr = >99:1; see Scheme 6).

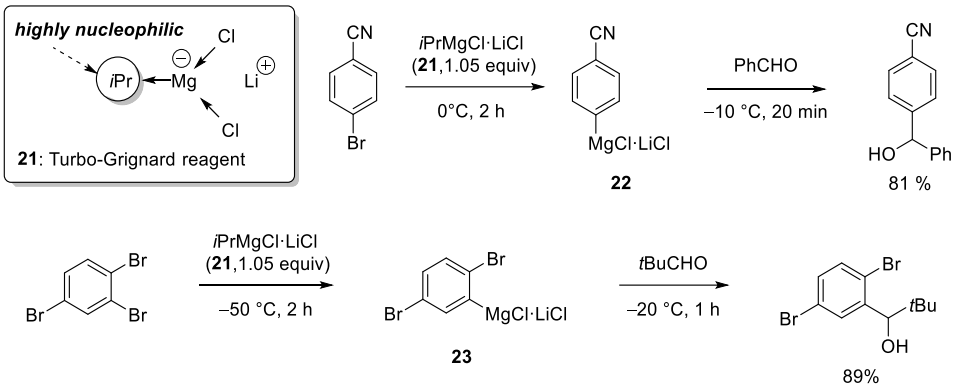


Scheme 6. Zn-insertions to alkyl iodides bearing an indolyl NH-group and (or) a β-*N*-pyrrolyl group.

[23] C. Feng, D. W. Cunningham, Q. T. Easter, S. A. Blum, *J. Am. Chem. Soc.* **2016**, *138*, 11156–11159.
[24] A. D. Benischke, G. Le Corre, P. Knochel, *Chem. Eur. J.* **2017**, *23*, 778–782.
[25] T. Mukhopadhyay, D. Seebach, *Helv. Chim. Acta* **1982**, *65*, 385–391.
[26] a) G. Manolikakes, M. A. Schade, C. M. Hernandez, H. Mayr, P. Knochel, *Org. Lett.* **2008**, *10*, 2765–2768; b) G. Manolikakes, C. Muñoz Hernandez, M. A. Schade, A. Metzger, P. Knochel, *J Org. Chem.* **2008**, *73*, 8422–8436; c) Z. Dong, G. Manolikakes, J. Li, P. Knochel, *Synthesis* **2009**, *2009*, 681–686; d) G. Manolikakes, M. S. Z. Dong, H. Mayr, J. Li, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 1324–1328.
[27] M. Leroux, W.-Y. Huang, Y. Lemke, T. J. Koller, K. Karaghiosoff, P. Knochel, *Chem. Eur. J.* **2020**, *26*, 8951–8957.
[28] T. Thaler, B. Haag, A. Gavryushin, K. Schober, E. Hartmann, R. M. Gschwind, H. Zipse, P. Mayer, P. Knochel, *Nat. Chem.* **2010**, *2*, 125–130.

3.2 The Halogen/Metal Exchange

The halogen/lithium exchange (Hal = I, Br) is a fast reaction which was independently discovered in 1939 by Gilman and Wittig.[29] In comparison, the halogen/magnesium-exchange is a much slower reaction, which had only found applications in the preparation of some heterocyclic Grignard reagents[30] and magnesium carbenoids.[31] However, by using organomagnesium halides complexed by LiCl such as *i*PrMgCl·LiCl (**21**, Turbo-Grignard reagent) fast I/Mg- and Br/Mg-exchanges took place producing functionalized aryl and heteroaryl magnesium reagents **22** or **23** under mild conditions (see Scheme 7).[32]



Scheme 7. Br/Mg-exchanges on functionalized aryl bromides using the Turbo-Grignard reagent (**21**).

The kinetics of the Br/Mg-exchange[33] as well as the mechanism of the reaction has been well studied.[34] It was postulated that the rate of a halogen/metal exchange depends on the ionic character of the carbon-metal bond: the more electro-positive the metal is, the faster the halogen/metal exchange takes place. This hypothesis led to the discovery of halogen/lanthanide exchange reactions.[35]

[29] H. Gilman, W. Langham, A. L. Jacoby, *J. Am. Chem. Soc.* **1939**, *61*, 106–109; G. Wittig, U. Pockels, *Ber. Dtsch. Chem. Ges.* **1939**, *72*, 884–886.

[30] a) M. Rottländer, L. Boymond, L. Bérillon, A. Leprêtre, G. Varchi, S. Avolio, H. Laaziri, G. Quéguiner, A. Ricci, G. Cahiez, P. Knochel, *Chem. Eur. J.* **2000**, *6*, 767–770; b) A. Boudier, L. O. Bromm, M. Lotz, P. Knochel, *Angew. Chem. Int. Ed.* **2000**, *39*, 4414–4435; c) P. Knochel, W. Dohle, N. Gommermann, F. F. Kneisel, F. Kopp, T. Korn, I. Sapountzis, V. A. Vu, *Angew. Chem. Int. Ed.* **2003**, *42*, 4302–4320.

[31] a) J. Villiéras, *Bull. Soc. Chim. Fr* **1967**, *5*, 1520; b) J. Villiéras, B. Kirschleger, R. Tarhouni, M. Rambaud, *Bull. Soc. Chim. Fr.* **1986**, 470–478; c) S. Avolio, C. Malan, I. Marek, P. Knochel, *Synlett* **1999**, 1820–1822; d) L. Boymond, M. Rottländer, G. Cahiez, P. Knochel, *Angew. Chem. Int. Ed.* **1998**, *37*, 1701–1703.

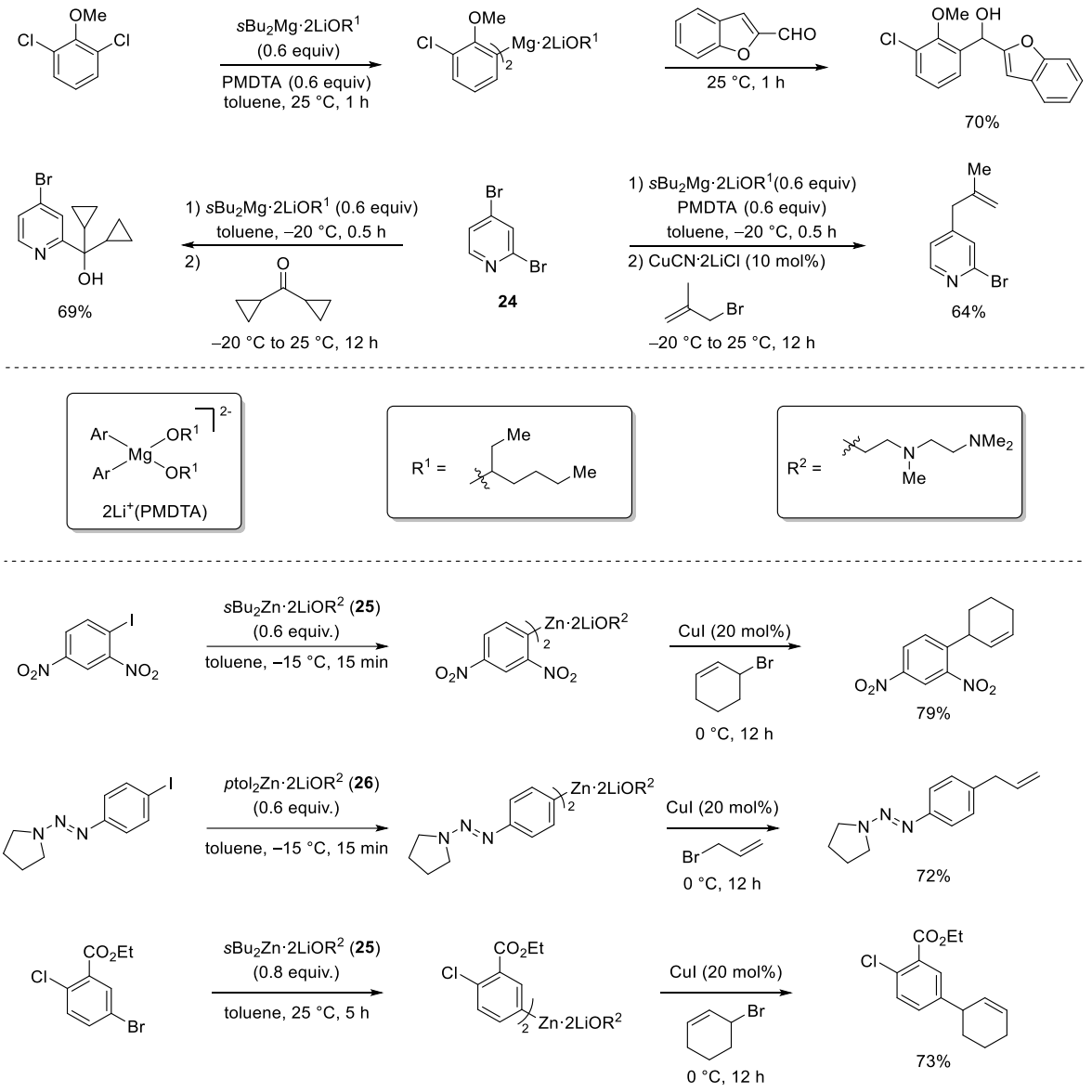
[32] A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333–3336.

[33] a) I. Hiriyakkanavar, B. Oliver, W. A. J., K. Paul, *Chem. Lett.* **2006**, *35*, 2–7; b) G. Dagousset, C. François, T. León, R. Blanc, E. Sansiaume-Dagousset, P. Knochel, *Synthesis* **2014**, *46*, 3133–3171; c) N. M. Barl, V. Werner, C. Samann, P. Knochel, *Heterocycles* **2014**, *88*, 827–844.

[34] a) A. Krasovskiy, B. F. Straub, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 159–162; b) L. Shi, Y. Chu, P. Knochel, H. Mayr, *Angew. Chem. Int. Ed.* **2008**, *47*, 202–204; c) L. Shi, Y. Chu, P. Knochel, H. Mayr, *Org. Lett.* **2009**, *11*, 3502–3505; d) L. Shi, Y. Chu, P. Knochel, H. Mayr, *Org. Lett.* **2012**, *14*, 2602–2605.

[35] a) A. D. Benischke, L. Anthore-Dalion, G. Berionni, P. Knochel, *Angew. Chem. Int. Ed.* **2017**, *56*, 16390–16394; b) A. D. Benischke, L. Anthore-Dalion, F. Kohl, P. Knochel, *Chem. Eur. J.* **2018**, *24*, 11103–11109; c) L. Anthore-Dalion, A. D. Benischke, B. Wei, G. Berionni, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58*, 4046–4050.

The replacement of LiCl in the Turbo-Grignard reagent (**21**) with lithium alkoxides (LiOR) led to even more powerful exchange reagents (*s*BuMgOR^1·LiOR^1 and *s*Bu$_2$Mg·2LiOR^1; R^1 = 2-ethylhexyl) soluble in toluene. These reagents allowed the performance of some Cl/Mg-exchanges[36] as well as regioselective exchanges on various dibromopyridines such as **24.**[37] Furthermore, the corresponding zinc reagents **25** or **26** were used for I/Zn-exchanges on aryl iodides in toluene (see Scheme 8).[38]



Scheme 8. Halogen/magnesium and zinc exchanges using the exchange reagents *s*Bu$_2$Mg·2LiOR^1, *s*Bu$_2$Zn·2LiOR^2 (**25**) or *p*Tol$_2$Zn·2LiOR^2 (**26**).

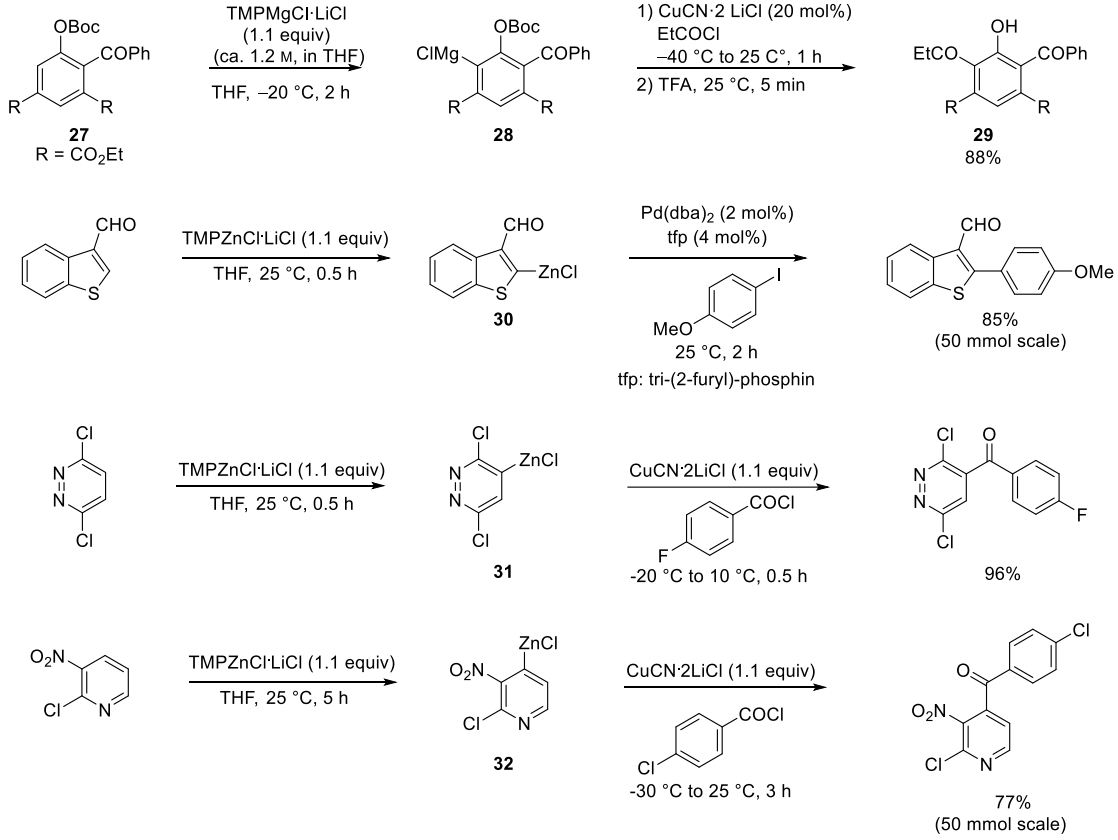
[36] D. S. Ziegler, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 6701–6704.

[37] A. Desaintjean, T. Haupt, L. J. Bole, N. R. Judge, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2021**, *60*, 1513–1518.

[38] M. Balkenhohl, D. S. Ziegler, A. Desaintjean, L. J. Bole, A. R. Kennedy, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58*, 12898–12902.

3.3 Directed Magnesiations and Zincations with TMP-Bases Complexed with LiCl

In general, magnesium amides (R_2NMgX or $(R_2N)_2Mg$) are poorly soluble in THF and display moderate kinetic basicity.[39] However, by using a sterically hindered amine (2,2,6,6-tetramethylpiperidine, TMP-H), it was possible to prepare a series of metallic amides complexed with LiCl (TMPMgCl·LiCl, TMP_2Mg·2LiCl, TMPZnCl·LiCl and TMP_2Zn·2LiCl) with high solubility in THF (1.2–1.4 M) and exceptional kinetic basicity.[40] The preparation of polyfunctional magnesium reagents became then possible from halide-free precursors. Thus, the highly functionalized arene **27** was magnesiated with TMPMgCl·LiCl at –20 °C leading to an arylmagnesium species **28** bearing several sensitive functional groups (OBoc, CO_2Et, COPh, see Scheme 9).[41]



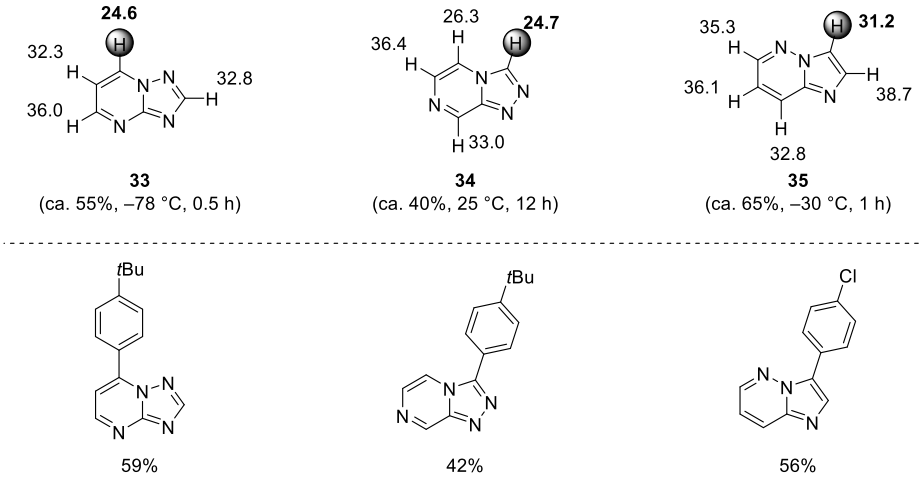
Scheme 9. Directed magnesiations and zincations using mixed Mg-Li or Zn-Li-TMP-bases.

[39] C. R. Hauser, H. G. Walker, *J. Am. Chem. Soc.* **1947**, *69*, 295–297.

[40] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958–2961; b) S. H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7685–7688; c) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794–9824; d) S. M. Manolikakes, N. M. Barl, C. Sämann, P. Knochel, *Z. Naturforsch. B* **2013**, *68*, 411–422.

[41] W. Lin, O. Baron, P. Knochel, *Org. Lett.* **2006**, *8*, 5673–5676.

A copper-mediated acylation afforded the penta-substituted arene **29** in 88% yield. By using TMPZnCl·LiCl, aryl and heteroaryl zinc organometallics **30**-**32** were produced.[42] Since a carbon-zinc bond is more covalent than a carbon-magnesium bond, the inherent reactivity of the carbon-zinc bond is much lower and therefore it becomes possible to prepare highly functionalized organozinc derivatives. Due to the presence of low lying p-orbitals at the zinc centre, various transmetalations with transition metal salts proceeded readily, providing transition metal intermediates which underwent new reaction pathways not possible for main-group organometallics (oxidative addition, reductive elimination, insertion reaction). This behaviour allowed an efficient reaction with numerous electrophiles. Furthermore, TMPZnCl·LiCl is less prone to undergo kinetic metalations and thermodynamic considerations are relevant for predicting the regioselectivity. Thus, the site of metalation can be readily determined by calculation of the pKa-values of various unsaturated substrates. The zincation of new heterocyclic systems such as **33**-**35** were predicted by this model and subsequent functionalizations were performed successfully (see Scheme 10).[43] In general, TMPMgCl·LiCl and TMPZnCl·LiCl are valuable reagents for the metalation of heterocycles.[44] Remarkably, the compatibility of these bases with various Lewis acids including BF_3·OEt_2 has also been reported.[45]



Scheme 10. Calculation of the pKa-values of condensed *N*-heterocycles to predict their reactivity with TMPZnCl·LiCl and subsequent quenching with electrophiles.

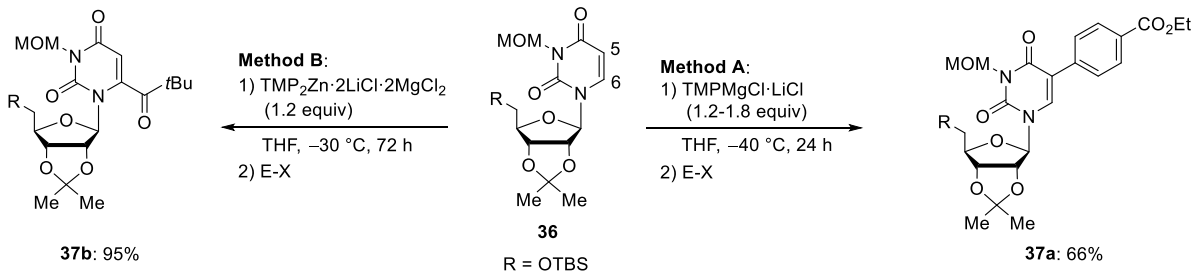
[42] a) M. Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837–1840; b) T. Bresser, G. Monzon, M. Mosrin, P. Knochel, *Org. Process Res. Dev.* **2010**, *14*, 1299–1303.

[43] M. Balkenhohl, H. Jangra, I. S. Makarov, S.-M. Yang, H. Zipse, P. Knochel, *Angew. Chem. Int. Ed.* **2020**, *59*, 14992–14999.

[44] K. Schwärzer, C. P. Tüllmann, S. Graßl, B. Górski, C. E. Brocklehurst, P. Knochel, *Org. Lett.* **2020**, *22*, 1899–1902.

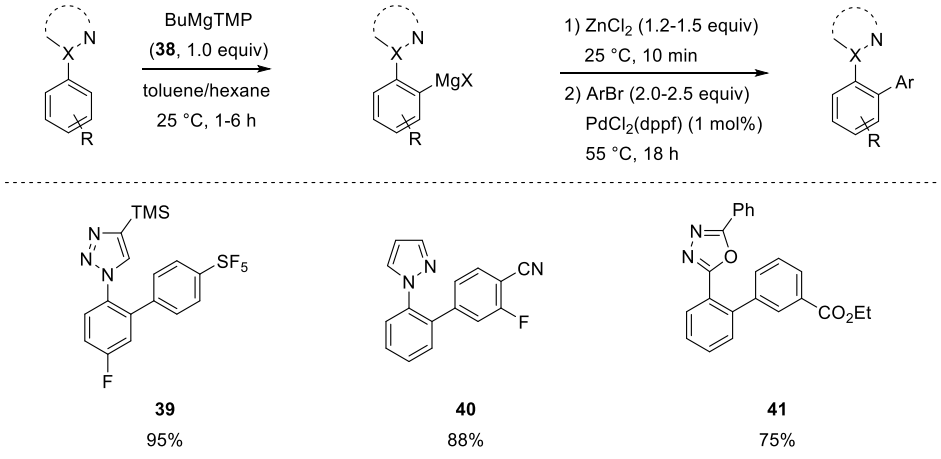
[45] a) M. Jaric, B. A. Haag, A. Unsinn, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2010**, *49*, 5451–5455; b) K. Groll, S. M. Manolikakes, X. M. du Jourdin, M. Jaric, A. Bredihhin, K. Karaghiosoff, T. Carell, P. Knochel, *Angew. Chem. Int. Ed.* **2013**, *52*, 6776–6780; c) S. M. Manolikakes, M. Jaric, K. Karaghiosoff, P. Knochel, *Chem. Commun.* **2013**, *49*, 2124–2126; d) A. Kremsmair, A. Hess, B. Heinz, P. Knochel *Chem. Eur. J.* **2022**, *28*, e202103269.

For example, the possibility of forming frustrated Lewis pairs has been exploited for the regioselective functionalization of uridines such as **36**. By using TMPMgCl·LiCl in THF, a complexation occured at the amide function directing the magnesiation at the adjacent position leading to products like **37a**. However, using $TMP_2Zn·2LiCl$ in the presence of $MgCl_2$ similarly led to a complexation of $MgCl_2$ at the amide function and hampered the approach of the zinc base which eventually deprotonated at position 6 leading to products like **37b** (see Scheme 11).[46]



Scheme 11. Regioselective magnesiations and zincations of uridines with TMP-bases.

The performance of kinetically controlled metalations (usually triggered by a pre-complexation of the base to a Lewis-basic centre of the substrate)[47] is often amplified by the use of a low polarity solvent such as toluene. Thus, designing a new toluene soluble base (BuMgTMP, **38**) allowed a regioselective kinetic metalation of various aryl azoles at the *ortho*-position of the aryl ring resulting in products **39-41** of great interest for pharmaceutical research (see Scheme 12).[48]



Scheme 12. Regioselective magnesiations of aryl azoles in toluene with BuMgTMP (**38**).

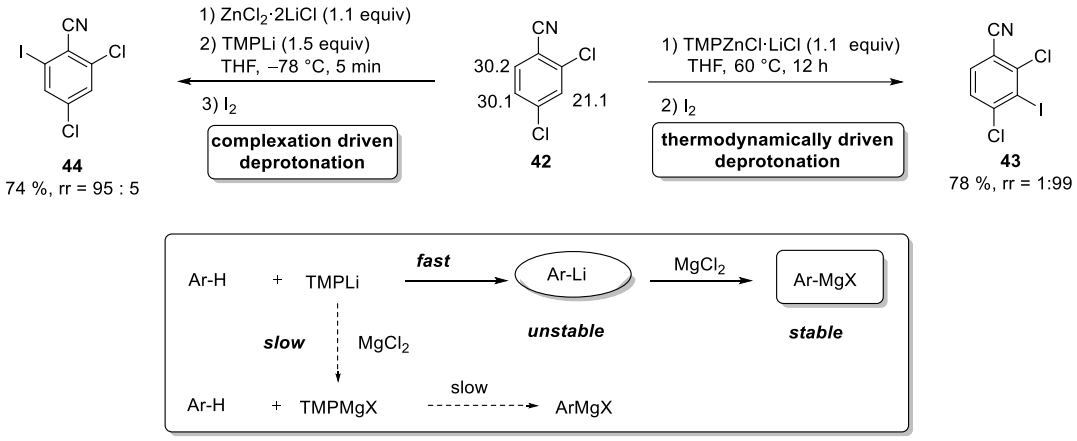
[46] L. Klier, E. Aranzamendi, D. Ziegler, J. Nickel, K. Karaghiosoff, T. Carell, P. Knochel, *Org. Lett.* **2016**, *18*, 1068–1071.

[47] M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem. Int. Ed.* **2004**, *43*, 2206–2225

[48] F. H. Lutter, L. Grokenberger, L. A. Perego, D. Broggini, S. Lemaire, S. Wagschal, P. Knochel, *Nat. Commun.* **2020**, *11*, 4443.

3.4 Lewis Pairs Involving Organozinc and Organomagnesium Reagents; New Barbier-Reactions

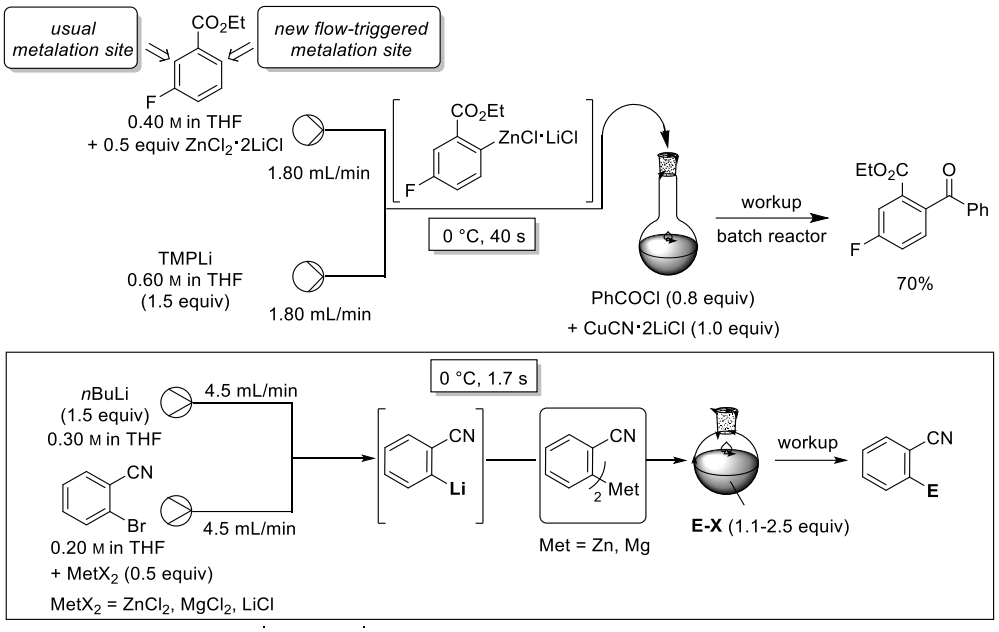
Various magnesium and zinc organometallics are compatible with strong Lewis acids such as $BF_3{\cdot}OEt_2$ and this behaviour has already been exploited for performing selective metalations.[49] The field of Barbier reactions remained largely unexplored although remarkable selectivities were achieved.[50] A recent example concerned the regioselective metalation of 2,4-dichlorobenzonitrile **42** (see Scheme 13).



Scheme 13. Kinetic and thermodynamic deprotonation of aryl nitrile **42**.

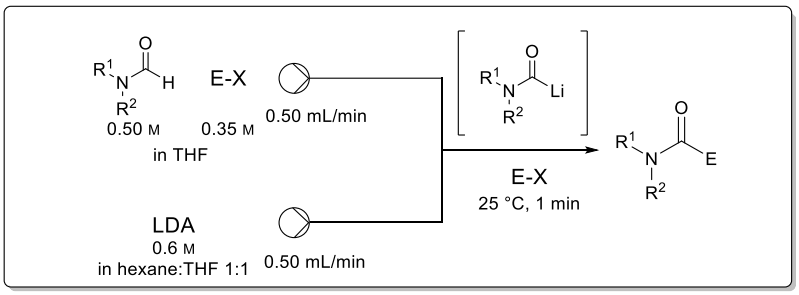
In accordance with the pKa-values of the aromatic ring protons, the most acidic 3-position of benzonitrile derivative **42** was readily zincated by TMPZnCl·LiCl. As indicated above, this base is especially prone to undergo thermodynamically driven metalations. After 12 h at 60 °C and subsequent iodolysis, nitrile **43** was obtained as the only regioisomer. However, with the strong lithium base TMPLi, a complexation driven deprotonation was triggered by coordination of this base to the cyano group inducing an *ortho*-deprotonation. Performing this lithiation only with TMPLi led to extensive decomposition due to the high reactivity of the resulting aryllithium species. However, mixing **42** with the THF-soluble salt $ZnCl_2{\cdot}2LiCl$ and adding TMPLi at –78 °C led to a fast kinetic deprotonation followed by a transmetalation with the zinc(II)-salt, providing a stable arylzinc reagent which after iodolysis produced regioselectively the iodonitrile **44**. This behaviour proved to be quite general and $MgCl_2$ or $CuCN{\cdot}2LiCl$ allowed similar reactions. However, the scale-up of these reactions proved to be difficult. This problem was solved by performing these metalations in continuous flow using micro-reactors (see Scheme 14).[51]

[49] C. Blomberg, *The Barbier reaction and related one-step processes*, Springer Verlag Berlin Heidelberg, **1993**.
[50] A. Frischmuth, M. Fernández, N. M. Barl, F. Achrainer, H. Zipse, G. Berionni, H. Mayr, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2014**, *53*, 7928–7932.
[51] a) M. R. Becker, P. Knochel, *Angew. Chem. Int. Ed.* **2015**, *54*, 12501–12505; b) M. Ketels, M. A. Ganiek, N. Weidmann, P. Knochel, *Angew. Chem. Int. Ed.* **2017**, *56*, 12770–12773.

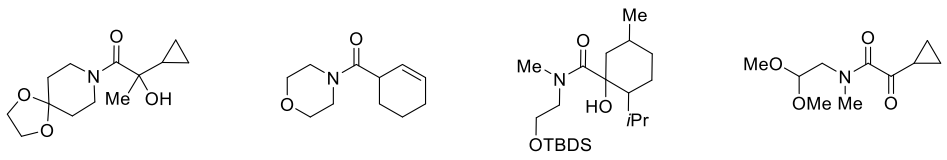


Scheme 14. Directed lithiations and Br/Li-exchanges in the presence of various metallic salts $MetX_2$.

It was possible to perform Barbier reactions by mixing the electrophile directly with the substrate bearing an acidic proton to avoid transmetalations. Thus, treatment of various formamides and electrophiles such as carbonyl electrophiles, disulfides and allylic bromides in continuous flow provided a convenient and scalable synthesis of functionalized amides (see Scheme 15).[52]



E-X = ketones, aldehydes allylic bromides, disulfides, morpholino- and Weinreb-amides



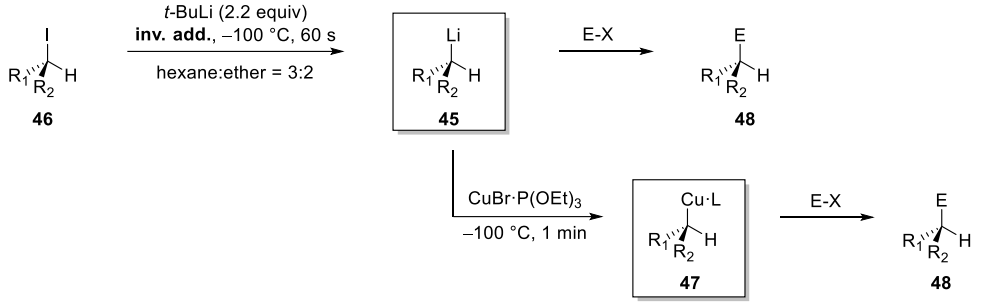
72% 60% 89% 76%

Scheme 15. Barbier reactions in continuous flow involving an *in situ* generation of carbamoyllithium derivatives.

[52] M. A. Ganiek, M. R. Becker, G. Berionni, H. Zipse, P. Knochel, *Chem. Eur. J.* **2017**, *23*, 10280–10284.

4 Previous Efforts on the Preparation of Chiral Alkyllithium Reagents

Organolithiums have been known since the beginning of the 20th century and were first used for the initiation of anionic polymerizations. They possess a highly polarized carbon-lithium bond, ensuring a high reactivity towards various electrophilic reagents.[53] These reactive organometallics were popularized in organic synthesis in *ca.* 1960[54] and soon a range of heteroatom-stabilized organolithium reagents became available.[55] Seebach introduced the concept of "Umpolung", which enables the performance of C-C bond formation by a formal inversion of polarity[56] and therefore, considerably facilitates the retrosynthesis of complex organic molecules.[57] A range of elegant methods were developed for the preparation of optically enriched chiral heteroatom-stabilized organolithium reagents.[58] However, non-stabilized secondary alkyllithium reagents of type **45** were prepared *via* an I/Li-exchange reaction proceeding with retention of configuration, starting from the corresponding secondary alkyl iodides of type **46**.[59] Reaction conditions were found allowing a stereoselective transmetalation of **45** to copper derivatives of type **47** using CuBr·P(OEt)$_3$ (see Scheme 16).[60]



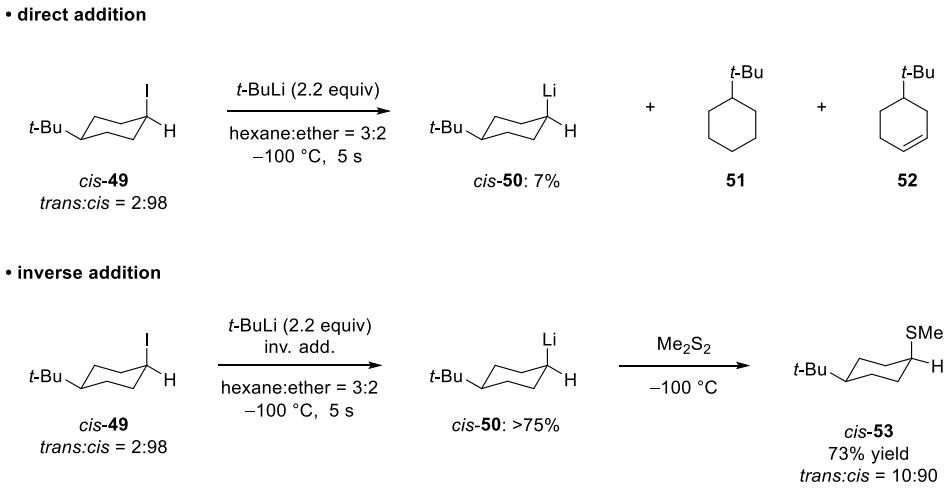
Scheme 16. Stereoselective reactions of chiral secondary alkyllithium reagents.

The transmetalation proceeded with retention of configuration and the resulting secondary alkyl organometallics (**45** or **47**) reacted stereoselectively with appropriate electrophiles (E-X) providing a range of chiral molecules of type **48** which are of interest for the preparation of natural products.[61]

[53] M. Majewski, et al. *Science of Synthesis*, 8a: Category 1, Organometallics Thieme, **2005**, 859 pp.
[54] a) J. Clayden, *Organolithiums: Selectivity for Synthesis*, Elsevier, Philadelphia, **2002**; b) D. V. Collum, A. J. McNeil, A. Ramirez, *Angew. Chem. Int. Ed*. **2007**, *46*, 3002–3017.
[55] A. T. Hase, *Umpoled Synthons: A Survey of sources and Uses in Synthesis*, John Wiley & Sons, Inc. New York, **1987**.
[56] D. Seebach, *Synthesis* **1969**, *1*, 17–36.
[57] D. Seebach, *Angew. Chem.* **1979**, *91*, 259–278.
[58] a) D. Hoppe, T. Hense, *Angew. Chem. Int. Ed*. **1997**, *36*, 2282–2316; b) D. Hoppe, *Synthesis* **2009**, 43–55; c) A. H. Cherney, N. T. Kadunce, S. E. Reisman, *Chem. Rev.* **2015**, *115*, 9587–9652.
[59] S. Seel, G. Dagousset, T. Thaler, A. Frischmuth, K. Karaghiosoff, H. Zipse, P. Knochel, *Chem. Eur. J.* **2013**, *19*, 4614–4622.
[60] K. Moriya, M. Simon, R. Mose, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed*. **2015**, *54*, 10963–10967.
[61] V. Morozova, J. Skotnitzki, K. Moriya, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed*. **2018**, *57*, 5516–5519.

4.1 Stereoselective Preparation of Secondary Alkyllithiums

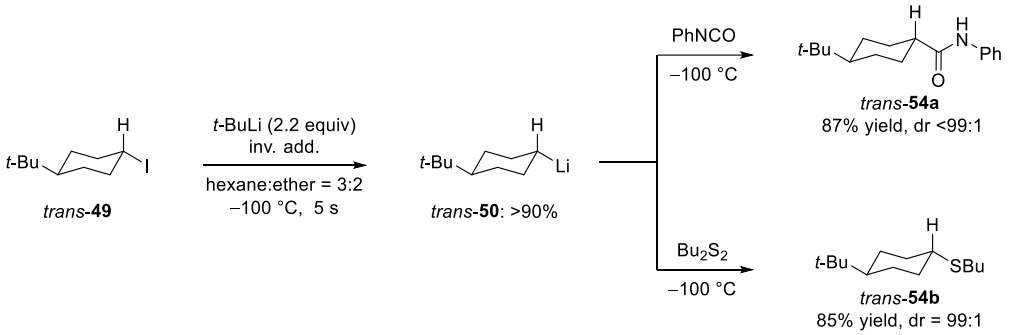
The performance of an I/Li-exchange on secondary alkyl iodides using *t*-BuLi is complicated by various side reactions due to the exceptionally high reactivity of the resulting secondary alkyllithium reagents, which are very close to the reactivity of *t*-BuLi. Bailey showed that the reaction of *cis*-4-*tert*-butylcyclohexyl iodide (*cis*-**49**) with *t*-BuLi at −100 °C in a hexane:ether mixture (3:2) produced the cyclic organolithium reagent *cis*-**50** in less than 7% yield. The main reaction products were cyclohexane **51** generated by the reaction of *cis*-**50** with iodide *cis*-**49** (protonation reaction) and the cyclohexene derivative **52** (elimination product of *cis*-**49**). These side reactions may be minimized by performing the reaction in the presence of a constant excess of *t*-BuLi. This can be experimentally realized by performing an inverse addition. Under these conditions, the lithium reagent *cis*-**50** could be generated in >75% yield. Trapping with Me_2S_2 at −100 °C provided the thioether *cis*-**53** with a diastereoselectivity of *trans*:*cis* = 10:90 (see Scheme 17).[59]



Scheme 17. Generation of the secondary alkyllithium reagent *cis*-**50** *via* direct or inverse addition of *t*-BuLi.

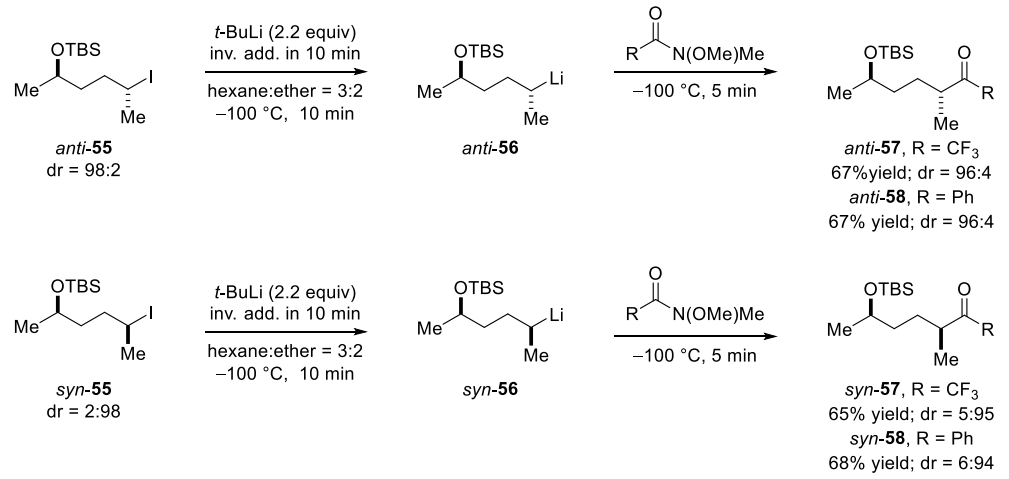
Further experiments demonstrated that *cis*-**50** displayed much lower thermodynamic stability than the corresponding diastereoisomer *trans*-**50** and fully equilibrated within 7 h at −100 °C.

As a consequence, starting from the cyclohexyl iodide *trans*-**49** allowed the preparation of *trans*-**50**, which reacted with phenyl isocyanate or Bu_2S_2 affording the *trans*-amide **54a** and the thioether *trans*-**54b** in 85-87% yield with very high stereoselectivity (dr up to 99:1; see Scheme 18).[59]



Scheme 18. Stereoselective preparation of *trans*-**50** and subsequent trapping with phenyl isocyanate and dibutyl disulfide.

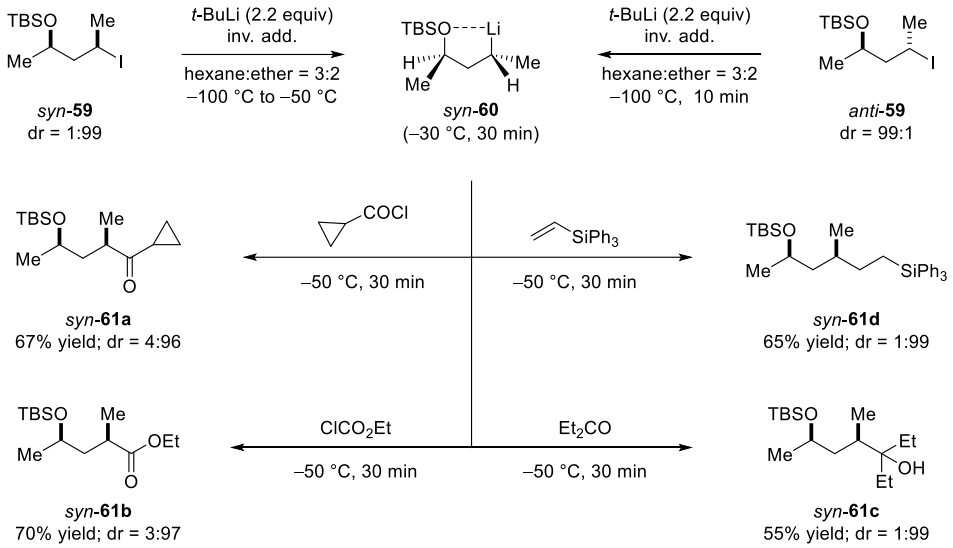
Remarkably, these reactions can also be extended to acyclic non-stabilized secondary alkyllithium reagents.[62] Thus, dropwise addition of the functionalized alkyl iodides *syn*-**55** and *anti*-**55** to a stirred solution of *t*-BuLi (2.2 equiv) in hexane:ether at −100 °C within 10 min afforded the corresponding alkyllithium species *syn*-**56** and *anti*-**56**. Their acylation with various Weinreb amides gave the corresponding ketones **57** and **58** with high retention of configuration (dr: ratio of *anti*:*syn* = up to 96:4; see Scheme 19).[62]



Scheme 19. Stereoselective generation of secondary open-chain alkyllithium reagents *syn*-**56** and *anti*-**56** and their stereoretentive trapping with Weinreb amides producing diastereomerically enriched ketones.

[62] G. Dagousset, K. Moriya, R. Mose, G. Berionni, K. Karaghiosoff, P. Knochel, *Angew. Chem, Int. Ed*. **2014**, *53,* 1425–1429.

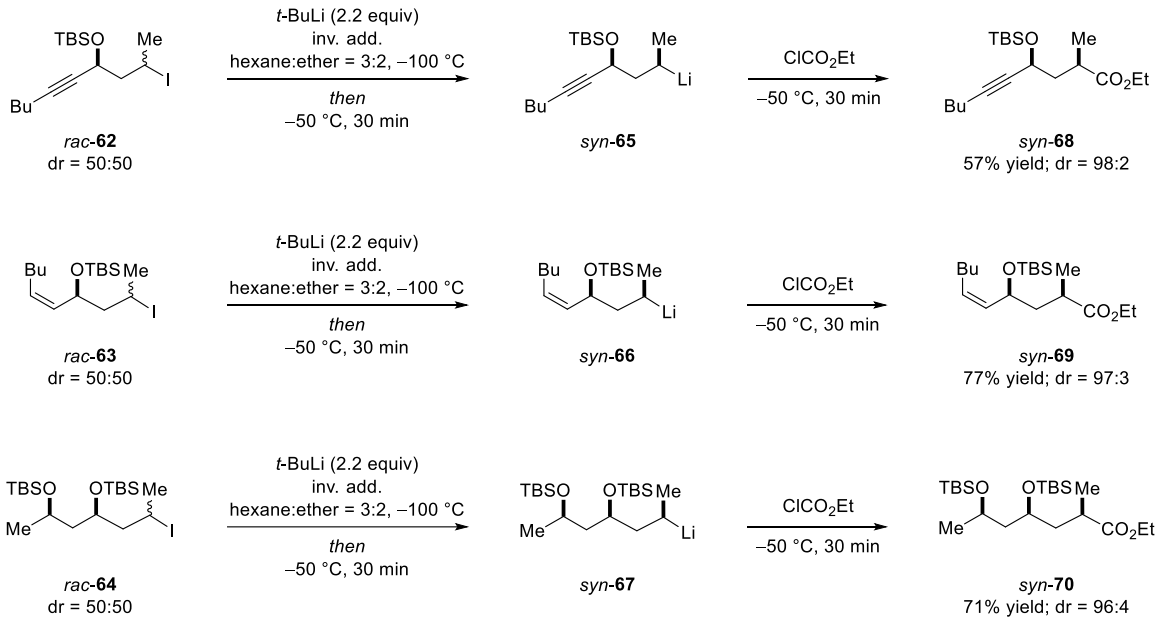
A similar approach was used to generate a broad range of diastereomerically pure non-stabilized secondary alkyl iodides and in all cases a retentive I/Li-exchange reaction took place. Thus, for example, the generation of *syn*-**56** or *anti*-**56** occured without significant interaction of the remote silyl ether function (OTBS) with the carbon-lithium bond. However, the diastereoselectivity of a lithium reagent is, in fact, strongly influenced by an OTBS-group in a close position, as it is the case for the secondary alkyl iodides *syn*- and *anti*-**59**.[63] Both lithium reagents, obtained after an I/Li-exchange, provided in a stereoconvergent manner the lithium species *syn*-**60**. Here, an intramolecular interaction between the silylether function and the lithium center took place and provided a significant stabilization.[60] The prepared lithium organometallic *syn*-**60** reacted with various carbonyl derivatives, such as cyclopropylcarbonyl chloride, ethyl chloroformate and pentan-3-one, furnishing the corresponding adducts *syn*-**61a-c** in 55-70% yield. Also, the addition to triphenylethenylsilane led to the silane *syn*-**61d** in 65% yield. In all cases, the products *syn*-**61a-d** were obtained with diastereoselectivities higher than 4:96 (see Scheme 20).[63]



Scheme 20. Stereconvergent preparation of the chelate-stabilized secondary alkyllithium *syn*-**60** and its stereoselective reactions with various electrophiles.

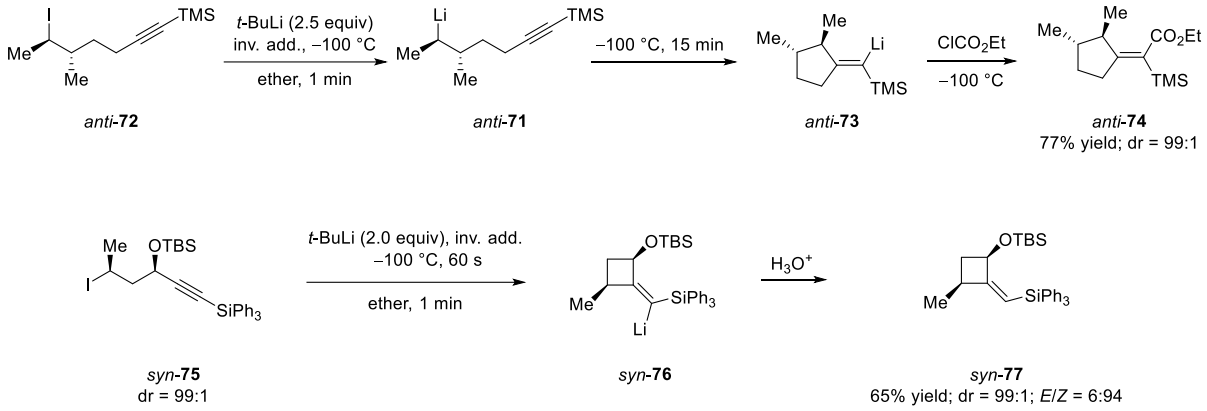
[63] K. Moriya, D. Didier, M. Simon, J. M. Hammann, G. Berionni, K. Karaghiosoff, H. Zipse, H. Mayr, P. Knochel, *Angew. Chem. Int. Ed.* **2015**, *54*, 2754–2757.

This approach can be extended to a range of γ-OTBS-substituted alkyl iodides. The epimeric mixtures of iodides *rac*-**62-64** were stereoconvergently converted to the expected secondary alkyllithium reagents *syn*-**65-67**. Further reaction with ethyl chloroformate at −50 °C furnished the desired polyfunctional esters *syn*-**68-70** in good yields and with very high diastereoselectivities (see Scheme 21).[62]



Scheme 21. Stereoconvergent synthesis of γ-OTBS-substituted secondary alkyllithium reagents *syn*-**65-67** and their stereoselective conversion to polyfunctional esters.

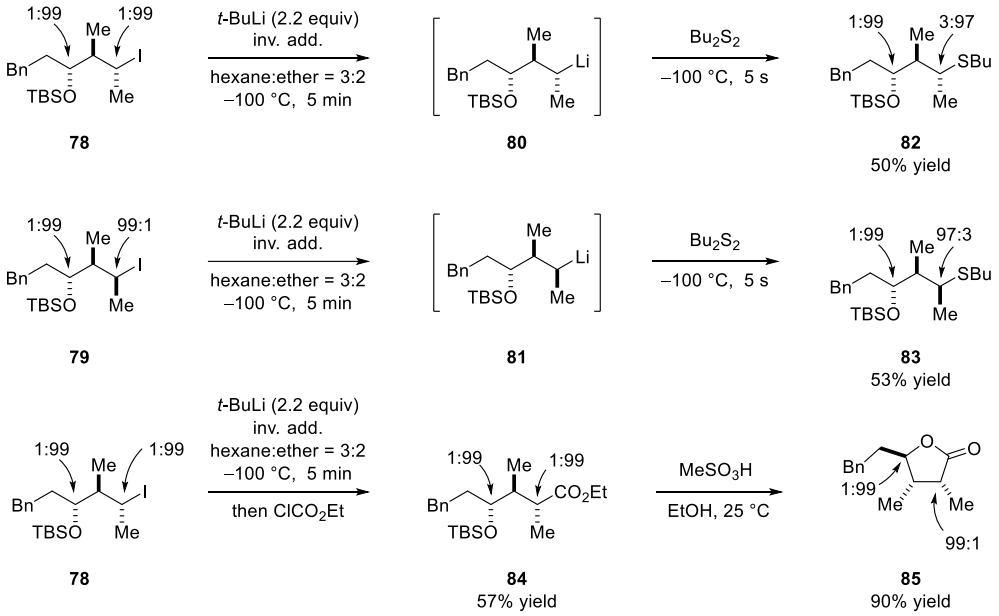
Additionally, diastereoselective intramolecular carbolithiations of secondary alkyllithiums such as *anti*-**71** was achieved if an alkynylsilane is present in a remote position. Thus, the treatment of the alkyl iodide *anti*-**72** (dr <1:99) with *t*-BuLi (2.5 equiv) in ether at −100 °C followed by 15 min of stirring at −100 °C afforded the cyclic lithiated alkenylsilane *anti*-**73** and after treatment with ethyl chloroformate the diastereomerically pure *exo*-alkylidene ester *anti*-**74** was obtained in 77% yield.[64] Chiral iodo-alkynylsilanes such as *syn*-**75** underwent a retentive *syn*-carbolithiation at −100 °C after an I/Li-exchange with *t*-BuLi leading to the lithiated alkenylsilane *syn*-**76**.[65] After quenching with a proton source, the *exo*-alkylidene cyclobutane *syn*-**77** was obtained in 65% yield, *E*/*Z* = 6:94 and dr = 99:1 (see Scheme 22).



Scheme 22. Intramolecular carbolithiation of an alkynyl silane *anti*-**72** and intramolecular carbolithiation of and alkynylsilane *syn*-**75**.

[64] M. Simon, K. Karaghiosoff, P. Knochel, *Org. Lett*. **2018**, *20*, 3518–3521.
[65] K. Moriya, K. Schwaerzer, K. Karaghiosoff, P. Knochel, *Synthesis* **2016**, *48*, 3141–3154.

An OTBS-group in γ-position with an additional methyl group in β-position strongly disfavours the stereoconvergent epimerization of these open-chain secondary alkyllithiums shown in Schemes 20 and 21. Thus, the reaction of both diastereomeric alkyl iodides **78** and **79** with *t*-BuLi in hexane:ether at −100 °C for 5 min provided the corresponding organolithium reagents **80** and **81**. Quenching with Bu_2S_2 provided the thioethers **82** (50% yield; dr = 3:97) and **83** (53% yield; dr = 97:3). Similarly, **78** could be stereoselectively converted by this method (reaction with *t*-BuLi, −100 °C followed by $ClCO_2Et$) into the diastereochemically pure ester **84**, which underwent lactonization furnishing **85** in 90% yield with full control of three adjacent chiral centers (see Scheme 23).[66]

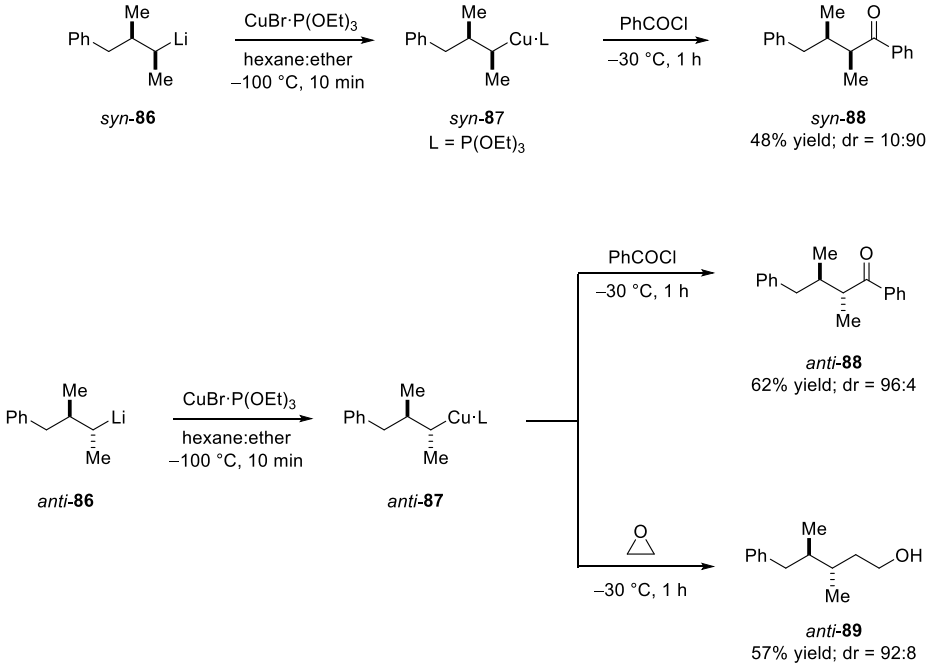


Scheme 23. Stereoselective I/Li-exchange of γ-OTBS substituted alkyl iodides **78** and **79** bearing an additional methyl group in β-position.

[66] V. Morozova, K. Moriya, P. Mayer, P. Knochel, *Chem. Eur. J.* **2016**, *22*, 9962–9965.

4.2 Preparation of Stereodefined Secondary Alkylcopper Reagents

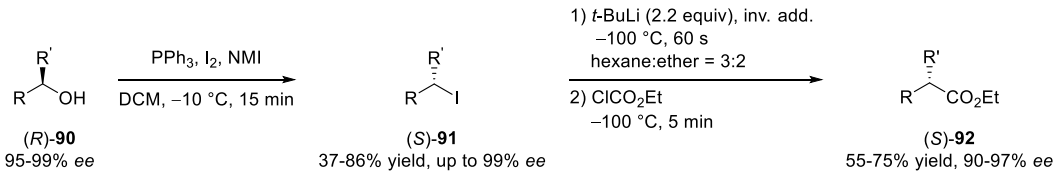
Although, the stereoselective preparation of secondary alkyllithiums and their subsequent trapping with electrophiles allows the preparation of numerous chiral molecules, it was found that several electrophilic reagents react only unselectively with these highly reactive species. Subsequently, transmetalations to new organometallics possessing a more covalent carbon-metal bond were envisioned. For example, the acylation of organolithiums with acid chlorides is complicated by further addition reactions to the generated intermediate. However, organocopper reagents are known to react chemoselectively with acid chlorides to produce exclusively the corresponding ketones.[67] Thus, the secondary alkyl iodides *syn*- and *anti*-**86** were converted into the corresponding alkylcopper reagents *syn*- and *anti*-**87** by addition of the ether soluble copper salt CuBr·P(OEt)$_3$ at −100 °C for 10 min. Treatment of *syn*- and *anti*-**87** with benzoyl chloride at −30 °C for 1 h produced the ketones *syn*- and *anti*-**88** in 48-62% yield and dr >10:90. In addition, the copper reagent *anti*-**87** reacted smoothly with ethylene oxide giving the alcohol *anti*-**89** in 57% yield and dr = 8:92 (see Scheme 24).[60]



Scheme 24. Stereoretentive transmetalation of alkyllithiums to the corresponding copper reagents using CuBr·P(OEt)$_3$.

[67] a) N. Krause, *Modern Organocopper Chemistry* Wiley-VCH Verlag GmbH, Weinheim **2002**. b) M. K. Eberle, G. G. Kahle *Tetrahedron Lett.* **1980**, *21*, 2303–2304; c) C. Kim, G. M. Rubottom, *J. Org. Chem.* **1983**, *48*, 1550–1552.

Improved transmetalation procedures were further developed.[61] It was shown, that a range of optically enriched alcohols of type (*R*)-**90** (95%-99% *ee*) could be converted to the corresponding secondary alkyl iodides (*S*)-**91** with full inversion of configuration. After a retentive I/Li-exchange reaction and subsequent trapping with ethyl chloroformate the corresponding ethyl esters (*S*)-**92** were produced with >90% *ee* (see Scheme 25).[61]



(*R*)-**90**
95-99% *ee*

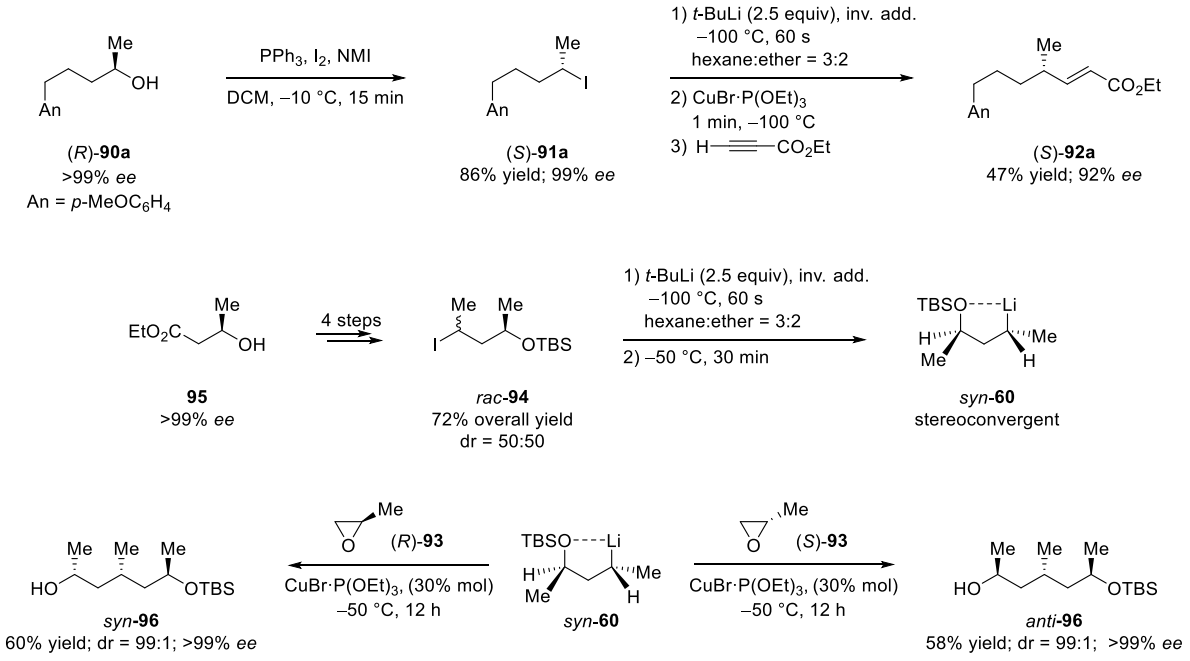
(*S*)-**91**
37-86% yield, up to 99% *ee*

(*S*)-**92**
55-75% yield, 90-97% *ee*

Scheme 25. Enantioselective synthesis of α-chiral esters (*S*)-**92** from optically enriched secondary alkyl alcohols (*R*)-**90**.

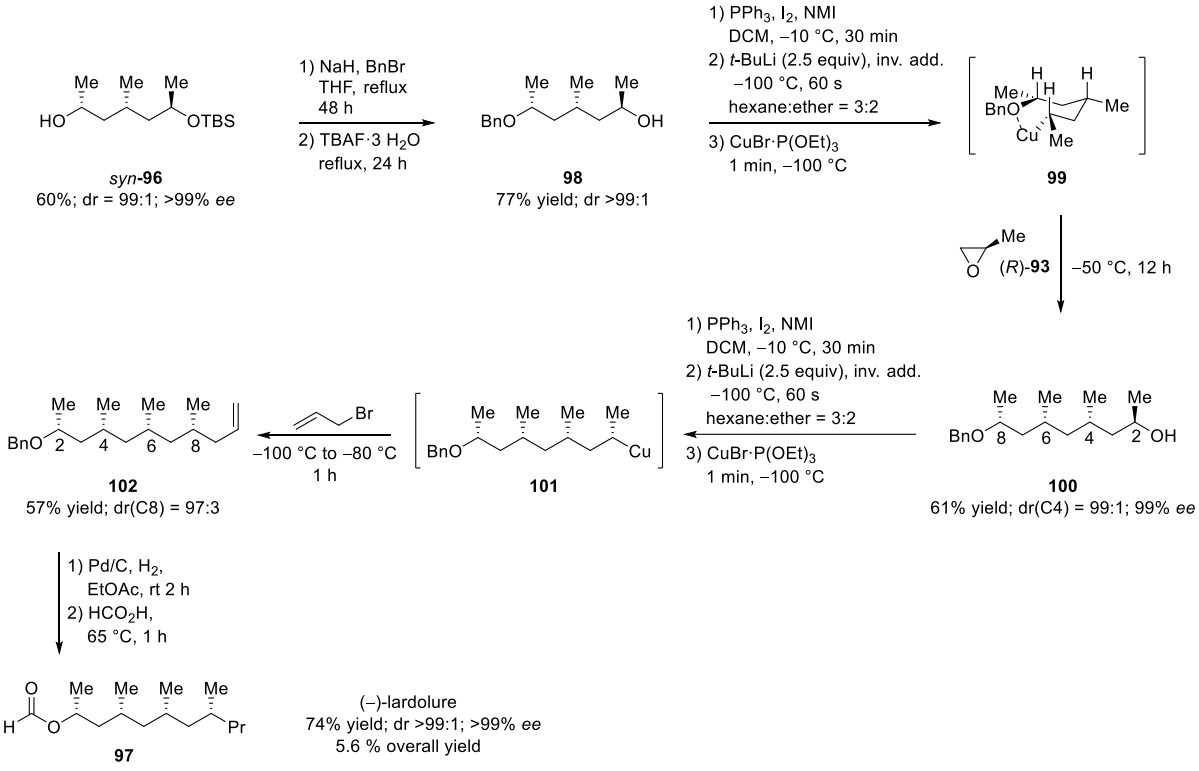
Thus, the optically enriched secondary alkyl alcohol (*R*)-**90a** (99% *ee*) was converted into the corresponding alkyl iodide (*S*)-**91a** with inversion of configuration. After an I/Li-exchange and subsequent transmetalation with CuBr·P(OEt)$_3$, the intermediate alkylcopper reagent underwent a carbocupration with ethyl propiolate affording the α,β-unsaturated ester (*S*)-**92a** in 47% yield and 92% *ee*.[61]

Especially impressive is the opening of chiral epoxides ((*R*)- and (*S*)-**93**) with secondary alkylcopper reagents. Therefore, the optically enriched secondary alkyllithium *syn*-**60** was obtained in 99% *ee* from the alkyl iodide *rac*-**94**, which was prepared from commercially available (*R*)-ethyl 3-hydroxybutyrate (**95**). In the presence of 30 mol% $CuBr{\cdot}P(OEt)_3$, this chelate stabilized lithium reagent triggered a smooth opening of either (*R*)- or (*S*)-propylene oxide ((*R*)- and (*S*)-**93**) leading to the selectively protected diols *syn*- and *anti*-**96** as diastereomerically and enantiomerically pure products (>99% *ee* and dr = 99:1; see Scheme 26).



Scheme 26. Stereoselective reactions of optically pure secondary alkylcopper reagents.

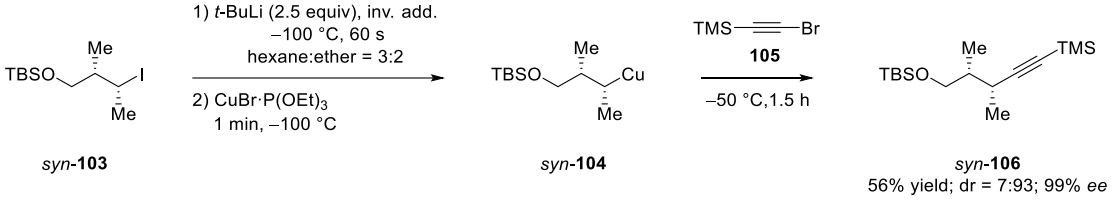
Especially *syn*-**96** is of great interest as it can be used for the preparation of the pheromone (−)-lardolure (**97**).[68] Thus, after benzylation, the silyl ether was cleaved using tetra-*n*-butylammoniumfluoride (TBAF·H_2O) leading to **98**. Conversion of the free alcohol into the corresponding iodide followed by the standard I/Li-exchange sequence and subsequent transmetalation with CuBr·$P(OEt)_3$ furnished the chelation-stabilized secondary alkylcopper reagent **99**. Opening of the epoxide (*R*)-**93** led to the chiral alcohol **100** in 61% yield with retention of the configuration (dr = 99:1 and >99% *ee*). The secondary alkylcoppper reagent **101**, prepared by an analogous iodination and I/Li-exchange sequence, was allylated with allyl bromide leading to the desired product **102** in 57% yield. Reduction of the allylic system and cleavage of the benzylic alcohol followed by formylation produced the pheromone (−)-lardolure **97** in 74% yield with a dr >99:1 and 99% *ee* (see Scheme 27).



Scheme 27. Iterative enantioselective synthesis of the pheromone (−)-lardolure (**97**).

[68] a) R. Des Mazery, M. Pullez, F. Lopez, S. R. Harutyunyan, A. J. Minnaard, B. L. Feringa, *J. Am. Chem. Soc*. **2005**, *127*, 9966–9967; b) J. S. Yadav, S. Sengupta, N. N. Yadav, C. D. Narasimha, A. A. Al Ghamdi, *Tetrahedron Lett*. **2012**, *53*, 5952–5954.

Alkylcopper derivatives can also undergo cross-couplings with 1-bromoalkynes.[69] Thus, the chiral secondary alkyl iodide *syn*-**103** was converted into the corresponding copper derivative *syn*-**104**, which reacted with the bromoacetylene derivative **105** providing the chiral alkyne *syn*-**106** in 56% yield with dr = 7:93 (see Scheme 28).[70]



Scheme 28. Cross-coupling of a chiral alkylcopper (*syn*-**104**) with a bromoalkyne.

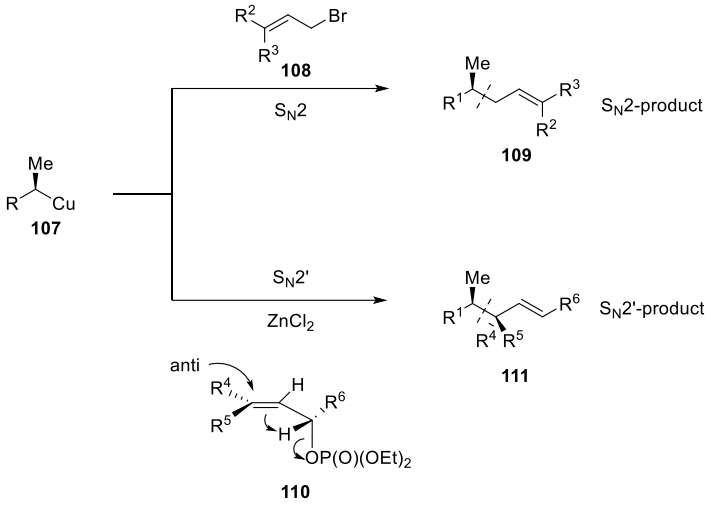
Remarkably, organocopper reagents undergo highly chemo- and stereoselective allylic substitution reactions in THF.[71] Thus, copper organometallics of type **107** react with unsymmetrical allylic bromides such as **108** with very high S_N2-selectivity furnishing allylated products of type **109**. Addition of $ZnCl_2$ to the same copper organometallics leads to mixed Zn/Cu-clusters, which react in an *anti*-S_N2'-selectivity with chiral allylic phosphates like **110** affording the corresponding (*E*)-alkenes **111** (see Scheme 29).[72]

[69] a) A. Commercon, J. F. Normant, J. Villieras, *Tetrahedron* **1980**, *36*, 1215–21; b) M. C. Yeh, P. Knochel, *Tetrahedron Lett*. **1989**, *30*, 4799–802; c) P. Knochel, N. Millot, A. L. Rodriguez, C. E. Tucker, *Org. React*. **2001**, *58*, 417–731; d) G. Cahiez, O. Gager, J. Buendia, *Angew. Chem. Int. Ed*. **2010**, *49*, 1278–1281.

[70] J. Skotnitzki, V. Morozova, P. Knochel, *Org. Lett*. **2018**, *20*, 2365–2368.

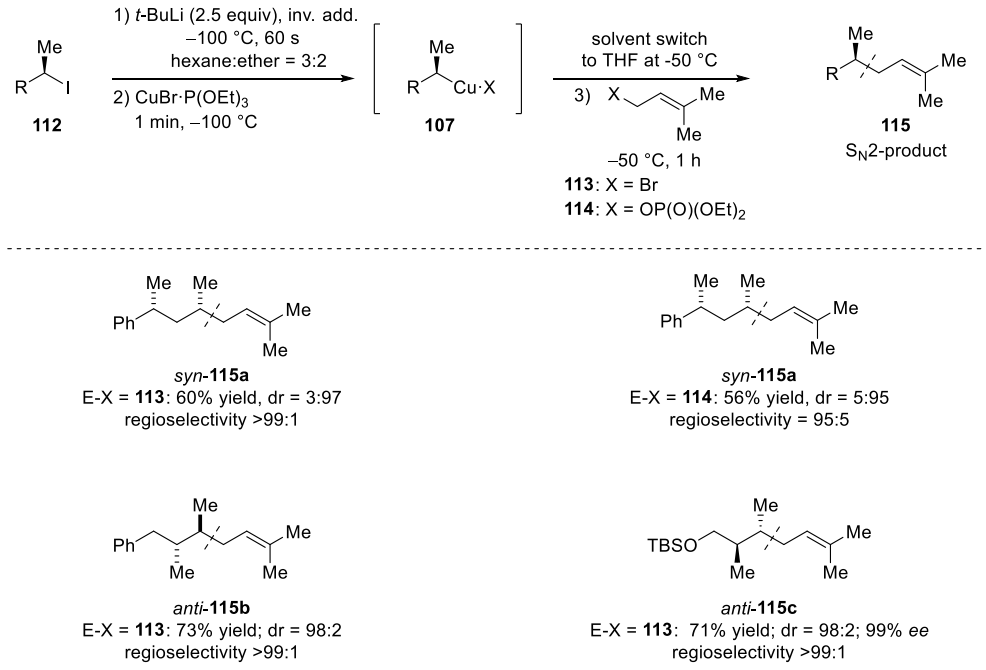
[71] a) N. Harrington-Frost, H. Leuser, M. I. Calaza, F. F. Kneisel, P. Knochel, *Org. Lett*. **2003**, *5*, 2111–2114; b) D. Soorukram, P. Knochel, *Org. Lett*. **2004**, *6*, 2409–2411; c) M. I. Calaza, E. Hupe, P. Knochel, *Org. Lett*. **2003**, *5*, 1059–1061; d) H. Leuser, S. Perrone, F. Liron, F. F. Kneisel, P. Knochel, *Angew. Chem. Int. Ed*. **2005**, *44*, 4627–4631; e) D. Soorukram, P. Knochel, *Angew. Chem. Int. Ed*. **2006**, *45*, 3686–3689; f) S. Perrone, P. Knochel, *Org. Lett*. **2007**, *9*, 1041–1044; g) B. Breit, P. Demel, *Tetrahedron* **2000**, *56*, 2833–2846; h) B. Breit, P. Demel, C. Studte, *Angew. Chem. Int. Ed.* **2004**, *43*, 3786–3789; i) T. Ibuka, H. Habashita, A. Otaka, N. Fujii, Y. Oguchi, T. Uyehara, Y. Yamamoto, *J. Org. Chem*. **1991**, *56*, 4370–4382; j) C. A. Falciola, K. Tissot-Croset, A. Alexakis, *Angew. Chem. Int. Ed.* **2006**, *45*, 5995–5998; k) H. Malda, A. W. van Zijl, L. A. Arnold, B. L. Feringa, *Org. Lett*. **2001**, *3*, 1169–1171; l) C. A. Luchaco-Cullis, H. Mizutani, K. E. Murphy, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2001**, *40*, 1456–1460; m) A. O. Larsen, W. Leu, C. N. Oberhuber, J. E. Campbell, A. H. Hoveyda, *J. Am. Chem. Soc*. **2004**, *126*, 11130–11131.

[72] J. Skotnitzki, L. Spessert, P. Knochel, *Angew. Chem. Int. Ed*. **2019**, *58*, 1509–1514.



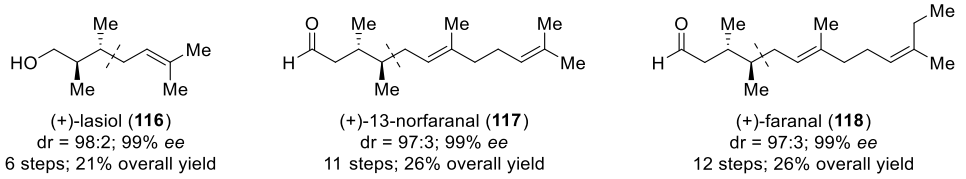
Scheme 29. Reactivity of organocopper reagents (**107**) with allylic halides and phosphates in the presence or absence of $ZnCl_2$.

Additionally, it was found that these chiral alkylcopper reagents (**107**), which were readily prepared from the corresponding alkyl iodides (**112**), are configurationally stable at up to −50 °C after a solvent-switch from hexane:ether to THF performed at this temperature. This procedure allowed smooth S_N2-reactions with prenylbromide **113** or prenyl phosphate **114** leading to allylated products of type **115** (dr = up to 98:2; see Scheme 30).



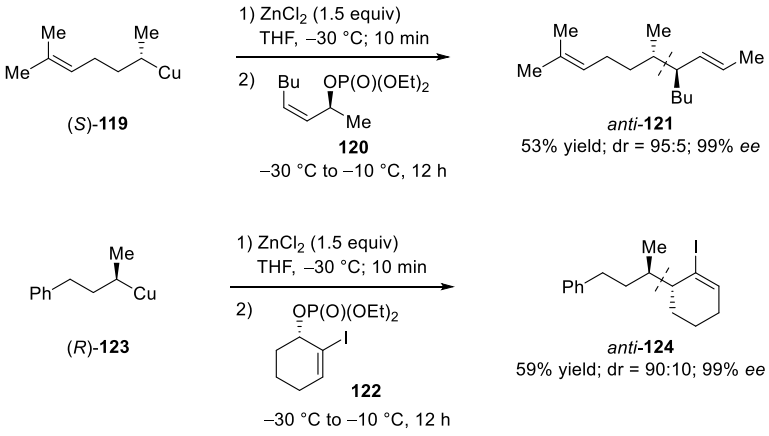
Scheme 30. Regioselective prenylation of chiral alkylcoppers *via* S_N2-substitution.

Deprotection of *anti*-**115c** with TBAF at 25 °C provided the pheromone (+)-lasiol (**116**) in 87% yield (dr = 98:2; 99% *ee*).[73] Using analogous approaches, the total syntheses of (+)-13-norfaranal (**117**) (dr = 97:3; 99% *ee*)[74] and (+)-faranal (**118**) (dr = 97:3; 99% *ee*)[75] were achieved (see Scheme 31).



Scheme 31. Synthesis of natural products (+)-lasiol (**116**), (+)-13-norfaranal (**117**) and (+)-faranal (**118**).

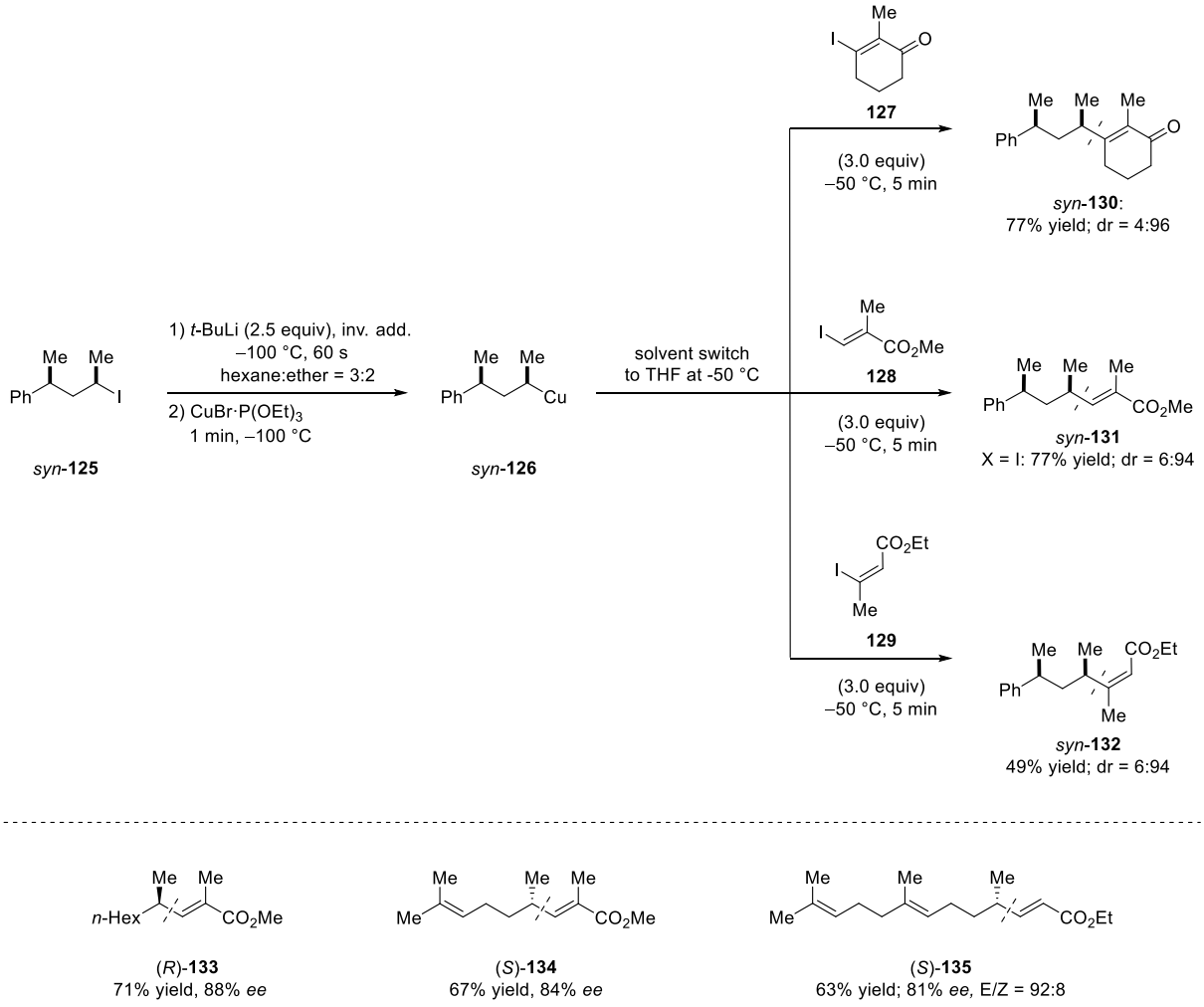
Adding a $ZnCl_2$ solution to the chiral secondary alkylcopper reagents **107** leads to mixed clusters, which display a very high *anti*-S_N2'-regioselectivity.[71] Thus, reaction of the non-stabilized secondary alkylcopper reagent (*S*)-**119** with the chiral allylic phosphate **120** led to S_N2'-substitution (S_N2'/S_N2 >99:1) products affording the diene *anti*-**121** in 53% yield (dr = 95:5; 99% *ee*) upon previous treatment with $ZnCl_2$. These allylic substitutions can also be extended to cyclic allylic substrates such as **122**. Therefore, the secondary alkyl copper reagent (*R*)-**123** reacted with **122** after the addition of $ZnCl_2$ (1.5 equiv) producing the chiral cyclohexenyl iodide *anti*-**124** in 59% yield (dr = 90:10, 99% *ee*) (see Scheme 32).



Scheme 32. S_N2'-regioselective *anti*-substitution of chiral alkylcoppers with chiral allylic phosphates.

[73] a) A. W. van Zijl, W. Szymanski, F. Lopez, A. J. Minnaard, B. L. Feringa, *J. Org. Chem*. **2008**, *73*, 6994–7002; b) J. Zhao, K. Burgess, *J. Am. Chem. Soc*. **2009**, *131*, 13236–13237.
[74] L. Poppe, L. Novak, P. Kolonits, A. Bata, C. Szantay, *Tetrahedron* **1988**, *44*, 1477–1487.
[75] T. Okochi, K. Mori, *Eur. J. Org. Chem*. **2001**, 2145–2150.

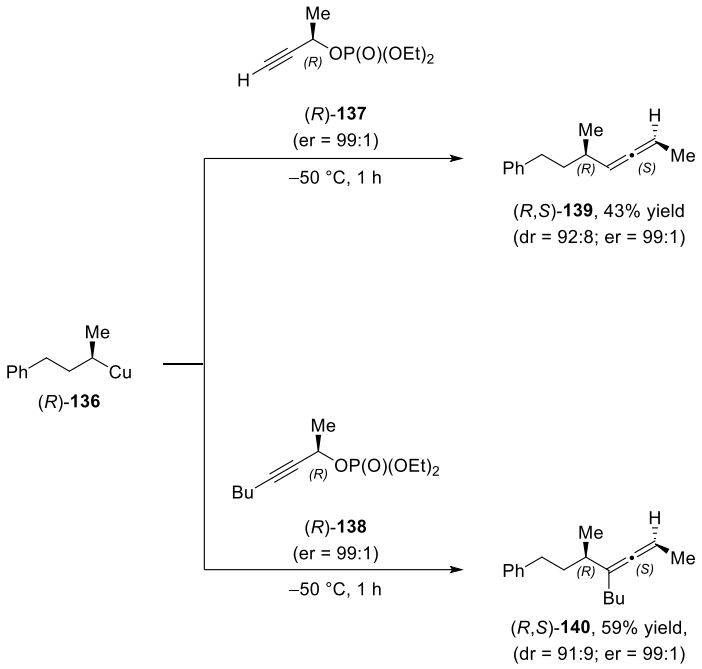
Furthermore, these chiral alkylcopper reagents reacted stereoretentively with several diversely substituted 3-iodo or 3-bromo unsaturated carbonyl derivatives. Thus, the reaction of *syn*-**125** with *t*-Buli and subsequent addition of CuBr·P(OEt)$_3$ provided *syn*-**126**, which reacted with the cyclic 3-iodo enone **127** or the acyclic 3-iodo enoates **128** and **129** providing the desired functionalized Michael acceptors *syn*-**130**-**132** in up to 77% yield and with up to dr = 96:4. Consequently, this method was used for the preparation of several advanced natural product intermediates. For example, (*R*)-**133**, (*S*)-**134** and (*S*)-**135** occuring in the total syntheses of Aranorosin,[76] (+)-Sorangicin A[77] and *ent*-Stelletamide A[78] respectively, were prepared in up to 71% yield and up to 88% *ee*[79] (see Scheme 33).



Scheme 33. Preparation of chiral Michael acceptors from chiral alkylcoppers and substituted 3-iodo or 3-bromo unsaturated carbonyl derivatives.

[76] a) W. H. Fehlhaber, H. Kogler, T. Mukhopadyay, E. K. S. Vijayakumar, B. N. Ganguli, *J. Am. Chem. Soc*. **1988**, *110*, 8242–8244; b) P. Wipf, Y. Kim, P. C. Fritch, *J. Org. Chem.* **1993**, *58*, 7195–7203.
[77] G. A. Whitlock, E. M. Carreira, *J. Org. Chem.* **1997**, *62*, 7916–7917.
[78] Y. Sridhar, P. Srihari, *Org. Biomol. Chem*. **2013**, *11*, 4640–4645.
[79] A. Kremsmair, J. Skotnitzki, P. Knochel, *Chem. Eur. J.* **2020**, *26*, 11971–11973.

In addition, we reported a highly regioselective *anti*-S_N2'-substitution of secondary alkylcopper reagents such as (*R*)-**136** with chiral propargylic phosphates (*R*)-**137** or (*R*)-**138** leading to α-chiral allenes (*R, S*)-**139** or (*R, S*)-**140** with retention of the configuration (see Scheme 34). Remarkably, this overall *anti*-S_N2'-substitution reaction proceeded directly with the alkylcopper reagent with transfer of chirality from the propargylic substrate to the allene and no further additive was needed.[80]



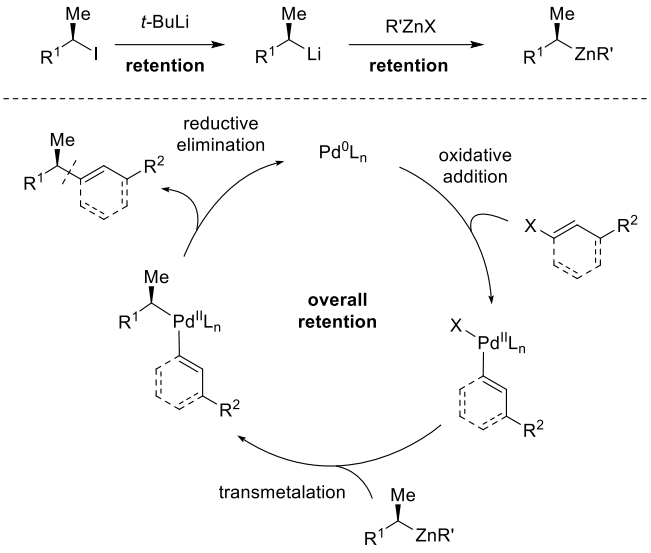
Scheme 34. Reaction of chiral alkylcopper (*R*)-**136** with propargyl phosphates (*R*)-**137** and (*R*)-**138** for the preparation of optically enriched α-chiral allenes (*R,S*)-**139** and (*R,S*)-**140**.

In summary, a range of secondary alkyl iodides can be converted to the corresponding secondary alkyllithiums with retention of the configuration. After stereoselective transmetalations to alkylcopper reagents, a wide variety of electrophiles react with these chiral organometallics affording chiral products of great interest for organic synthesis. Applications toward the preparation of natural products have been demonstrated.

[80] J. Skotnitzki, A. Kremsmair, D. Keefer, F. Schüppel, B. Le Cacher de Bonneville, R. De Vivie-Riedle, P. Knochel, *Chem. Sci.* **2020**, *11*, 5328-5332.

5 Objectives

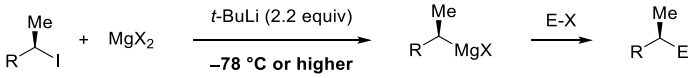
The preparation of chiral organolithiums from chiral secondary alkyl iodides using *t*-BuLi is highly interesting but limited in applicability, scalability and compatibility with electrophiles. Thus, stereoretentive transmetalations to new chiral organometallics should be investigated. The stereoretentive preparation of chiral alkylzinc reagents from the corresponding secondary alkyl iodides *via* I/Li-exchange using *t*-BuLi would greatly broaden the scope of chiral alkyl organometallics. With these reagents in hand highly stereoretentive Negishi-type cross-couplings with alkenyl halides and aryl halides could be performed using an appropriate transition metal catalyst. The obtained chiral secondary alkylzinc reagents should possess a more covalent carbon-zinc bond allowing these cross-couplings to be performed at elevated temperatures. Their configurational stability and the scope of suitable electrophiles should be tested (see Scheme 35).



Scheme 35. Stereoretentive preparation of chiral secondary alkylzincs and their potential use in Negishi cross-couplings.

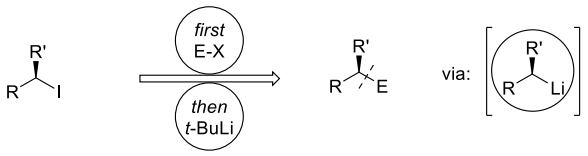
Furthermore, improving the practicability of this stereoretentive I/Li-exchange reaction should be investigated in terms of realizing a more robust and practical procedure. Thus, Barbier-conditions, in which the chiral secondary alkyl iodide is mixed with a suitable transmetalation reagent before addition of *t*-BuLi could allow the performance of the I/Li-exchange at more convenient temperatures as the resulting configurationally labile chiral alkyllithiums would be immediately transmetalated to more stable organometallics. The obtained new organometallics could then be used in electrophilic quenching reactions at elevated temperature in comparison to the corresponding alkyllithiums.

This could be realized in the case of magnesium derivatives as their reactivity should be comparable to lithium organometallics, but the carbon-magnesium bond is less polarized than the carbon-lithium bond, resulting in a reagent less prone to epimerization (see Scheme 36). Furthermore, the preparation of chiral Grignard reagents represents a major challenge in the past and so far, no general procedure for their generation has been reported. The temperature stability of the obtained optically enriched secondary alkylmagnesium reagents as well as their reactivity towards several classes of electrophiles should be investigated.



Scheme 36. Barbier-type preparation of chiral secondary alkylmagnesium reagents at temperatures above −100 °C.

If such I/Li-exchanges take place under Barbier-conditions, the reaction should be investigated considering the use of functionalized secondary alkyl iodides bearing sensitive functional groups, which have not been compatible with the previously described conditions. These reactions should be performed in batch and if successful, performed in continuous flow conditions, leading to a reliable and scalable method for the utilization of highly reactive, but configurationally labile chiral alkyllithiums. The scope of suitable electrophiles as well as the temperature should be explored (see Scheme 37).



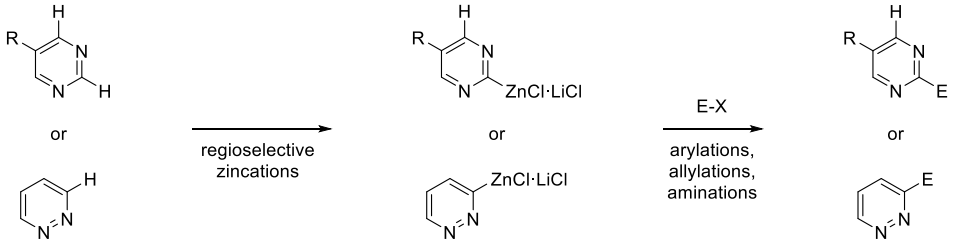
***in situ* quench (ISQ) reaction:**

- reaction temperature: up to 0 °C
- tolerance of sensitive FGs (ester, nitrile)
- scale-up possible in continuous flow

Scheme 37. *In situ* quench (ISQ) reaction of chiral secondary alkyliodides with electrophiles *via* chiral alkyllithiums.

A successful development of new transmetalations as well as performing the I/Li-exchange under Barbier conditions would allow a fast, scalable and broadly applicable preparation of highly optically enriched molecules, which could be useful for agrochemical and pharmaceutical research.

Also, a mild and regioselective functionalization of important classes of *N*-Heterocycles such as pyrimidines and pyridazine should be investigated. So far, these substrates can only be zincated using bimetallic TMP-bases in the presence of highly toxic Lewis acids such as $BF_3 \cdot OEt_2$. Thus, industrial and other large scale-processes require new ideas for such metalations.



B. Results and Discussion

1 Stereoselective Csp^3-Csp^2 Cross-Couplings of Chiral Secondary Alkylzinc Reagents with Alkenyl and Aryl Halides

1.1 Introduction

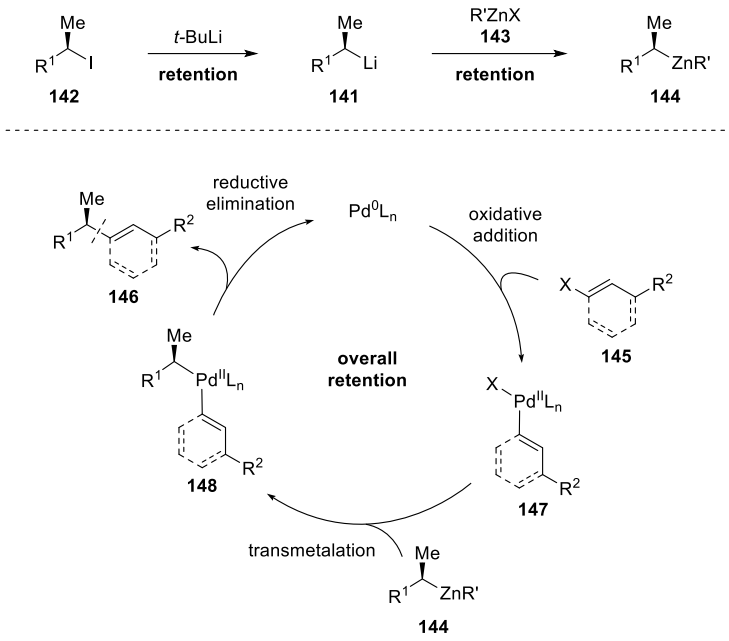
Transition-metal-catalyzed cross-coupling reactions are widely used for the construction of complex organic molecules.[81] Although a range of Csp^3-Csp^2 coupling reactions have been developed, only a few are stereoselective.[82,58c] In this context, highly stereoretentive cross-couplings of enantioenriched α-chiral alkylzinc reagents are desirable as these reagents are known for their broad functional group tolerance. However, their preparation proved to be challenging since oxidative addition of zinc powder into the carbon-halogen bond proceeds with a loss of stereoinformation.[82g] A stereoselective palladium-catalyzed cross-coupling reaction after hydroboration of trisubstituted alkenes followed by a boron-zinc exchange reaction has been reported, but proved to be of limited scope.[83] Lately, a diastereoselective palladium-catalyzed cross-coupling reaction of cyclic alkylzinc reagents, where the stereoselectivity of the cross-coupling is thermodynamically controlled has been reported.[28] This method leads to high selectivities only with cyclic substrates, which drastically limits the utility of such stereoselective palladium-catalyzed cross-couplings. So far, the preparation of non-stabilized optically pure open-chain organometallic reagents is a challenge for organic synthesis.

Recently, we have reported that chiral secondary alkyllithiums **141** can be readily prepared from the corresponding optically enriched α-chiral secondary alkyl iodides **142** *via* a stereoretentive I/Li-exchange reaction (see Scheme 38). The configurational stability of these secondary alkyllithiums is rather moderate (ca. 1 h at –100 °C in a hexane:ether mixture).[59, 62, 63] However, transmetalation to the corresponding secondary alkylcopper reagents significantly increases this configurational stability (several hours at –50 °C in THF). These chiral alkylcopper organometallics react with activated alkynes, epoxides, 1-bromoalkynes and allylic halides with high retention of configuration.[60, 61, 70, 72] Furthermore, these organocopper reagents were used in the total synthesis of several pheromones with high control of all stereocenters.[61, 70]

[81] a) E.-i. Negishi, *Handbook of Organopalladium Chemistry for Organic Synthesis*, Wiley-Interscience, New York, **2002**; b) A. De Meijere, S. Bräse, M. Oestreich, *Metal-Catalyzed Cross-Coupling Reactions and More*, Wiley-VCH, Weinheim, **2013**; c) for a review see: R. Jana, T. P. Pathak, M. S. Sigman, *Chem. Rev.* **2011**, *111*, 1417–1492.

[82] a) Y. Hatanaka, T. Hiyama, *J. Am. Chem. Soc.* **1990**, *112*, 7793−7794. b) B. Hölzer, R. W. Hoffmann, *Chem. Commun.* **2003**, 732−733. c) T. K. Beng, R. E. Gawley, *Org. Lett.* **2011**, *13*, 394–397. d) L. Li, S. Zhao, A. Joshi-Pangu, M. Diane, M. R. Biscoe, *J. Am. Chem. Soc.* **2014**, *136*, 14027–14030. e) C. Sandford, V. K. Aggarwal, *Chem. Commun.* **2017**, 5481–5494. f) J. P. G. Rygus, C. M. Crudden, *J. Am. Chem. Soc.* **2017**, *139*, 18124–18137. g) S. Zhao, T. Gensch, B. Murray, Z. L. Niemeyer, M. S. Sigman, M. R. Biscoe, *Science* **2018**, *362*, 670–674.

[83] A. Boudier, P. Knochel, *Tetrahedron Lett.* **1999**, *40*, 687−690.



Scheme 38. Stereoretentive preparation of secondary alkylzinc reagents **144** and subsequent palladium-catalyzed cross-coupling reaction with alkenyl or aryl halides **145**.

Nevertheless, the configurational stability of these chiral secondary alkylcopper reagents is restricted to low temperature reactions. Thus, we envisioned the performance of a stereoretentive transmetalation of chiral alkyllithiums of type **141** with an appropriate ether soluble zinc reagent R'ZnX (**143**), leading to the mixed dialkylzinc reagents of type **144** (see Scheme 38). These chiral mixed dialkylzinc reagents may undergo a stereoselective palladium-catalyzed cross-coupling with alkenyl and aryl halides of type **145**, which would afford α-chiral products of type **146**. To achieve such a stereoselective cross-coupling several requirements should be fulfilled: (1) both the transmetalation step (conversion of **147** to **148**) and the reductive elimination step (converting **148** to **146**) of the catalytic cycle have to be stereoselective; (2) the secondary dialkylzinc reagent **144** must be configurationally stable at the cross-coupling temperature and should contain a group R', which does not easily participate in the catalytic cycle. After several preliminary experiments,[84] we chose $Me_3SiCH_2ZnBr{\cdot}LiBr$ (**143a**) as transmetalating zinc reagent since it is highly soluble in diethyl ether and readily prepared.[85] To our delight, these conditions allow for the first time a highly stereoselective cross-coupling of chiral non-stabilized open-chain secondary alkylzinc reagents with various alkenyl and aryl halides.

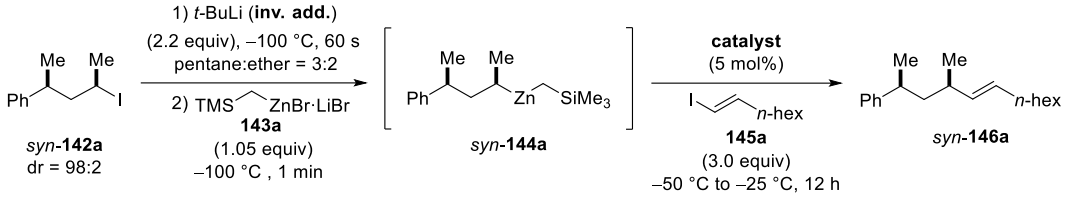
[84] For details, see Experimental Part.

[85] a) S. H. Bertz, M. Eriksson, G. Miao, J. P. Snyder, *J. Am. Chem. Soc.* **1996**, *118*, 10906−10907. b) S. Berger, F. Langer, C. Lutz, P. Knochel, T. A. Mobley, C. K. Reddy, *Angew. Chem. Int. Ed.* **1997**, *36*, 1496−1498. c) C. Lutz, P. Knochel *J. Org. Chem.* **1997**, *62*, 7895−7898.

1.2 Optimization of Reaction Conditions

Hence, we treated the diastereomerically enriched secondary alkyl iodide *syn*-**142a**[63] with *t*-BuLi (2.2 equiv) in a 3:2 mixture of pentane:diethyl ether at –100 °C for 60 s leading to an intermediate alkyllithium species (see Table 1). Addition of $Me_3SiCH_2ZnBr{\cdot}LiBr$ (**143a**; 0.95 M in diethyl ether, 1.05 equiv) at –100 °C provided the mixed dialkylzinc species *syn*-**144a**. For performing a subsequent stereoselective palladium-catalyzed cross-coupling, the choice of the palladium catalyst proved to be essential.

Table 1. Optimization for palladium-catalyzed cross-coupling reaction of racemic secondary alkylzinc reagent *syn*-**144a**.



entry	catalyst	yield of *syn*-**146a**[a]	dr of *syn*-**146a**[a]
1	$Pd(PPh_3)_4$	39%	89:11
2	$Pd(OAc)_2$/CPhos	51%	92:8
3	Pd-PEPPSI-iPent	60%	96:4
4	$Pd_2I_2(Pt\text{-}Bu_3)_2$	58%	98:2

[a] The yield and diastereoselectivity (dr: *syn*:*anti* ratio was determined by GC-analysis using dodecane as internal standard.

Addition of 5 mol% $Pd(PPh_3)_4$ and (*E*)-1-iodooct-1-ene (**145a**; 3.0 equiv) as a typical substrate at −50 °C followed by warming to –25 °C and stirring for 12 h at this temperature provided the desired cross-coupling product *syn*-**146a** with a diastereoselectivity of *syn*:*anti* = 89:11 (entry 1).[86] Using the catalytic system $Pd(OAc)_2$/CPhos introduced by *Buchwald* for the coupling of secondary alkylzinc halides[87] improved the stereoselectivity of the cross-coupling to *syn*:*anti* = 92:8 (entry 2). A further improvement was observed with the NHC-based catalyst Pd-PEPPSI-iPent reported by *Organ*,[88] which provided the desired product *syn*-**146a** with a dr = 96:4 (entry 3).

[86] Nickel catalysts afforded only traces of *syn*-**146a**;

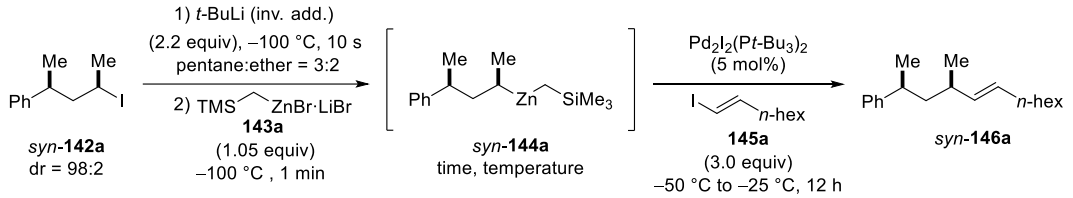
[87] a) C. Han, S. L. Buchwald, *J. Am. Chem. Soc.* **2009**, *131*, 7532−7533. b) Y. Yang, K. Niedermann, C. Han, S. L. Buchwald, *Org. Lett.* **2014**, *16*, 4638−4641.

[88] S. Çalimsiz, M. G. Organ, *Chem. Comm.* **2011**, 5181–5183; Pd-PEPPSI-iPr afforded *syn*-**146a** in 23% yield and dr = 91:9; for details see Experimental Part.

Finally, the Pd(I)-catalyst $Pd_2I_2(Pt\text{-}Bu_3)_2$ used by *Schoenebeck*[89] gave the product *syn*-**146a** with complete retention of configuration (entry 4; dr = 98:2).

In order to obtain a deeper insight into the configurational stability of these chiral non-stabilized secondary alkylzincs of type **144**, we prepared *syn*-**144a** at –100 °C and kept it at various temperatures (–50 °C to 25 °C) for a certain time, followed by the stereoselective cross-coupling with **145a**, leading to *syn*-**146a** (see Table 2). We observed high stability of the zinc species *syn*-**144a** up to –10 °C (dr of *syn*-**146a** = 97:3). Furthermore, keeping the alkylzinc reagent *syn*-**144a** at 25 °C for 1 h and performing a palladium-catalyzed cross-coupling provided *syn*-**146a** with dr = 96:4. However, stirring *syn*-**144a** at 25 °C for 4 h led to a minimal epimerization (dr of *syn*-**146a** = 89:11). This indicated a high configurational stability of these chiral secondary mixed dialkylzinc reagents (several hours at 25 °C).

Table 2. Stability of racemic secondary alkylzinc reagent *syn*-**144a** and subsequent cross-coupling reaction with alkenyl iodide **145a**.



entry	temperature	time	yield of *syn*-**146a**[a]	dr of *syn*-**146a**[a]
1	–50 °C	10 min	61%	97:3
2	–30 °C	10 min	58%	97:3
3	–10 °C	10 min	50%	97:3
4	25 °C	60 min	51%	96:4
5	25 °C	240 min	53%	89:11

[a] The yield and diastereoselectivity (dr: *syn*:*anti* ratio was determined by GC-analysis using dodecane as internal standard.

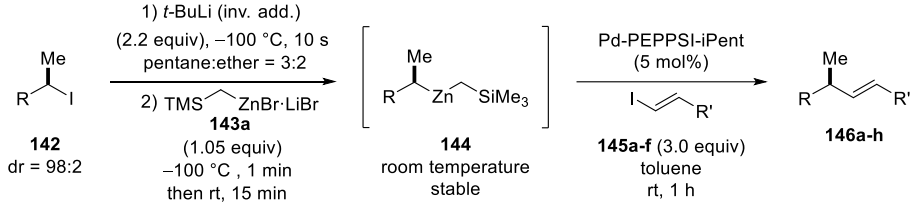
With this result in hand, we slightly modified the experimental procedure to the effect that the cross-coupling reaction could be performed at room temperature. Under these conditions, Pd-PEPPSI-iPent showed superior results compared to the Pd(I)-dimer catalyst regarding β-hydride elimination and formation of side products such as dimerization.

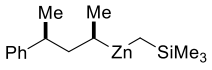
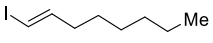
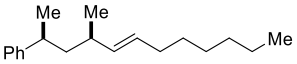
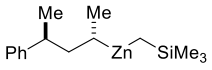
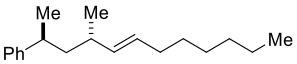
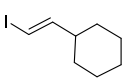
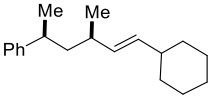
[89] a) I. Kalvet, T. Sperger, T. Scattolin, G. Magnin, F. Schoenebeck, *Angew. Chem. Int. Ed.* **2017**, *56*, 7078–7082. b) S. T. Keaveney, G. Kundu, F. Schoenebeck, *Angew. Chem. Int. Ed.* **2018**, *57*, 12573–12577.

1.3 Palladium-Catalyzed Cross-Couplings with Alkenyl Iodides

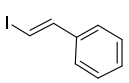
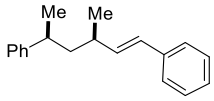
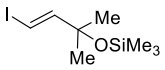
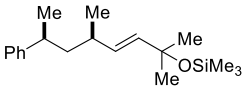
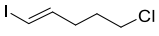
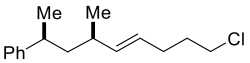
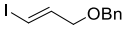
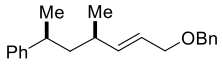
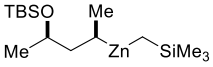
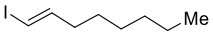
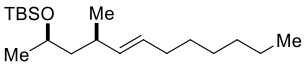
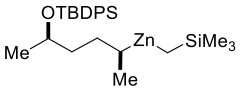
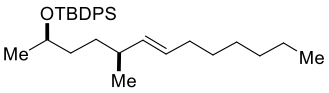
In a typical procedure, the chiral mixed dialkylzinc reagents (**144a-c**) were generated as described above and subsequently warmed to room temperature within 15 min (see Table 3). The dialkylzinc reagent was then added dropwise to a stirring solution of 5 mol% Pd-PEPPSI-iPent and the alkenyl iodide of type **145** (3.0 equiv) in toluene. After stirring for 1 h at room temperature the corresponding α-chiral cross-coupling products were isolated in up to 52% yield and with high retention of configuration (dr up to 98:2). In this way, the stereodefined alkenes *syn*-**146a**[90] and *anti*-**146a** were prepared from the corresponding iodides in 43% and 39% yield, respectively (dr = 98:2 and dr = 5:95). Interestingly, the thermodynamically more stable alkylzinc reagent *anti*-**144a** afforded the corresponding (*E*)-alkene *anti*-**146a** in lower yield and with less retention of configuration compared to the *syn*-product. In most other cases a high retention of configuration (dr >94:6) was achieved. Thereby, the *E*/*Z*-configuration of the alkenyl iodides of type **145** turned out to be highly important. All attempts to use (*Z*)-alkenyl iodides as cross-coupling partners were unsuccessful presumably due to steric hindrance in the palladium(II)-intermediates **147** and **148**.

Table 3. Stereoretentive cross-coupling reactions of racemic secondary alkylzinc reagents **144** with alkenyl iodides **145a-f** leading to α-chiral alkenes **146a-h**.



entry	alkylzinc	electrophile	product of type **146**[a]
1	 *syn*-**144a**	 **145a**	 *syn*-**146a**, 43%, dr = 98:2
2	 *anti*-**144a**	**145a**	 *anti*-**146a**, 39%, dr = 5:95
3	*syn*-**144a**	 **145b**	 *syn*-**146b**, 45%, dr = 94:6

[90] The use of octenyl bromide as electrophile afforded *syn*-**146a** in 23% yield and dr = 94:6.

4	*syn*-**144a**	 **145c**	 *syn*-**146c**, 52%, dr = 98:2
5	*syn*-**144a**	 **145d**	 *syn*-**146d**, 39%, dr = 94:6
6	*syn*-**144a**	 **145e**	 *syn*-**146e**, 44%, dr = 98:2
7	*syn*-**144a**	 **145f**	 *syn*-**146f**, 43%, dr = 96:4
8	 *syn*-**144b**	 **145a**	 *syn*-**146g**, 43%, dr = 93:7
9	 *syn*-**144c**	**145a**	 *syn*-**146h**, 46%, dr = 96:4

[a] The diastereoselectivity (dr; syn:*anti* ratio) was determined by ^{1}H-NMR spectroscopy and GC-analysis.

These conditions were broadly applicable. Hence, we performed such a cross-coupling reaction with other secondary alkylzinc reagents **144b-c** (see entries 8 and 9). The 1,3-functionalized secondary alkyl iodide *rac*-**142b** was prepared according to literature procedure, followed by an I/Li-exchange reaction, which after epimerization (–50 °C, 30 min) led to the chelate-stabilized lithium species.[63] Subsequent transmetalation to the corresponding dialkylzinc reagent *syn*-**144b** followed by cross-coupling with **145a** afforded the silyl-protected alkene *syn*-**146g** in 43% yield (dr = 93:7). Furthermore, the 1,4-functionalized dialkylzinc reagent *syn*-**144c** was suitable for cross-coupling reaction leading to *syn*-**146h** in 46% yield and dr = 96:4.

1.4 Palladium-Catalyzed Cross-Couplings with Aryl Bromides

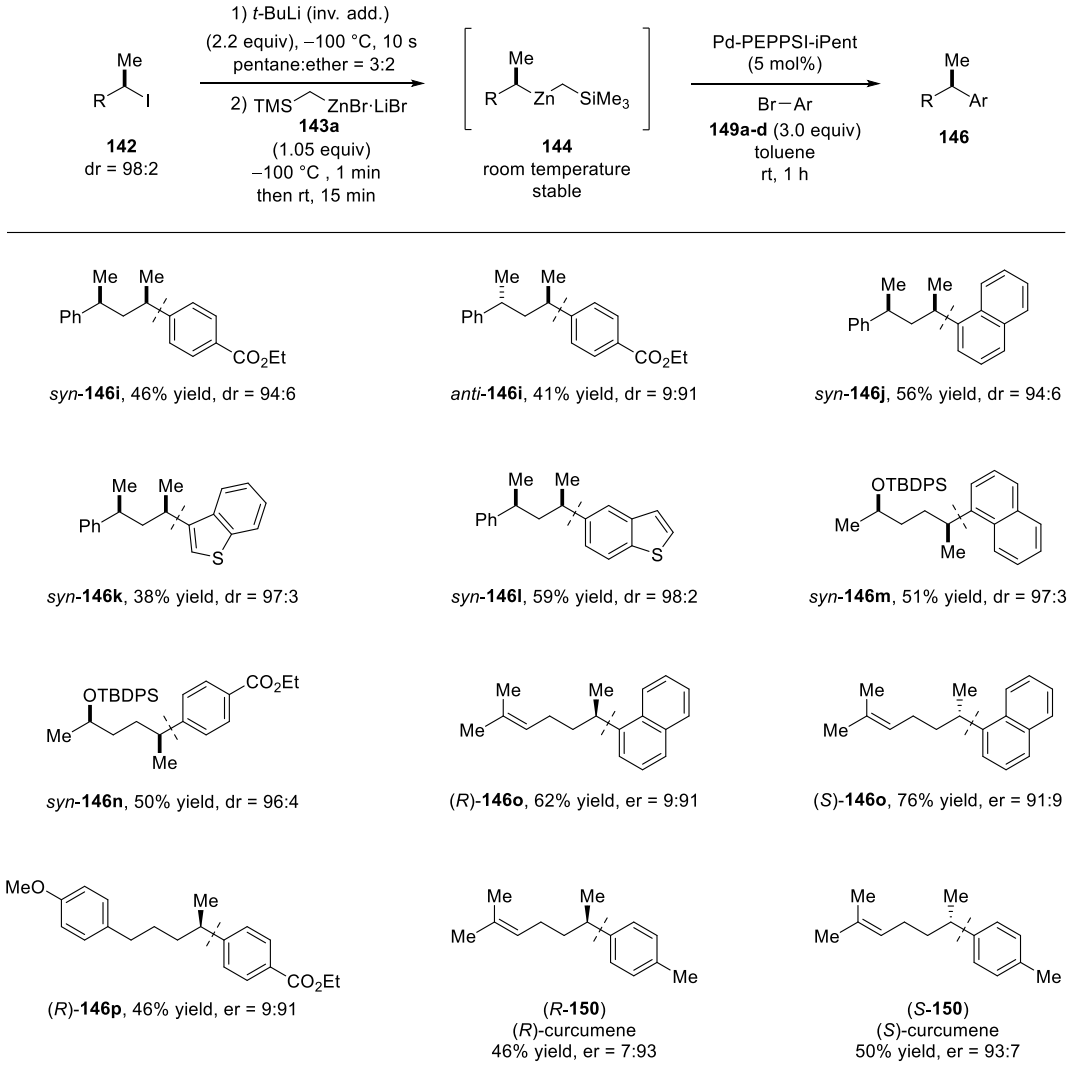
As many pharmaceuticals and natural products contain aromatic moieties, the preparation of chiral arenes and heteroarenes is of great interest. Thus, we extended our method to palladium-catalyzed cross-couplings with aryl bromides of type **149** leading to the corresponding chiral arenes and heteroarenes (see Scheme 39). Various aryl bromides with electron donating and electron withdrawing substituents were used, leading to products **146i-n** (38–59% yield; dr up to 98:2). Thus, the cross-coupling reaction of *syn*-**144a** with bromothiophene derivatives[91] afforded *syn*-**146k-l** in 38-59% yield and with high retention of configuration (dr up to 98:2). In addition, 1-bromonaphthalene was used for the cross-coupling reaction with the dialkylzinc reagents *syn*-**144a** and *syn*-**144c** leading to α-chiral naphthalenes *syn*-**146j** and *syn*-**146m** in good yields (51-56% yield) and high stereoretention (dr up to 97:3). This cross-coupling was also extended to optically enriched alkylzinc reagents leading to the corresponding α-chiral arenes (*R*)-**146o,** (*S*)-**146o** and (*R*)-**146p** (up to 76% yield, er = 91:9).[92] To demonstrate the synthetic utility of the method, we performed the natural product synthesis of the two enantiomers of α-curcumene **150**, an aromatic sesquiterpene.[93] Both enantiomers can be found in nature, e.g. in essential oils or in the pheromone produced by the red-shoulder stink bug.[94] Starting from the readily available chiral secondary alkyl iodide (*S*)- or (*R*)-**142d**, the corresponding chiral secondary alkylzinc reagents (*S*)- or (*R*)-**144d** were prepared. Subsequent palladium-catalyzed cross-coupling reaction with 4-bromotoluene afforded the natural products (*S*)-curcumene ((*S*)-**150**; 50% yield; er = 93:7) and (*R*)-curcumene ((*R*)-**150**; 46% yield; er = 7:93).

[91] In this point, 2-bromothiophenes and *N*-heterocyclic halides were not suitable for cross-coupling reaction. For a detailed screening table, see Experimental Part.

[92] The *enantiomeric ratio* was determined by chiral GC-analysis or chiral HPLC-analysis. The (*S*)-enantiomer of **146p** was also prepared: 54% yield, er = 83:17. For details, see supplementary information.

[93] a) B. Rao, J. L. Simonsen, *J. Chem. Soc.* **1928**, 2496–2505. b) L. Wu, J.-C. Zhong, S.-K. Liu, F.-P. Liu, Z.-D. Gao, M. Wang, Q.-H. Bian, *Tetrahedron: Asymmetry* **2016**, *27*, 78–83.

[94] a) G. Uhde, G. Ohloff, *Helv. Chim. Acta* **1972**, *55*, 2621–2625. b) H. L. McBrien, J. G. Millar, R. E. Rice, J. S. McElfresh, E. Cullen, F. G. Zalom, *J. Chem. Ecol.* **2002**, *28*, 1797–1818.

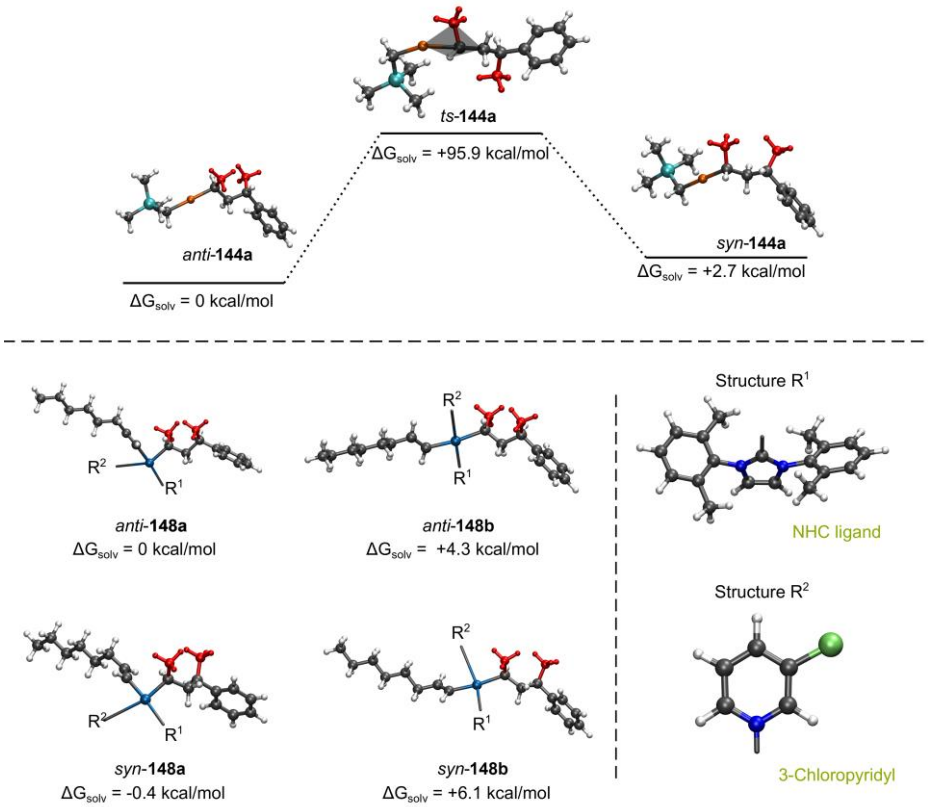


Scheme 39. Cross-coupling reaction of chiral alkylzinc reagents **144** with aryl bromides **149** leading to α-chiral arenes and heteroarenes (**146i-p**). [a] The diastereoselectivity (dr: *syn*:*anti* ratio) was determined by ^{1}H-NMR spectroscopy and GC-analysis.

1.5 DFT Calculations

Furthermore, DFT-calculations were performed to gain insight into the high retention of configuration of secondary alkylzinc reagents. Therefore, the configurational stability of the chiral alkylzinc reagents *syn*-**144a** and *anti*-**144a** was investigated. Solvation effects were accounted for by the *Polarizable Continuum Model* (PCM) as well as by explicit treatment with diethyl ether molecules.[95] Comparison of the free energies between the two isomers showed that *anti*-**144a** is thermodynamically more stable than the corresponding alkylzinc reagent *syn*-**144a** (ΔG = +2.7 kcal/mol). Coordination of one solvent molecule (diethyl ether) to the zinc site leads to a marginal rise of energy both for *syn*-**144a** and *anti*-**144a**, which suggests that solvent coordination is not relevant for the epimerization pathway. This result is in agreement with the fact that the cross-coupling reaction proceeded also in other solvents, such as toluene or THF, with high retention of configuration. We examined two possible pathways, which could lead to epimerization from *syn*-**144a** to *anti*-**144a** and *vice versa*, namely *via* a planar transition state *ts*-**144a** (see Scheme 40) or by cleavage of the carbon-zinc bond. Both the transition state energy of 95.5 kcal/mol and the carbon-zinc bond energy of ca. 35 kcal/mol corroborate the high stability of **144a** towards epimerization at 25 °C. Another important step in this catalytic cross-coupling cycle, where stereoretention is crucial, is the configurational stability of the Pd(II)-intermediate **148** (see Scheme 38). We performed an analogous analysis of potential epimerization channels on **148** using Pd-PEPPSI. To stay within the computational feasibility of our quantum chemical method, we simplified the catalyst by replacing the four experimentally used isopentyl residues in Pd-PEPPSI-iPent with methyl groups. This allowed slightly more steric flexibility, while the electronic nature around the Pd(II) and the carbon stereocenter is unaltered. Starting from a tetrahedral geometry of the four ligands around the Pd(II) center, the optimization ends in an energetic minimum which exhibits a nearly planar tetragonal structure. Thus, there are four possible species for **8**, with either the *syn*- or the *anti*-isomer in *cis* (**148a**) or *trans* (**148b**) position to the alkene (see Scheme 3). A comparison of configurational stabilities of the four species showed that the *cis*-conformer **148a** is more stable than the *trans*-conformer **148b**, which is encouraging since reductive elimination can only occur from the *cis*-configuration **148a**.

[95] a) M. J. Frisch *et al.* Gaussian16 Revision B.01, **2016**. b) for details of calculations, see Experimental Part.



Scheme 40. Theoretical calculations of the epimerization of secondary alkylzinc reagent *anti*-**144a** to *syn*-**144a** and Pd(II)-intermediates of type **148**. Molecular geometries and Gibbs free energies ΔG_{solv} in solution. **Top:** Stabilities of *anti*-**144a** and *syn*-**144a**. **Bottom:** Stabilities of *syn*- and *anti*-**148a** and **148b**.

With respect to the finding of our study again the high energy of the transition states *ts*-**148a** (41.8 kcal/mol; *anti*-**148a** to *syn*-**148a**) and *ts*-**148b** (39.7 kcal/mol; *anti*-**148b** to *syn*-**148b**) and carbon-palladium bonding energies of *syn*-**148a** (47.7 kcal/mol), *anti*-**148a** (47.2 kcal/mol), *syn*-**148b** (41.6 kcal/mol), and *anti*-**148b** (40.1 kcal/mol) corroborate the experimentally found retention of configuration. Interestingly, the energy barrier is significantly lower for *ts*-**148a** and *ts*-**148b** than it is for *ts*-**144a**, which suggests that a potential loss of stereoinformation occurs more likely at the Pd(II)-intermediate **148**. Nevertheless, we presume that the minimal epimerization of the secondary alkylzinc reagents may be due to polymolecular exchange reactions between these zinc reagents, which may involve the salts LiBr and LiI.

2 General Stereoretentive Preparation of Chiral Secondary Mixed Alkylmagnesium Reagents and Their Use for Enantioselective Electrophilic Aminations

2.1 Introduction

Organomagnesium reagents are key intermediates in organic synthesis, which have found numerous applications.[30c, 40c, 96] Nevertheless, a general and practical enantioselective preparation of secondary alkylmagnesium reagents is still pending. To date, only one example of a non-heteroatom-stabilized α-chiral Grignard reagent has been reported, which was prepared *via* a sulfoxide-magnesium exchange.[82b, 97] Furthermore, deracemization of a mixture of endo- and exo- norbornylmagnesium bromide using benzophenone[98] or exploiting the different reactivities of menthylmagnesium chloride epimers[99] have been reported.

Recently, we have shown that various enantiomerically enriched secondary alkyl iodides of type **142** underwent an I/Li-exchange[100] at −100 °C in pentane:ether mixtures furnishing the corresponding chiral alkyllithiums of type **141** with retention of configuration (Scheme 41a).[59, 62, 63, 101] After transmetalations with appropriate ether soluble Cu,[60, 61, 70, 79, 80] and Zn[102] salts at −100 °C, chiral organometallics of type **143** were obtained, which reacted with various electrophiles (**145** or **151**) providing products of type **146** after cross-coupling or products of type **152** after direct quench with high retention of configuration. Although chiral building blocks and natural products were available by these procedures,[60, 72] such reaction sequences required very low temperatures (−100 °C) due to the occurrence of configurationally labile alkyllithium reagents (**141**), which epimerized readily at temperatures above −100 °C[62] and tolerated no sensitive functional groups.

[96] a) H. G. Richey, *Grignard Reagents: New Developments*, John Wiley & Sons, Ltd. New York, **1999**; b) Z. Rappoport, I Marek *PATAI's Chemistry of Functional Groups: The Chemistry of Organomagnesium Compounds*, John Wiley & Sons, Ltd. New York, **2008**; c) A. Kremsmair, J. H. Harenberg, K. Schwärzer, A. Hess, P. Knochel, *Chem. Sci.* **2021**, *12*, 6011–6019.

[97] a) R. W. Hoffmann, B. Hölzer, O. Knopff, K. Harms, *Angew. Chem. Int. Ed.* **2000**, *39*, 3072–3074; b) R. W. Hoffmann, B. Hölzer, *Chem. Commun.* **2001**, 491–492; c) R. W. Hoffmann, B. Hölzer, O. Knopff, *Org. Lett.* **2001**, *3*, 1945–1948; d) R. W. Hoffmann, B. Hölzer, *J. Am. Chem. Soc.* **2002**, *124*, 4204–4205;

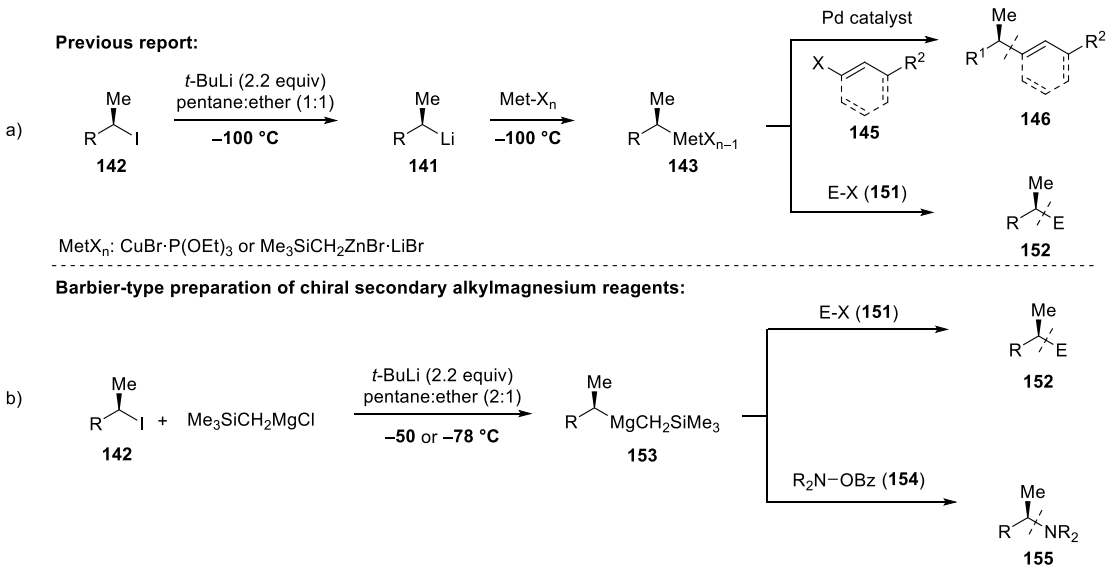
[98] a) F. R. Jensen, K. L. Nakamaye, *J. Am. Chem. Soc.* **1966**, *88*, 3437–3438; b) J. San Filippo, J. W. Nicoletti, *J. Org. Chem. 1977*, **42**, 1940–1944.

[99] J. Beckmann, D. Dakternieks, M. Dräger, A. Duthie, *Angew. Chem. Int. Ed.* **2006**, *45*, 6509–6512.

[100] We used 2.2 equiv of *t*-BuLi for best results (formation of lithium reagent and formation of isobutylene and isobutene as side-products); see: M. Schlosser, *Organometallics in Synthesis: Third Manual*, John Wiley & Sons, Ltd. New York, **2013**.

[101] J. Skotnitzki, A. Kremsmair, P. Knochel, *Synthesis* **2020**, *52*, 189–196.

[102] J. Skotnitzki, A. Kremsmair, D. Keefer, Y. Gong, R. de Vivie-Riedle, P. Knochel, *Angew. Chem. Int. Ed.* **2020**, *59*, 320–324.



Scheme 41. a) Previous preparation of chiral secondary alkyl organometallics of type **143** *via* I/Li-exchange and subsequent transmetalation at −100 °C; b) Barbier-type preparation of chiral secondary alkylmagnesium reagents (**153**) *via* I/Li-exchange and *in-situ* transmetalation with Me_3SiCH_2MgCl at −50 °C or −78 °C.

Thus, Barbier conditions involving the generation of the organometallic species in the presence of an electrophile or transmetalation reagent might circumvent the configurational lability and high reactivity of these secondary alkyllithiums.[49,103] Lately, we have shown that Barbier conditions were broadly applicable for the directed lithiation of (hetero)aromatics with TMPLi (TMP = 2,2,6,6,-tetramethylpiperidyl) in the presence of various salts.[50] With these previous reports in mind, we have envisioned Barbier conditions, that would overcome the use of unpractical very low temperatures for the preparation of chiral secondary alkylmagnesium reagents (**153**) by generating the chiral secondary alkyllithiums in the presence of an appropriate magnesium reagent. Herein, we report a general and practical preparation of non-stabilized enantiomerically enriched mixed alkylmagnesium reagents of type **153** from optically enriched secondary alkyl iodides in the presence of commercially available Me_3SiCH_2MgCl using *t*-BuLi at convenient temperatures of up to −50 °C (Scheme 41b). These enantiomerically enriched Grignard reagents (**153**) reacted with a range of electrophiles (**151**) including ketones, aldehydes, acid chlorides, isocyanates, *S*-methyl methanethiosulfonate, chlorophosphines and *O*-benzoyl hydroxylamines (**152**) providing products of type **152** such as α-chiral tertiary alcohols, ketones, amides, thioethers, phosphines and tertiary amines (**155**) in up to 89% yield (over 3 reaction steps) with high retention of configuration (up to 99% *ee*).

[103] S. Goto, J. Velder, S. El Sheikh,Y. Sakamoto, M. Mitani, S. Elmas, A. Adler, A. Becker, J-M Neudörfl, J. Lex, H-G. Schmalz, *Synlett* **2008**, *9*, 1361–1365.

2.2 Optimization of Reaction Conditions

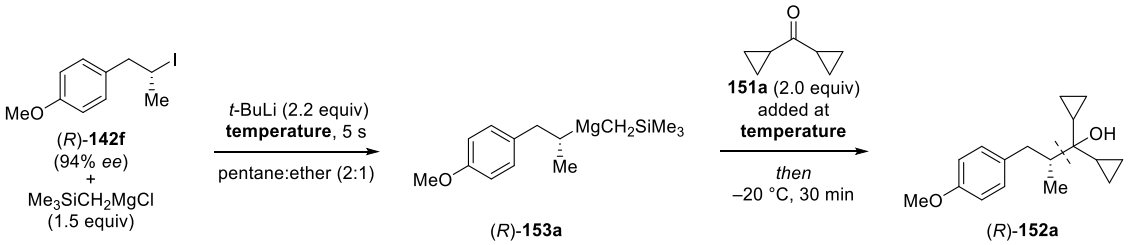


Table 4. Optimization of reaction conditions

Entry	Temperature [°C]	Yield of (*R*)-**152a**[a]	*ee* of (*R*)-**152a**[b]
a) *reaction condition optimization*			
1	−100	80%	91%
2	−78	80% (75%)[c]	91%
3	−78	78%[d]	12%
4	−60	73%	90%
5	−40	71%	82%
6	−20	59%	52%
7	−20[e]	52%	78%
8	−40[e]	67%	84%
*b) configurational stability evaluation of (R)-**153a***			
9	−78[f]	75%	91%
10	−50[f]	71%	86%
11	−50[g]	64%	69%
12	−20[f]	66%	60%

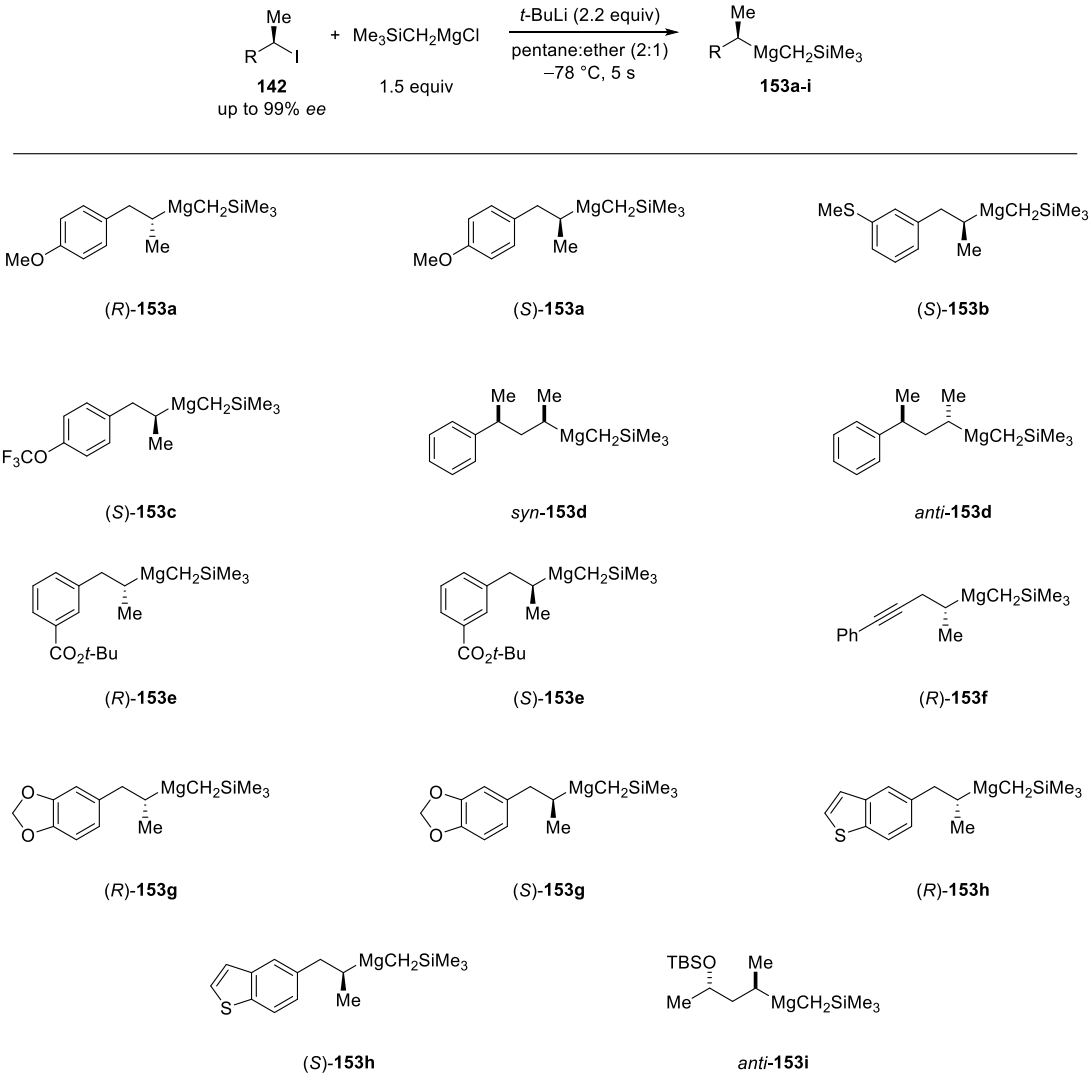
Stereoretentive preparation of (*R*)-**153a** at various reaction temperatures under Barbier conditions. [a] The yield was determined by GC-analysis of reaction aliquotes. [b] The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis. [c] Yield of analytically pure isolated product. [d] The reaction was performed without Me_3SiCH_2MgCl. [e] Me_3SiCH_2MgCl (2.0 equiv) was used. [f] The chiral Grignard reagent (*R*)-**153a** was kept for 1 h at this temperature before quenching. [g] The chiral Grignard reagent (*R*)-**153a** was kept for 3 h at this temperature before quenching.

Thus, in preliminary experiments, we have mixed the chiral secondary alkyl iodide (*R*)-**142f** with Me_3SiCH_2MgCl and have subsequently added *t*-BuLi (2.2 equiv) at various temperatures (see Table 4). The resulting secondary alkylmagnesium species (*R*)-**153a** was quenched with dicyclopropyl ketone (**151a**) and stirred at −20 °C for 30 min. The desired tertiary alcohol (*R*)-**152a** was obtained in 80% yield and 91% *ee* at a reaction temperature of −100 °C (entry 1). To our delight, the same enantioselectivity was achieved by performing the I/Li-exchange at −78 °C (entry 2). As expected, if the reaction was performed at −78 °C without Me_3SiCH_2MgCl, (*R*)-**152a** was obtained in comparable yield (78%) but only with 12% *ee* (entry 3). A slight erosion of enantioselectivity was observed if the reaction was carried out at −60 °C (73% yield; 90% *ee*, entry 4). However, higher temperatures led to a significant loss of enantiomeric purity as a reaction at −40 °C afforded (*R*)-**152a** in 71% yield and 82% *ee* (entry 5). Further raising the reaction temperature and performing the exchange at −20 °C gave (*R*)-**152a** in 59% yield with 52% *ee* (entry 6). Interestingly, using 2.0 equiv of Me_3SiCH_2MgCl considerably reduced the racemization rate at −20 °C, since the tertiary alcohol (*R*)-**152a** was obtained in 78% *ee* and 52% yield (entry 7). Lowering the reaction temperature to −40 °C again and using 2.0 equiv of Me_3SiCH_2MgCl did not give any improved result (67% yield, 84% *ee*, entry 8). Alternative transmetalating reagents may also be used for this reaction, however with less satisfactory results.[104] Next, we have examined the configurational stability of such chiral secondary alkylmagnesium reagents of type **153**. Therefore, we have generated the mixed dialkylmagnesium reagent (*R*)-**153a** at −78 °C and kept it at this temperature for 1 h before adding **151a,** yielding the corresponding alcohol (*R*)-**152a** in 75% yield and 91% *ee* (entry 9). A detectable racemization was observed after stirring the reaction mixture of (*R*)-**153a** for 1 h (71% yield, 86% *ee;* entry 10) or 3 h (64% yield, 69% *ee*; entry 11) at −50 °C. Furthermore, a large loss of enantioselectivity was observed by keeping (*R*)-**153a** for 1 h at −20 °C (66% yield, 60% *ee*, entry 12). These results indicated, that mixed non-stabilized secondary alkylmagnesium reagents of type **153** were configurationally stable up to ca. −50 °C for ca. 1 h and in comparison with the corresponding alkyllithium reagents (configurationally stable only below −100 °C for some minutes)[101] were better suited for synthetic applications.

[104] For further optimization see Experimental Part.

2.3 Reactions of Chiral Grignard Reagents with Electrophiles

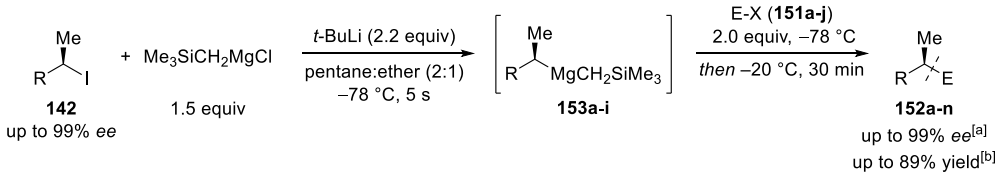
With these optimized conditions in hand (Table 4, entry 2), we have prepared several chiral Grignard reagents (**153a-i**) with high retention of configuration starting from the corresponding enantiomerically enriched secondary alkyl iodides (**142**; see Scheme 42).

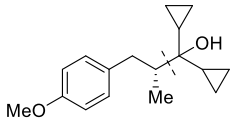


Scheme 42. Prepared optically enriched Grignard reagents (**153a-i**) *via* I/Li-exchange and *in situ* transmetalation using Me_3SiCH_2MgCl.

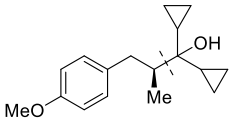
Thus, using (*S*)-**153a** (ca. 92-94% *ee*[105] instead of (*R*)-**153a**), obtained from the alkyl iodide (*S*)-**142e** (95% *ee*), gave the alcohol (*S*)-**152a** after quenching with **151a** in 81% yield and 90% *ee* (see Scheme 43). Related Grignard reagents such as (*S*)-**153b** (ca. 99% *ee*) or (*S*)-**153c** (ca. 98% ee) add similarly to **151a** or **151b** providing the alcohols (*S*)-**152b** and (*S*)-**152c** in 65-73% yield and 98-99% *ee*. Also, diastereomerically enriched Grignard reagents *syn*-**153d** (dr = 99:1) and *anti*-**153d** (dr = 1:99) provided after addition to **151a** the alcohols *syn*- and *anti*-**152d** respectively in 74% yield and dr = 96:4 as well as 70% yield and dr = 5:95. Remarkably, functionalized alkylmagnesium species bearing a *tert*-butyl ester function such as (*R*)- and (*S*)-**153e** or an alkynyl group like (*R*)-**153f** reacted with excellent stereoretention with **151a** giving the alcohols (*R*)-**152e** (65% yield, 93% *ee*) or (*S*)-**152e** (72% yield, 93% *ee*) and (*R*)-**152f** (73% yield, 93% *ee*). Although enolizable ketones did not give satisfactory results, addition of Grignard reagents (*R*)-**153a**, (*R*)- and (*S*)-**153g** and (*R*)-**153h** to aldehydes such as *c*-hexylcarboxaldehyde (**151c**), (*S*)-(−)-citronellal (**151d**) and (1*R*)-(−)-myrtenal (**151e**) afforded after Dess-Martin oxidation the corresponding ketones (*R*)-**152g** (68%, 89% *ee*), (2*R*,5*S*)-**152h** (74%, dr = 95:5), (2*S*,5*S*)-**152h** (75%, dr = 5:95) as well as (*R*,*R*,*S*)-**152i** (46%, dr = 95:5) and (*S*,*R*,*S*)-**152i** (49%, dr = 3:97). Performance of acylations did not require Weinreb amides as used for the acylation of chiral alkyllithiums[63], but commercially available acid chlorides were employed. Thus, (*R*)-**153a** reacted with (*S*)-tetrahydrofuran-2-carbonyl chloride (**151f**) affording (2*S*,2'*R*)-**152j** in 89% yield and dr = 11:89. Similarly, acylation of *anti*-**153i** with 3-fluorobenzoyl chloride (**151g**) led to *anti*-**152k** in 52% yield and dr = 5:95. Further functionalizations of these optically enriched Grignard reagents were realized by addition of (*R*)- and (*S*)-**153g**, (*S*)-**153b** and (*S*)-**153e** to cyclohexyl isocyanate (**151h**) and the commercial chiral (*S*)-(−)-α-methylbenzyl isocyanate (**151i**, 96% *ee*) or (*R*)-(−)-1-(1-naphthyl)ethyl isocyanate (**151j**, 95% *ee*) providing under our standard conditions, the chiral amides (*R*)-**152l** (80%, 94% *ee*) or (*S*)-**152l** (81%, 94% *ee*) as well as the diastereomerically enriched amides (3*S*,2'*S*)-**152m** (71%, dr = 96;4) and (3*R*,2'*R*)-**152n** (53%, dr = 96:4).

[105] The enantiopurity was estimated based on the enantiopurity of the obtained tertiary alcohols after reaction with the ketones **151a** or **151b**.

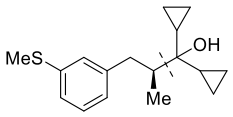




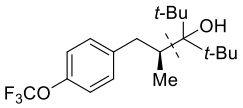
(*R*)-**152a:** 75%, 91% *ee*



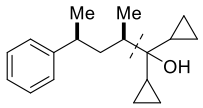
(*S*)-**152a:** 81%, 90% *ee*



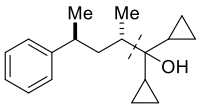
(*S*)-**152b**: 73%, 99% *ee*



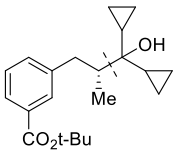
(*S*)-**152c:** 65%, 98% *ee*



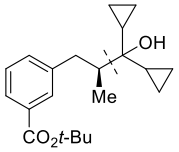
syn-**152d:** 74%, dr = 96:4



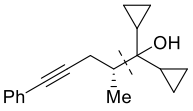
anti-**152d:** 70%, dr = 5:95



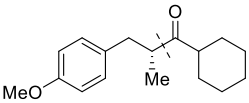
(*R*)-**152e**: 65%, 93% *ee*



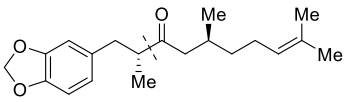
(*S*)-**152e:** 72%, 93% *ee*



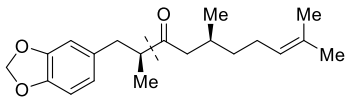
(*R*)-**152f:** 73%, 93% *ee*



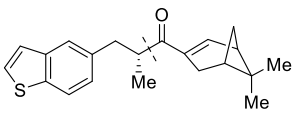
(*R*)-**152g:** 68%, 89% *ee*



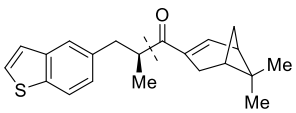
(2*R*,5*S*)-**152h**: 74%, dr = 95:5



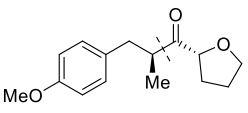
(2*S*,5*S*)-**152h:** 75%, dr = 5:95



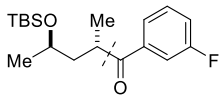
(*R*,*R*,*S*)-**152i:** 46%, dr = 95:5



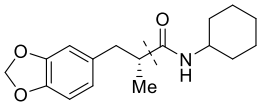
(*S*,*R*,*S*)-**152i:** 49%, dr = 3:97



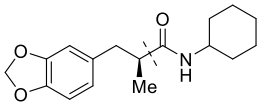
(2*S*,2'*R*)-**152j**: 89%, dr = 11:89



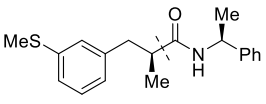
anti-**152k:** 52%, dr = 5:95



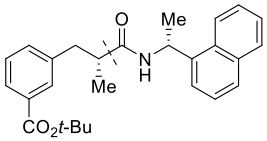
(*R*)-**152l:** 80%, 94% *ee*



(*S*)-**152l:** 81%, 94% *ee*



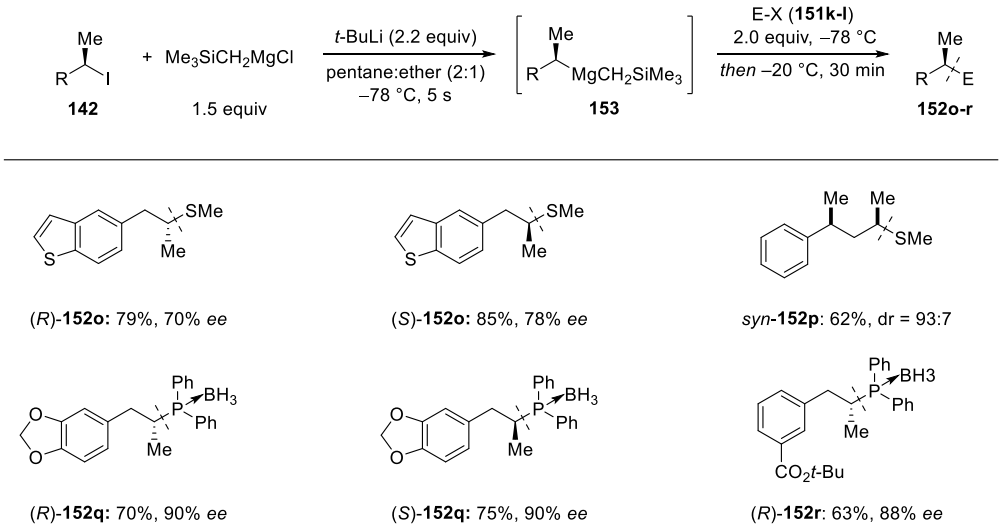
(3*S*,2'*S*)-**152m**: 71%, dr = 96:4



(3*R*,2'*R*)-**152n:** 53%, dr = 96:4

Scheme 43. Prepared enantiomerically and and diastereomerically enriched products **152a-n** from secondary alkylmagnesium reagents **153a-i** and electrophiles (**151a-j**). [a] The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis. The diastereomeric ratio (dr; *syn/anti* ratio) was determined by ^{1}H-NMR spectroscopy and GC-analysis. [b] Yield refers to isolated analytically pure compounds

We further investigated the formation of carbon-heteroatom bonds (see Scheme 43). Thus, the enantioselective preparation of carbon-sulfur bonds was briefly examined since it proceeded also directly with chiral secondary alkyllithiums.[59, 62] We observed that the coupling of (*R*)- or (*S*)-**153h** and *syn*-**153d** with $MeSO_2SMe$ (**151k**) led to the thioethers (*R*)- or (*S*)-**152o** and *syn*-**152p** in up to 85% yield, but moderate stereoselectivity (up to 78% *ee* or dr = 93:7). However, phosphorus electrophiles such as Ph_2PCl (**151l**) reacted with high stereoretention with chiral Grignard reagents. Thus, (*R*)- and (*S*)-**153g** or (*R*)-**153e** led, after protection with $BH_3 \cdot SMe_2$,[106] to a practical synthesis of chiral phosphine BH_3-complexes (*R*)- and (*S*)-**152q** as well as (*R*)-**152r** in up to 75% yield and up to 90% *ee*. These optically enriched phosphines could be of interest for asymmetric catalysis.



Scheme 44. Prepared enantiomerically and diastereomerically enriched products **152o-r** from secondary alkylmagnesium reagents **153** and electrophiles (**151k-l**). [a] The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis. The diastereomeric ratio (dr; *syn/anti* ratio) was determined by ^{1}H-NMR spectroscopy and GC-analysis. [b] Yield refers to isolated analytically pure compounds.

[106] F. Langer, P. Knochel, *Tetrahedron Lett.* **1995**, *36*, 4591–4594

2.4 Electrophilic Aminations Using Chiral Grignard Reagents

α-Chiral alkyl amines are of considerable interest due to their presence in natural products, pharmaceuticals and other biologically active molecules.[107] Inspired by pioneering work of Johnson,[108] we envisioned using *O*-benzoyl hydroxylamines[109] as electrophilic amination reagents with chiral dialkyl Grignard reagents of type **153**. After optimization, we have found that at a reaction temperature of −50 °C, the desired α-chiral amines **155a-j** were obtained with high stereoretention (see Scheme 45). Remarkably, all these reactions occurred chemoselectively without any transition metal additive and only minimal amounts of usual side-products (ketone)[110] were observed. Thus, (*R*)- and (*S*)-**153a** reacted with 4-(pyrimidin-2-yl)piperazin-1-yl benzoate (**154a**) affording the corresponding α-chiral tertiary amines (*R*)- and (*S*)-**155a** in 73% yield and 88−91% *ee*. Furthermore, sertraline, a commercially available drug molecule,[111] was successfully aminated *via* **154b** and (*S*)-**153a** using this procedure, giving (2'*S*,1*S*,4*S*)-**155b** in 52% yield and dr = 91:9. Also, the chiral Grignard reagents (*R*)- and (*S*)-**153g** were generated at −50 °C and trapped with 6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl benzoate (**154c**) and non-cyclic *O*-benzoyl-*N*,*N*-bis(2-methoxyethyl) hydroxylamine (**154d**) yielding (*R*)- and (*S*)-**155c** as well as (*R*)- and (*S*)-**155d** in 70-85% yield and 84-93% *ee*. The functionalized secondary alkylmagnesium reagent (*R*)-**153e** was also aminated with **154c** providing (*R*)-**155e** in 68% yield and 83% *ee*. Additionally, the aminated benzothiophene derivatives (*R*)- and (*S*)-**155f-g** were prepared in up to 85% yield and up to 97% *ee* from optically enriched Grignard reagents (*R*)- and (*S*)-**153h** and the *O*-benzoyl hydroxylamines **154c** and *N*-morpholino benzoate (**154e**).

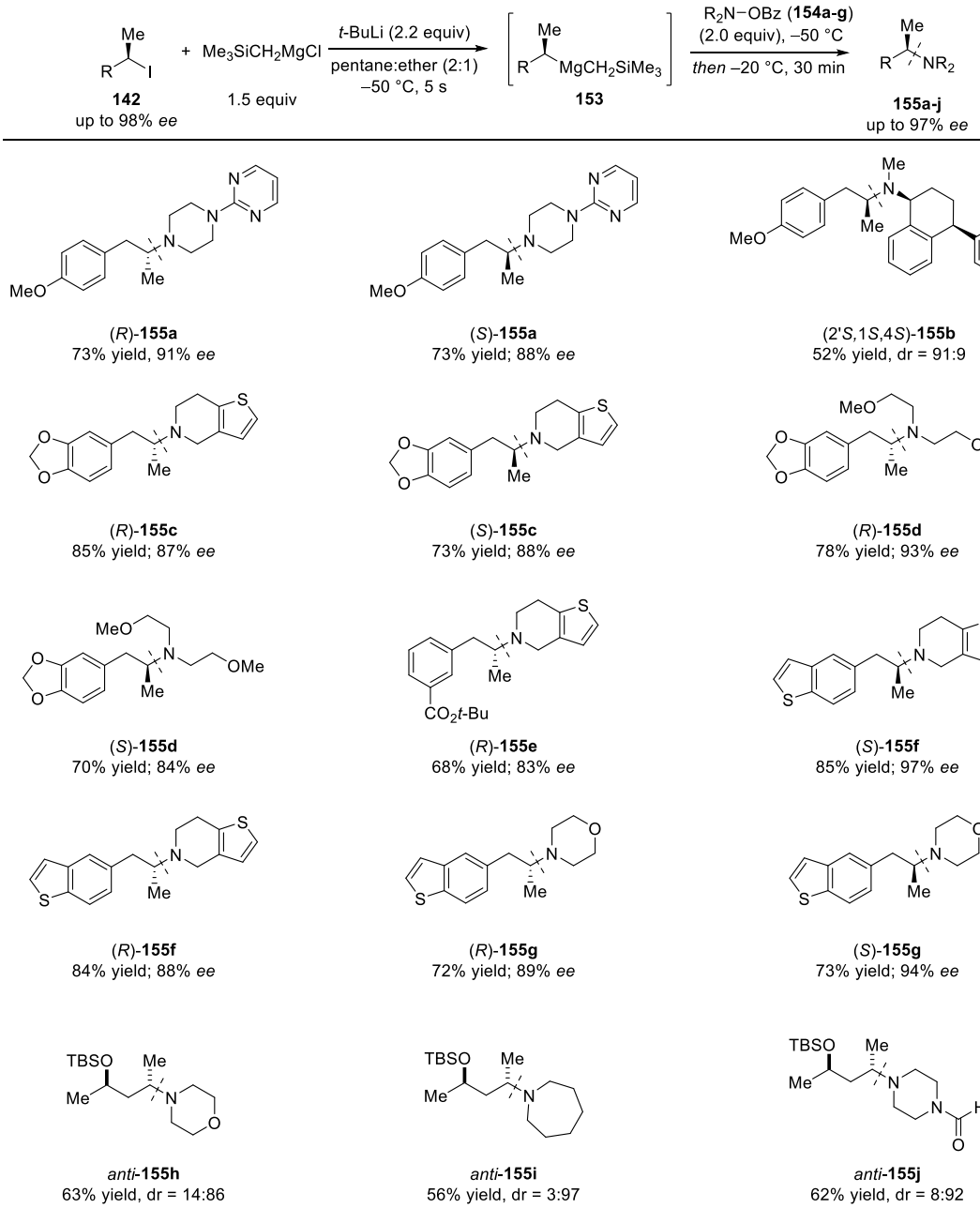
[107] a) N. E. Lee, S. L. Buchwald, *J. Am. Chem. Soc*. **1994**, *116*, 5985–5986; b) T. C. Nugent, M. El-Shazly, *Adv. Synth. Catal.* **2010**, *352*, 753–819; c) G-H. Hou, J-H. Xie, P-C. Yan, Q-L. Zhou, *J. Am. Chem. Soc*. **2009**, *131*, 1366–1371; d) D. Matheau-Raven, P. Gabriel, J. A. Leitch, Y. A. Almehmadi, K. Yamazaki, D. J. Dixon, *ACS Catalysis*, **2020**, *10*, 8880–8897; e) A. Trowbridge, S. M. Walton, M. J. Gaunt, *Chem. Rev.* **2020**, *120*, 2613–2692.

[108] a) A. M. Berman, J. S. Johnson, *J. Am. Chem. Soc.* **2004**, *126*, 5680–5681; b) A. M. Berman, J. S. Johnson, *J. Org. Chem.* **2005**, *70*, 364–366; c) A. M. Berman, J. S. Johnson, *J. Org. Chem.* **2006**, *71*, 219–224.

[109] a) S. L. McDonald, C. E. Hendrick, Q. Wang, *Angew. Chem. Int. Ed.* **2014**, *53*, 4667–4670; b) K. Shen, Q. Wang, *Chem. Sci.* **2015**, *6*, 4279–4283; c) B. N. Hemric, K. Shen, Q. Wang, *J. Am. Chem. Soc.* **2016**, *138*, 5813–5816; d) C. E. Hendrick, K. J. Bitting, S. Cho, Q. Wang, *J. Am. Chem. Soc.* **2017**, *139*, 13110–13116; e) Y-H. Chen, S. Graßl, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 1108–1111; f) S. Graßl, Y-H. Chen, C. Hamze, C. P. Tüllmann, P. Knochel, *Org. Lett.* **2019**, *21*, 494–497; g) Z. Xiong, P. Cai, Y. Mei, J. Wang, *RSC Adv.* **2019**, *9*, 42072–42076; h) V. A. Van der Puyl, J. Derosa, K. M. Engle, *ACS Catal.* **2019**, *9*, 224–229; i) S. Graßl, P. Knochel, *Org. Lett.* **2020**, *22*, 1947–1950; j) J. He, Y. Xue, B. Han, C. Zhang, Y. Wang, S. Zhu *Angew. Chem. Int. Ed*. **2020**, *59*, 2328–2332; k) Y. Kwon, Q. Wang, *Org. Lett.* **2020**, *22*, 4141–4145; l) B. N. Hemric, C. K. Ku, Q. Wang, *Encyclopedia of Reagents for Organic Synthesis*, Wiley VCH **2020**, doi: 10.1002/047084289X.rn02290.

[110] M. J. Campbell, J. S. Johnson, *Org. Lett*. **2007**, *9*, 494-497.

[111] M. W. Welch, A. R. Kraska, R. Sarges, B. K. Koe, *J. Med. Chem.* **1984**, *27*, 1508–1515.



Scheme 45. Scope of prepared enantiomerically and diastereomerically enriched α-chiral tertiary amines **155a-j** obtained by electrophilic amination of secondary alkylmagnesium reagents **153a-i** with *O*-benzoyl hydroxylamines (**154a-g**). The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis. The diastereomeric ratio (dr; *syn*/anti ratio) was determined by ^{1}H-NMR spectroscopy and GC-analysis.

Also, the diastereomerically enriched secondary alkylmagnesium reagent *anti*-**153i** was successfully quenched with **154e**, azepan-1-yl benzoate (**154f**) and even the sensitive formamide 4-formylpiperazin-1-yl benzoate (**154g**) affording *anti*-**155h-j** in 56-63% yield and up to dr = 3:97. This preparation of tertiary amines was found to be superior to standard nucleophilic substitutions of chiral secondary alkyl iodides, phosphates and tosylates by metallic amides, which gave erratic results in our hands.[112] The determination of the absolute configuration was made in the case of the amine hydrochloride derivative of (*S*)-**155g** using X-ray diffraction (Flack parameter method)[113] confirming the (*S*)-configuration of **155g** as well as the retention of configuration of this electrophilic amination (Figure 3).

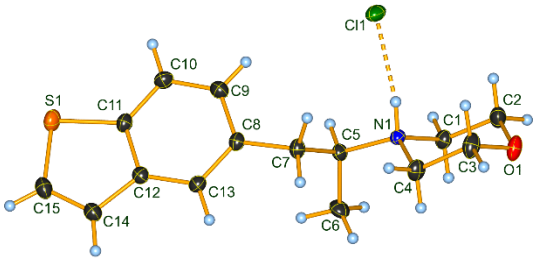


Figure 3. X-ray structure of (*S*)-**155g** crystallized as the corresponding amine hydrochloride as a representative example of the overall stereoretention of the electrophilic amination

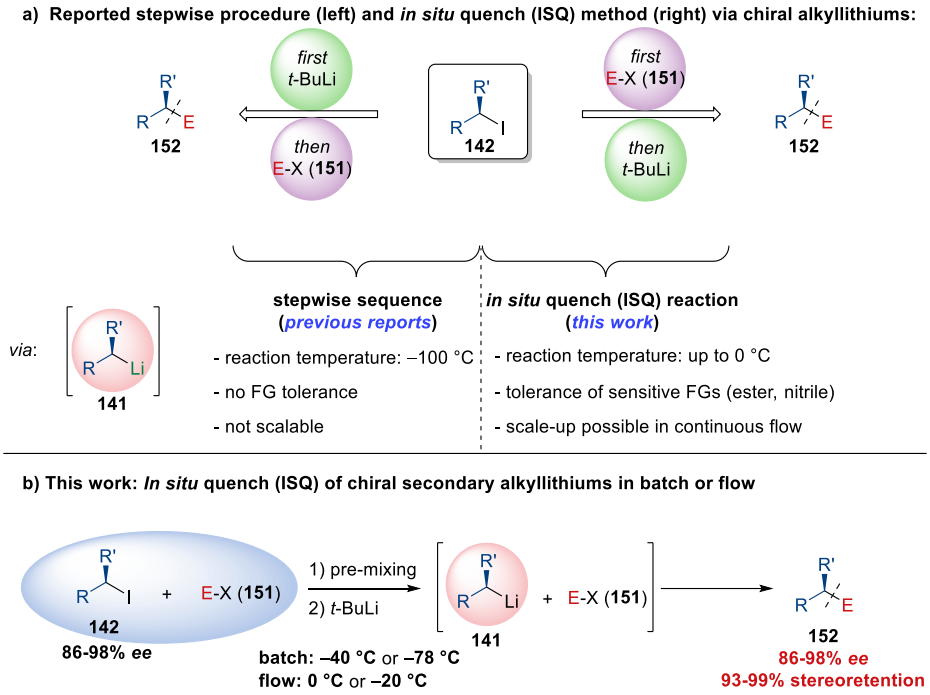
[112] For a detailed comparison of electrophilic and nucleophilic aminations see Experimental Part.

[113] a) H. D. Flack, *Acta Crystallogr.* **1983**, *39*, 876–881; b) E. C. Constable, C. E. Housecroft, *Chemistry* **2020**, *2*, 759–776.

3 In Situ Quench Reactions of Chiral Secondary Alkyllithium Reagents in Batch and Continuous Flow

3.1 Introduction

The enantioselective synthesis of small molecules has attracted increasing interest in pharmaceutical and agrochemical research.[114] Especially, the preparation of enantioenriched organometallics is an important goal as it gives straightforward access to various enantiopure compounds after quenching with numerous electrophiles.[115] Nevertheless, many reported chiral maingroup organometallics bear a heteroatom in α-position for stabilization, preventing fast epimerization.[58a, 58b, 116] Recently, we have reported the preparation of chiral non-heteroatom stabilized secondary alkyllithiums (**141**) from the corresponding iodides (**142**) *via* an I/Li-exchange with *t*-BuLi. The resulting organolithium species were either trapped after stereoretentive transmetalations[60, 61, 66, 70, 72, 79, 80, 102] or directly quenched[59, 62, 63, 101] with electrophiles (**151**) leading to various products of type **152** (see Scheme 46a, left).



Scheme 46. Highly stereoretentive *in situ* quench (ISQ) reactions involving secondary alkyllithium intermediates.

[114] a) H-J. Federsel, *Nat. Rev. Drug. Discov.* **2005**, *4*, 685–697; b) N. A. McGrath, M. Brichacek, J. T. Njardason, *J. Chem. Educ.* **2010**, *87*, 1348–1349; c) J. R. Cossy, *Compr. Chirality* **2012**, *1*,1–7; d) P. Jeschke, *Pest. Manag. Sci.* **2018**, *74*, 2389-2404; e) C. W. Lindsley, *ACS Chem. Neurosci.* **2019**, *10*, 115.

[115] G. Eppe, D. Didier, I. Marek, *Chem. Rev.* **2015**, *115*, 9175–9206.

[116] a) W. C. Still, C. Sreekumar, *J. Am. Chem. Soc.* **1980**, *102*, 1201–1202; b) H. J. Reich, M. D. Bowe, *J. Am. Chem. Soc.* **1990**, *112*, 8994–8995; c) H. J. Reich, K. J. Kulicke, *J. Am. Chem. Soc.* **1995**, *117*, 6621–6622; d) P. J. Rayner, P. O'Brien, R. A. J. Horan, *J. Am. Chem. Soc.* **2013**, *135*, 8071–8077.

However, the drawback of such approaches is the very low temperatures required for the generation of the organolithium species (−100 °C).[59, 62, 63, 101] Furthermore, the functional group tolerance was limited and the scale-up of these reaction sequences proved to be difficult affording poor yields and low optical purities. Thus, we have found that an *in situ* quench (ISQ)[103, 104] of chiral alkyl iodides in the presence of a suitable magnesium reagent with *t*-BuLi allowed the performance of the I/Li-exchange at up to −50 °C with high stereoretention (up to 99%) providing, upon transmetalation, several chiral secondary Grignard reagents.[117] Yet, the resulting chiral alkylmagnesiums proved to be unreactive towards some important classes of electrophiles (**151**) including enolizable or sterically hindered ketones.

Hence, we envisioned an ISQ-reaction involving the treatment of enantioenriched secondary alkyl iodides (**142**) with electrophiles (**151**) using *t*-BuLi as an exchange reagent at −78 °C or higher temperatures (Scheme 46a, right). These conditions combined with the use of a continuous flow set-up might allow even higher temperatures and previously impossible reaction scales. These perspectives would greatly improve the practicability of our method. Herein, we report such an *in situ* quench (ISQ) reaction of chiral alkyl iodides (**142**), including for the first time highly functionalized substrates, in the presence of a broad range of electrophiles such as aldehydes, ketones, Weinreb amides, isocyanates, sulfides, or boronates (**151**). Addition of *t*-BuLi at −78 °C or even −40 °C allowed the facile preparation of diversely functionalized chiral products of type **152** with high enantiomeric purity (up to 98% *ee*) *via* intermediate alkyllithiums of type (**141**, Scheme 46b). Furthermore, we were able to transfer the reaction into continuous flow conditions, in which it was scaled up to a 40-fold.

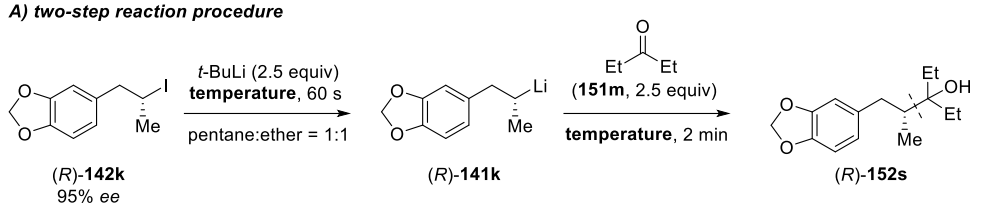
[117] A. Kremsmair, H. R. Wilke, M. M. Simon, Q. Schmidt, K. Karaghiosoff, P. Knochel, *Chem. Sci.* **2022**, *13*, 44–49.

3.2 Optimization of Reaction Conditions

In preliminary experiments, we have converted the chiral secondary alkyl iodide (*R*)-**142k** (95% *ee*) into the corresponding organolithium (*R*)-**141k** at −100 °C (addition of (*R*)-**142k** to *t*-BuLi within 60 s) resulting, after immediate quench with diethyl ketone (**151m**, 2.5 equiv), in the formation of the alcohol (*R*)-**152s** in 67% GC-yield and 92% *ee* (Table 5A, entry 1). Increasing the reaction temperature to −78 °C or −40 °C led to significant racemization of (*R*)-**152a** showing the limitations of the two-step procedure (entries 2 and 3 of table 5A). In contrast, using the ISQ-procedure, mixing the iodide (*R*)-**142k** (95% ee, 1.0 equiv) with Et_2CO (**151m**, 2.5 equiv) in 3:2 pentane:ether and adding *t*-BuLi (2.1 M in pentane) within 10 s at −78 °C gave (*R*)-**152s** in 60% isolated yield and 93% *ee* (entry 4). A temperature increase to −60 °C led to (*R*)-**152s** in 52% GC-yield and still 92% *ee* (entry 5). A slight erosion of enantioselectivity was observed at −40 °C, providing (*R*)-**152s** in 54% GC-yield and 90% *ee* (entry 6). A significant decrease in optical purity of (*R*)-**152s** was observed when the reaction was done at −20 °C (44% GC-yield, 86% *ee*, entry 7) or at 0 °C (41% GC-yield, 69% *ee*, entry 8). Increasing or decreasing the amount of electrophile used in the ISQ-procedure led to lower yields of (*R*)-**152s**.

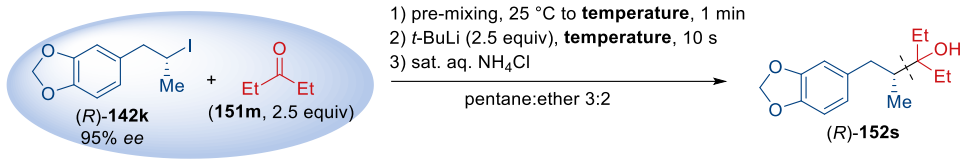
Table 5. Preparation of the enantioenriched alcohol (*R*)-**152s** using a two-step sequence *via* alkyllithium (*R*)-**141k** followed by the addition of diethyl ketone (**151m**) or *via* the *in situ* generation of (*R*)-**141k** in the presence of **151m**.

A) two-step reaction procedure



Entry	Temperature [°C]	GC-Yield of (*R*)-**152s**[a]	*ee* of (*R*)-**152s**[b]
1	−100	67%	92%
2	−78	61%	53%
3	−40	54%	0%

B) in situ quench (ISQ) procedure



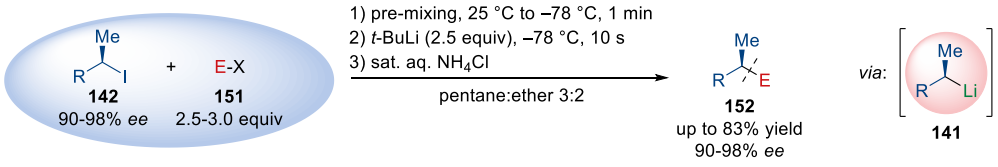
Entry	Temperature [°C]	GC-Yield of (*R*)-**152s**[a]	*ee* of (*R*)-**152s**[b]
4	**−78**	**60%**[c]	**93%**
5	−60	52%	92%
6	−40	54%	90%
7	−20	44%	86%
8	0	41%	69%

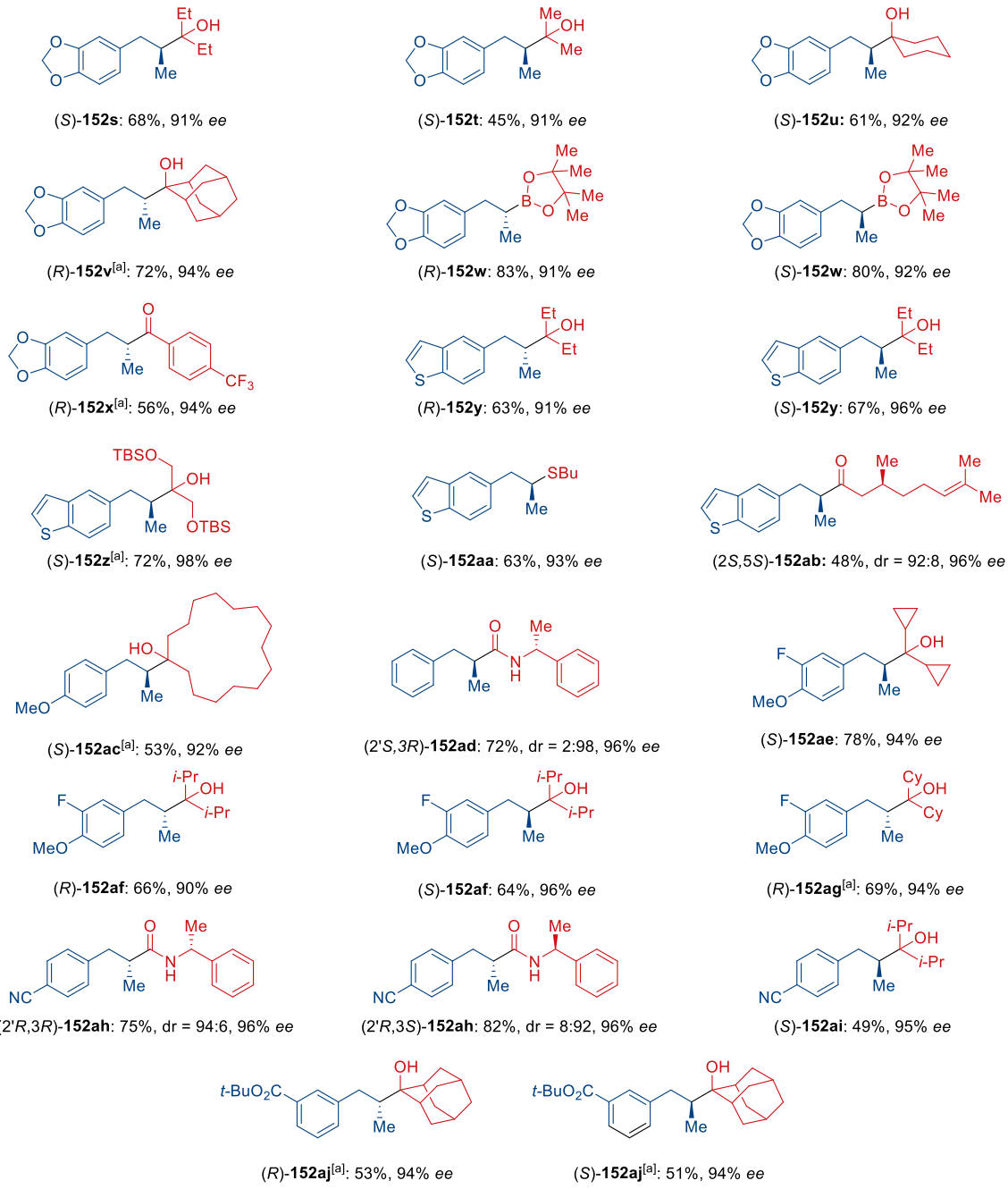
[a] The yield was determined by GC-analysis; [b] The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis; [c] Yield of isolated analytically pure product.

3.3 Scope of the ISQ-Reactions of Chiral Secondary Alkyllithiums in Batch

Based on these preliminary experiments, we have designed a general procedure for the *in situ* quench of various functionalized chiral secondary alkyl iodides of type **142** in the presence of electrophiles (E-X) of type **151** such as ketones, boronates, Weinreb amides, disulfides, aldehydes and isocyanates leading to functionalized chiral products of type **152** (see Scheme 47). Thus, mixing (*S*)-**142k** and diethyl ketone (**151m**) in pentane:ether and adding *t*-BuLi within 10 s at −78 °C followed by an immediate quench with sat. aq. NH_4Cl solution, gave the expected alcohol (*S*)-**152s** in 68% yield and 91% *ee*. Using (*S*)-**142k** in the presence of other enolizable ketones such as acetone (**151n**) or cyclohexanone (**151o**) led to the chiral alcohols (*S*)-**152t** and (*S*)-**152u** in 45-61% yield and 91-92% *ee*. In the case of solid electrophiles such as adamantanone (**151p**), the reaction was performed at −40 °C due to the limited solubility of the reaction mixture at lower temperatures. Nevertheless, the desired alcohol (*R*)-**152v** was isolated in 72% yield and 94% *ee*. Also, transmetalations to boronic acid esters like (*R*)- or (*S*)-**152w** were achieved with high stereoretention in up to 83% yield and up to 92% ee starting from (*R*)- or (*S*)-**142k** and methoxyboronic acid pinacol ester (**151q**). Although, the Weinreb amide *N*-methoxy-*N*-methyl-4-(trifluoromethyl)benzamide (**151r**) showed only limited solubility under our standard conditions (−78 °C), the ISQ reaction could be performed at −40 °C providing the α-chiral ketone (*R*)-**152x** in 56% yield and 94% *ee*. Employing the benzothiophene derived alkyl iodides (*R*)- or (*S*)-**142l** in the presence of diethyl ketone (**151m**) and adding *t*-BuLi at −78 °C gave the corresponding alcohols (*R*)- and (*S*)-**152y** in 63-67% yield and 91-96% *ee*. Also, a mixture of the chiral alkyl iodide (*S*)-**142l** and the silyl protected dihydroxyacetone derivative **151s** was only soluble at −40 °C and therefore *t*-BuLi was added at this temperature affording (*S*)-**152z** in 72% yield with high stereoretention (98% *ee*). Electrophiles like BuSSBu (**151t**) or citronellal (**151d**) reacted with (*S*)-**142l** providing the sulfide (*S*)-**152aa** (63%, 93% *ee*) or (2*S*,5*S*)-**152ab** (after oxidation with Dess-Martin periodinane;[118] 48% yield, dr = 92:8, 96% *ee*). Furthermore, the chiral alcohol (*S*)-**152ac** was isolated after mixing (*S*)-**142f** with cyclotetradecanone (**151u**) and adding *t*-BuLi at −40 °C in 53% yield and 92% *ee*. Isocyanates like (*R*)-**151i** also proved to be suitable electrophiles when mixed with the secondary alkyl iodide (*S*)-**142m** yielding, under standard conditions, the desired amide (2'*S*,3*R*)-**152ad** in 72% yield with dr = 2:98 and 98% *ee*. Moreover, the optically enriched iodides (*R*)- and (*S*)-**142n** underwent the ISQ reaction with dicyclopropyl ketone (**151a**), di-*iso*-propyl ketone (**151v**) or dicyclohexyl ketone (**151w**, at −40 °C) providing the alcohols **152ae-ag** in up to 78% yield and up to 96% ee.

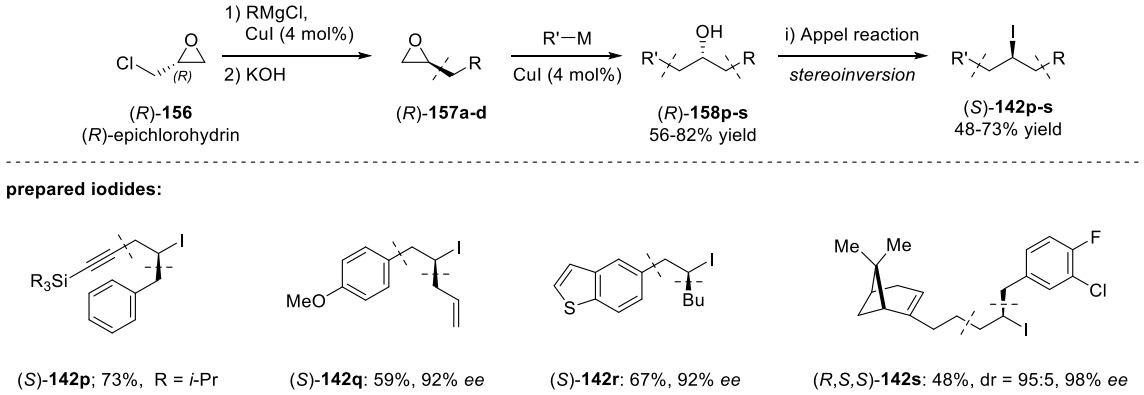
[118] D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155–4156.





Scheme 47. Prepared chiral products **152s-aj** by *in situ* quench (ISQ) of optically enriched secondary alkyl iodides (**142**) in the presence of electrophiles (**151**) using *t*-BuLi. Yields refer to isolated analytically pure products. The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis. The diastereomeric ratio (dr = *syn*/*anti*) was determined *via* GC- or NMR-analysis. [a] The reaction was performed at −40 °C using 3.0 equiv of electrophile.

To our delight, chiral secondary alkyl iodides bearing sensitive functional groups like a nitrile ((*R*)- and (*S*)-**142o**) or an ester ((*R*)- and (*S*)-**142i**) were compatible with this method. Thus, the amides (2'*R*,3*R*)-**152ah** (75%, dr = 94:6, 96% *ee*) and (2'*R*,3*S*)-**152ah** (82%, dr = 8:92, 96% *ee*) as well as the alcohol (*S*)-**152ai** (49%, 95% *ee*) were isolated after ISQ-reaction using (*R*)- or (*S*)-**142o** and (*R*)-**151i** or (*S*)-**151i** as well as **151v**. Likewise, (*R*)- and (*S*)-**152aj** were obtained after reaction of the ester-containing alkyl iodide (*R*)- or (*S*)-**142i** with adamantanone (**151p**) after addition of *t*-BuLi in up to 53% yield and 94% *ee* at −40 °C. While the reaction proceeded smoothly with chiral iodides of type AlkCH(Me)I, we have also demonstrated that more substituted alkyl iodides may be used. The required alkyl iodides were prepared from commercially available (*R*)-epichlorohydrin ((*R*)-**156**) in a three step sequence (see Scheme 48).[119] Thus, (*R*)-**156** was treated with various Grignard reagents (RMgCl) in the presence of 4 mol% CuI[120] affording after treatment with KOH the chiral epoxides of type **157**. Another ring opening of **157** with Grignard reagents (R'MgCl) or alkynyllithiums in the presence of 4 mol% CuI provided the chiral alcohols of type **158** in 56-82% yield (over 3 steps). A stereoinvertive Appel reaction[121] afforded the desired secondary alkyl iodides (*S*)-**142p-s** in 48-73% yield and 92-98% *ee*.

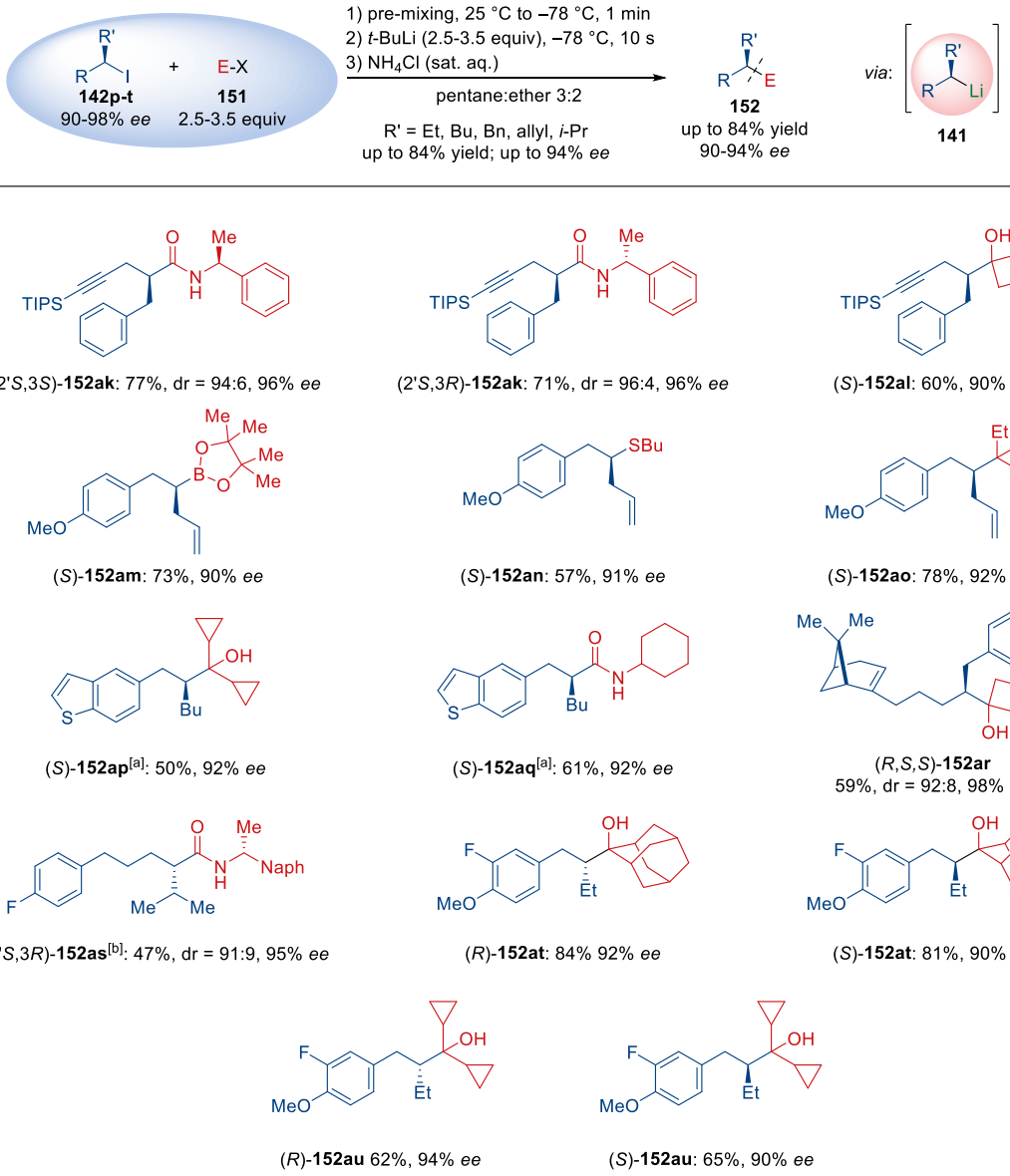


Scheme 48. Modular preparation of optically enriched secondary alkyl iodides (*S*)-**142p-s** from (*R*)-epichlorohydrin ((*R*)-**156**) *via* epoxide opening and closing sequences followed by stereoinvertive Appel reaction. i) (1.2 equiv PPh_3, 1.2 equiv I_2, 1.2 equiv NMI, −78 °C, 30 min).

[119] P. Gupta, P. Kumar, *Tetrahedron: Asymmetry* **2007**, *18*, 1688–1692.
[120] B. H. Lipshutz, S. Sengupta, *Org. React.* **1992**, *41*, 135–296.
[121] R. Appel, *Angew. Chem. Int. Ed.* **1975**, *14*, 801–811.

With these chiral secondary alkyl iodides in hand, we performed several ISQ-reactions (see Scheme 49). Thus, the chiral homobenzylic secondary alkyl iodide (*S*)-**142p** smoothly underwent the ISQ-reaction in the presence of the isocyanates (*R*)-**151i** or (*S*)-**151i** providing the diastereomerically and enantiomerically enriched amides (2'*S*,3*R*)-**152ak** in 71% with dr = 94:6 and 96% *ee* as well as (2'*S*,3*R*)-**152s** in 77%, dr = 4:96, 96% *ee*. Furthermore, ISQ of (*S*)-**142p** with cyclobutanone (**151x**) at −78 °C gave the chiral alcohol (*S*)-**152al** in 60% yield and 90% *ee*. Also, treating the allyl substituted iodide (*S*)-**142q** with *t*-BuLi in the presence of methoxyboronic acid pinacol ester (**151q**), BuSSBu (**151t**) or diethyl ketone (**151m**), led to the expected optically enriched boronic acid ester (*S*)-**152am** (73%, 90% *ee*), to the sulfide (*S*)-**152an** (57%, 91% *ee*) or the alcohol (*S*)-**152ao** (78%, 92% *ee*). In the case of the chiral secondary alkyl iodide (*S*)-**142r,** bearing a butyl substitutent, we observed that dropwise addition of 2.5 equiv of *t*-BuLi led to a low conversion of this iodide to the corresponding alkyllithium reagent. However, raising the amounts of *t*-BuLi and electrophile to 3.5 equiv led to the expected alcohol (*S*)-**152ap** and amide (*S*)-**152aq** in up to 61% yield with full stereoretention (92% *ee*) when using dicyclopropyl ketone (**151a**) or cyclohexyl isocyanate (**151h**) as electrophiles. Also the terpene derived optically enriched iodide (*R*,*S*,*S*)-**142s** underwent the ISQ-reaction providing after mixing with cyclobutanone (**151x**) and addition of *t*-BuLi the desired alcohol (*R*,*S*,*S*)-**152ar** in 59% yield with dr = 92:8 and 98% *ee*. Even the sterically demanding secondary alkyl iodide (*S*)-**142t**, bearing an *iso*-propyl substituent,[122] reacted with (*R*)-(−)-1-(1-naphthyl)ethyl isocyanate (**151j**) with high stereoretention providing (2'*S*,3*R*)-**152as** in 47% yield and a of dr = 91:9 and 95% *ee*. Moreover, the optically enriched alcohols (*R*)- and (*S*)-**152at** as well as (*R*)- and (*S*)-**152au** were isolated after this ISQ-reaction from (*R*)- and (*S*)-**142u** in the presence of either adamantanone (**151p**) or dicyclopropyl ketone (**151a**) in up to 84% yield and up to 94% *ee*.

[122] H. Hattori, J. Roesslein, P. Caspers, K. Zerbe, H. Miyatake-Ondozabal, D. Ritz, G. Rueedi, K. Gademann, *Angew. Chem. Int. Ed.* **2018**, *57*, 11020–11024.



Scheme 49. Chiral products **152** prepared by *in situ* quench (ISQ) of functionalized optically enriched secondary alkyl iodides **142p-t** in the presence of electrophiles (**151**) using *t*-BuLi at −78 °C. Yields refer to isolated analytically pure products. The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis. The diastereomeric ratio (dr = *syn*/*anti*) was determined *via* GC- or NMR-analysis. [a] The reaction was performed using 3.5 equiv of *t*-BuLi and 3.5 equiv of electrophile; [b] Naph = naphthyl.

3.4 ISQ-Reactions of Chiral Secondary Alkyllithiums in Continuous Flow

Although these ISQ-procedures provided various highly enantioenriched products, a scale-up above 0.3 mmol was complicated and gave erratic results. Recently, the use of continuous-flow setups and microreactors has led to a revolution in the field of thermally labile organometallics, and pioneering works by Ley,[123] Yoshida,[124] Organ,[125] and others[126] have popularized the performance of reactions involving highly reactive organometallics in continuous flow.

Therefore, we envisioned that this ISQ-reaction might benefit from the fast mixing properties and the efficient heat transfer of micro reactor technology. We utilized a commercial two pump system[127] in which the afforehand prepared solution of *t*-BuLi (0.20 M in hexane) and the premixed solution of alkyl iodides of type **142** (0.08 M) and electrophiles of type **151** (0.20 M in hexane:Et_2O = 2:1) were passed through precooling loops (2.0 mL) using two peristaltic pumps. The streams were combined in a T-shaped mixer and pumped through a coil reactor (1.0 mL). Upon reaching steady state, the reaction mixture was collected in a flask charged with *sat*. *aq*. NH_4Cl.

[123] a) A. Polyzos, M. O'Brien, T. P. Petersen, I. R. Baxendale, S. V. Ley, *Angew. Chem. Int. Ed.* **2011**, *50*, 1190–1193; b) D. L. Brown, M. Baumann, B. H. Harji, I. R. Baxendale, S. V. Ley, *Org. Lett.* **2011**, *13*, 3312–3315; c) T. Brodmann, P. Kroos, A. Metzger, P. Knochel, S. V. Ley, *Org. Process Res. Dev.* **2012**, *16*, 1102–1113; d) S. V. Ley, D. E. Fitzpatrick, R. J. Ingham, R. M. Myers, *Angew. Chem. Int. Ed.* **2015**, *54*, 3449–3464.

[124] a) H. Wakami, J.-i. Yoshida, *Org. Process Res. Dev.* **2005**, *9*, 787–791; b) J.-i. Yoshida, *Chem. Rec.* **2010**, *10*, 332; c) H. Kim, A. Nagaki, J.-i. Yoshida, *Nat. Commun.* **2011**, *2*, 264; d) H. Kim, Y. Yonekura, J.-i. Yoshida, *Angew. Chem. Int. Ed.* **2018**, *57*, 4063–4066.

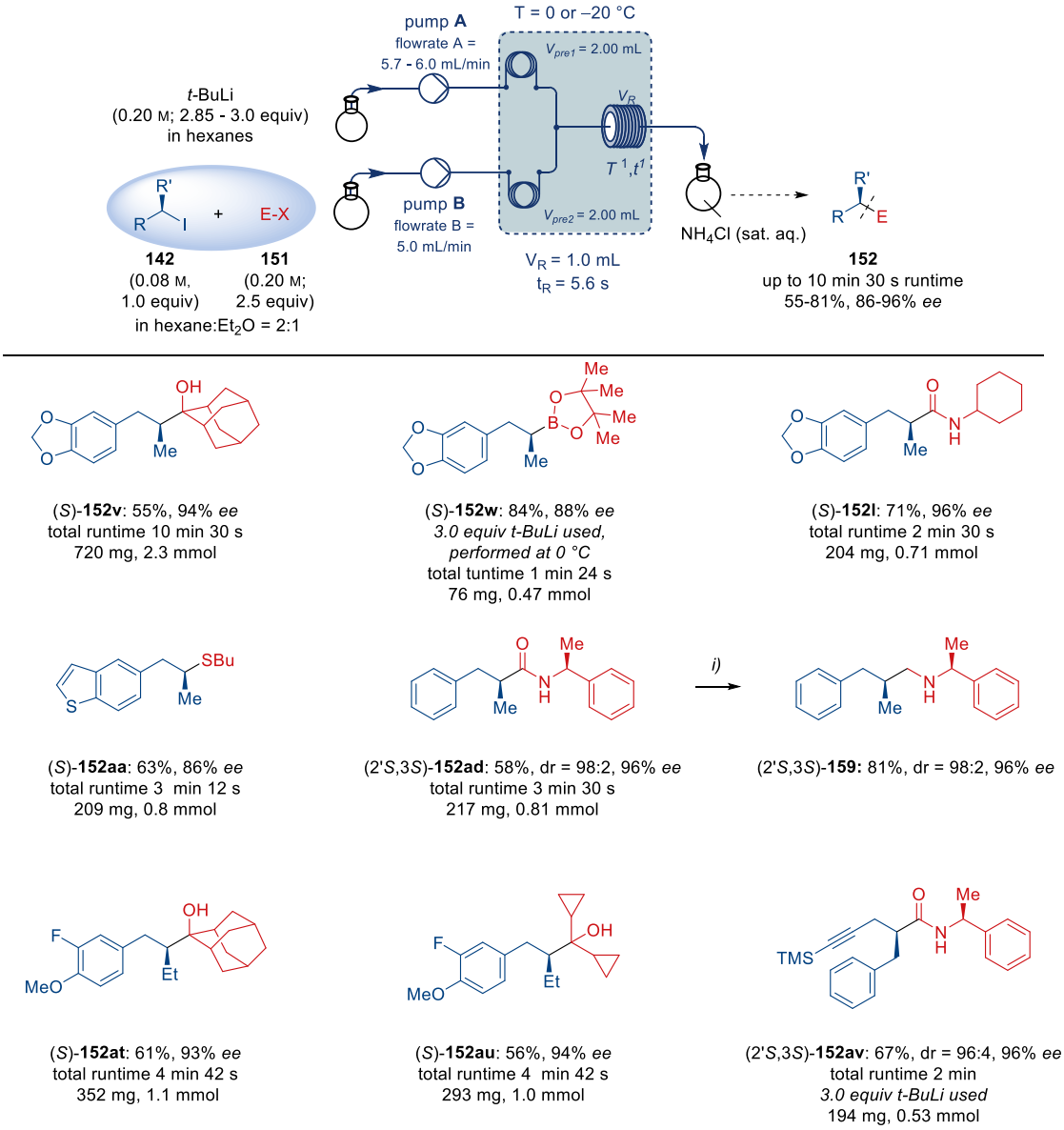
[125] a) E. Comer, M. G. Organ, *J. Am. Chem. Soc.* **2005**, *127*, 8160–8167; b) G. A. Price, A. R. Bogdan, A. L. Aguirre, T. Iwai, S. W. Djuric, M. G. Organ, *Catal. Sci. Technol.* **2016**, *6*, 4733–4742; c) G. A. Price, A. Hassan, N. Chandrasoma, A. R. Bogdan, S. W. Djuric, M. G. Organ, *Angew. Chem. Int. Ed.* **2017**, *56*, 13347–13350.

[126] a) D. Cantillo, C. O. Kappe, *ChemCatChem* **2014**, *6*, 3286–3305; b) M. Movsisyan, E. I. P. Delbeke, J. K. E. T. Berton, C. Battilocchio, S. V. Ley, C. V. Stevens, *Chem. Soc. Rev.* **2016**, *45*, 4892–4928; c) L. Degennaro, C. Carlucci, S. De Angelis, R. Luisi, *J. Flow Chem.* **2016**, *6*, 136–166; d) N. Weidmann, M. Ketels, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 10748–10751; e) M. Colella, A. Nagaki, R. Luisi, *Chem. Eur. J.* **2020**, *26*, 19–32; f) N. Weidmann, J. H. Harenberg, P. Knochel, *Org. Lett.* **2020**, *22*, 5895–5899; g) J. H. Harenberg, N. Weidmann, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2021**, *60*, 731–735; h) J. H. Harenberg, N. Weidmann, A. J. Wiegand, C. A. Hoefer, R. R. Annapureddy, P. Knochel, *Angew. Chem. Int. Ed.* **2021**, *60*, 14296–14301; i) J. H. Harenberg, R. R. Annapureddy, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2022**, e202203807.

[127] For details see Experimental part.

After a short optimization, based on the previously found conditions, we observed that the continuous flow set-up allowed to raise the reaction temperature at which the ISQ was performed to −20 °C. Best results were obtained when pumping the premixed alkyl iodide and electrophile solution at a flowrate of 5.0 mL/min. Whereas the *t*-BuLi solution was pumped at a flowrate of 5.7 to 6.0 mL/min depending on the substrate (see Scheme 50). Therefore, the residence time in the coil reactor varied between 5.5 to 5.6 s. Thus, also moderately soluble electrophiles like adamantanone (**151p**) in the presence of the secondary alkyl iodide (*S*)-**142k** were employed and after mixing with *t*-BuLi the corresponding alcohol (*S*)-**152v** was isolated in 55% with 94% *ee*. No clogging of the reactor was observed and the reaction mixture was collected for a total of 10 min 30 s, resulting in a 40-fold scale-up in comparison to the batch conditions. The high optical purity of (*S*)-**152v** indicated that the elevated temperatures do not lead to any significant epimerization of the intermediate alkyllithium (**141k**). Furthermore, X-ray diffraction analysis of (*S*)-**4d** using Flack parameter method[113] confirmed the (*S*)-configuration and an overall stereoretention of our method. When (*S*)-**142k** was mixed with other electrophiles like boronic acid ester **151q** the temperature could be increased even further to 0 °C preventing precipitation in the precooling loop. Under these conditions, the optical purity decreased only slightly and (*S*)-**152w** was obtained in 84% isolated yield and 88% *ee*. Also, (*S*)-**142k** was treated with cyclohexyl isocyanate (**151h**) upon addition of *t*-BuLi in and after collecting for 2 min 30 s the desired amide (*S*)-**152l** was isolated in 71% yield and 96% *ee*. The reactions of (*S*)-**142l** in the presence of BuSSBu (**151t**) or (*S*)-**142m**, which was mixed with the isocyanate (*S*)-**151i,** and *t*-BuLi provided the sulfide (*S*)-**152aa** (63%, 86% *ee*) or the amide (2'*S*,3*S*)-**152ad** (58%, dr = 98:2, 96% *ee*). Furthermore, the optically enriched iodides (*S*)-**142u** and (*S*)-**142v** were also compatible with this continuous flow set-up and the scale-up of their reactions with either adamantanone (**151p**), dicyclopropyl ketone (**151a**) as well as (*S*)-(−)-1-phenylethyl isocyanate (*S*)-**151i** gave (*S*)-**152at**, (*S*)-**152au** and (2'*S*,3*S*)-**152av** in up to 67% yield with up to dr = 96:4 and up to 96% *ee*. To demonstrate the value of our obtained products, we aimed to prepare β-chiral secondary amines, a valuable motif in drug discovery and agrochemical products.[128] Thus, we treated the optically enriched amide (2'*S*,3*S*)-**152ad** with a solution of lithium aluminum hydride in THF,[129] affording the desired amines (2'*S*,3*S*)-**159** in up to 81% yield without loss of optical purity.

[128] P. Matzel, S. Wenske, S. Merdivan, S. Günther, M. Höhne, *ChemCatChem* **2019**, *11*, 4281–4285.
[129] B. M. Trost, A. Maruniak, *Angew. Chem. Int. Ed.* **2013**, *52*, 6262–6264.



Scheme 50. Preparation of optically enriched products of type **152** *via in situ* quench of optically enriched secondary alkyl iodides (**142**) in the presence of electrophiles (**151**) using *t*-BuLi in continuous flow. Yields refer to isolated analytically pure products. The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis. The diastereomeric ratio (dr = *syn*/*anti*) was determined *via* GC- or NMR-analysis. i) $LiAlH_4$ (3.0 equiv), 0 °C to 60 °C, 14 h.

4 Exploiting Coordination Effects for the Regioselective Zincation of Diazines Using TMPZnX·LiX (X = Cl, Br)

4.1 Introduction

N-heterocycles are among the most valuable synthetic scaffolds for pharmaceutical and agrochemical research.[130] Their general functionalization has been thoroughly studied[131] and various cross-couplings[132] or metalations of these *N*-heterocycles have been reported for such purpose.[8, 22, 32, 96c, 133] A powerful tool for the preparation of *N*-heteroaryl organometallics is the directed C-H metalation using sterically hindered, non-nucleophilic metallic amide bases.[134] Zinc and magnesium derived TMP-bases (TMP = 2,2,6,6-tetramethylpiperidyl) have recently emerged as useful reagents for the preparation of highly functionalized *N*-heterocycles.[40a-c, 42a, 44, 45c-d, 135] Diazine building blocks are of special importance for the pharmaceutical industry.[136]

[130] a) R. D. Taylor, M. MacCoss, A. D. G. Lawson, *J. Med. Chem.* **2014**, 57, 5845–5859; b) D. C. Blakemore, L. Castro, I. Churcher, D. C. Rees, A. W. Thomas, D. M. Wilson, A. Wood, *Nature Chem.* **2018**, *10*, 383–394.

[131] a) K. R. Campos, *Chem. Soc. Rev.* **2007**, *36*, 1069–1084; b) W. Guo, J. E. Gómez, A. Cristòfol, J. Xie, A. W. Kleij, *Angew. Chem. Int. Ed.* **2018**, *57*, 13735–13747; c) G-Q. Xu, J-T. Xu, Z-T. Feng, H. Liang, Z-Y. Wang, Y. Qin, P-F. Xu, *Angew. Chem. Int. Ed.* **2018**, *57*, 5110–5114; d) J. Diesel, A. M. Finogenova, N. Cramer, *J. Am. Chem. Soc*. **2018**, *140*, 4489–4493; e) M. Balkenhohl, B. Heinz, T. Abegg, P. Knochel, *Org. Lett.* **2018**, *20*, 8057–8060; f) N. Zeidan, T. Beisel, R. Ross, M. Lautens, *Org. Lett.* **2018**, *20*, 7332–7335; g) H. Wang, Y. Li, Q. Lu, M. Yu, X. Bai, S. Wang, H. Cong, H. Zhang, A. Lei, *ACS Catal.* **2019**, *9*, 1888–1894; h) A. Grozavu, H. B. Hepburn, P. J. Smith, H. K. Poukuchi, P. J. Lindsay-Scott, T. J. Donohoe, *Nature Chem.* **2019**, *11*, 242–247; i) Z. Yang, M. Möller, R. M. Koenigs, *Angew. Chem. Int. Ed*. **2020**, *59*, 5572–5576.

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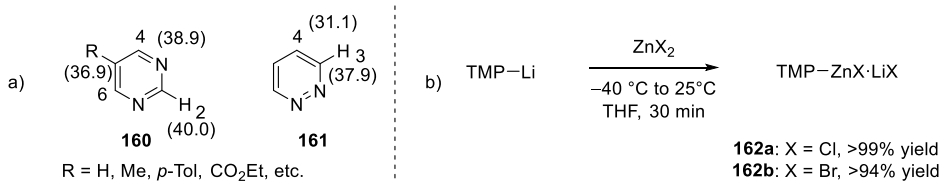
[135] a) R. E. Mulvey, F. Mongin, M. Uchiyama, Y. Kondo, *Angew. Chem. Int. Ed.* **2007**, *46*, 3802-3824; b) G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed*. **2007**, *46*, 7681–7684; c) P. Fleming, D. F. O'Shea, *J. Am. Chem. Soc.* **2011**, *133*, 1698–1701.

[136] a) F. Chevallier, F. Mongin, *Chem. Soc. Rev.* **2008**, *37*, 595-609; b) E. Vitaku, D. T. Smith, J. T. Njardarson, *J. Med. Chem.* **2014**, 57, 10257–10274.

Thus, the metalation of substituted pyrimidines of type **160** has been studied by using TMPLi and TMPMgCl·LiCl and proceeded with good regioselectivity at the positions 4–6.[137] However, their metalation at the 2-position is poorly investigated and was only achieved in the presence of strong Lewis acid additives.[45b] Furthermore, the regioselective functionalization of non-substituted pyrimidine (**160a**) and pyridazine (**161**; Scheme 51a) represents a major challenge since it lacks directing groups generally needed for regioselective control.[138] The addition of appropriate Lewis acids represents a well-established method for improving regio- and stereoselectivies.[139] $BF_3{\cdot}OEt_2$ proved particularly effective allowing high metalation regioselectivities by coordinating to the nitrogen lone pair *via* the formation of frustrated Lewis-pairs[140] with various metallic amides.[45a] However, this approach has several drawbacks such as the formation of mixed boron intermediates of moderate reactivity[45c] as well as the need for stoichiometric amounts of this strong and hazardous Lewis acid. Therefore, a mild, practical and regioselective functionalization of *N*-heterocycles of type **160** and **161** is highly desirable.



Scheme 51. a) Diazines such as pyrimidines (**160**) and pyridazine (**161**) and their respective pka values[141]; b) Preparation of the TMP-bases TMPZnCl·LiCl (**162a**) and TMPZnBr·LiBr (**162b**).

[137] a) A. Wada, J. Yamamoto, S. Kanatomo, *Heterocycles* **1987**, *26*, 585–589; b) A. Turck, N. Plé, G. Quéguiner, *Heterocycles* **1994**, *37*, 2149–2172; c) M. Mosrin, P. Knochel, *Org. Lett.* **2008**, *10*, 2497–2500; d) M. Mosrin, N. Boudet, P. Knochel, *Org. Biomol. Chem*. **2008**, *6*, 3237–3239; e) M. Mosrin, M. Petrera, P. Knochel, *Synthesis* **2008**, *22*, 3697–3702; f) M. Mosrin, P. Knochel, *Chem. Eur. J*. **2009**, *15*, 1468–1477; g) T. A. Moss, B. R. Hayter, I. A. Hollingsworth, T. Nowak, *Synlett* **2012**, *23*, 2408–2412; h) M. Balkenhohl, P. Knochel, *SynOpen* **2018**, *2*, 78–95.

[138] a) N. Plé, A. Turck, K. Couture, G. Quéguiner, *J. Org. Chem.* **1995**, *60*, 3781–3786; b) A. Seggio, F. Chevallier, M. Vaultier, F. Mongin, *J. Org. Chem.* **2007**, *72*, 6602–6605.

[139] a) B. Maji, M. Baidya, H. Yamamoto, *Chem. Sci.* **2014**, *5*, 3941–3945; b) L. Yin, H. Takada, S. Lin, N. Kumagai, M. Shibasaki, *Angew. Chem. Int. Ed*. **2014**, *53*, 5327–5331; c) C. Wang, H. Yamamoto, *Angew. Chem. Int. Ed*. **2015**, *54*, 8760–8763; d) W. Gati, H. Yamamoto, *Acc. Chem. Res.* **2016**, *49*, 1757–1768; e) S. Bhadra, H. Yamamoto, *Chem. Rev.* **2018**, *118*, 3391–3446.; f) W. Muramatsu, T. Hattori, H. Yamamoto, *J. Am. Chem. Soc.* **2019**, *141*, 12288–12295.

[140] a) G. C. Welch, R. R. San Juan, J. D. Masuda, D. W. Stephan, *Science* **2006**, *314*, 1124–1126; b) D. W. Stephan, G. Erker, *Angew. Chem. Int. Ed.* **2010**, *49*, 46–76; c) M. Bakos, Á. Gyömöre, A. Domján, T. Soós, *Angew. Chem. Int. Ed.* **2017**, *56*, 5217–5221.

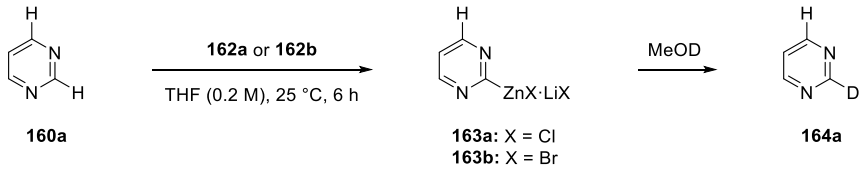
[141] K. Shen, Y. Fu, J-N. Li, L. Liu, Q-X. Guo, *Tetrahedron* **2007**, *63*, 1658–1576.

Since *alpha*-metalated *N*-heterocyclic intermediates are thermally fragile when generated using polar bases such as lithium amides,[136a] we envisioned the use of TMPZnCl·LiCl (**162a**) or TMPZnBr·LiBr (**162b**, Scheme 51b) as possible metalating systems that would allow direct zincation of these sensitive substrates in the presence or absence of additional Lewis acids. Herein, we report the practical and effective zincation of various functionalized and non-substituted pyrimidines (**160**) and pyridazine (**161**) using TMPZnCl·LiCl (**162a**). Reactions showed an excellent regioselective control enabling the C2 and C3 zincation of pyrimidines and pyridazine respectively. The synthetic potential and versatility of this approach was demonstrated by electrophilic interception furnishing a wide range of newly functionalized pyrimidines and pyridazines. These studies have revealed an interesting effect in the reactivity of these zincated species on the addition of metal salts. Combining NMR reaction monitoring studies with X-ray crystallographic studies has shed some light on the constitution of organometallic species participating in these transformations and on the possible origins behind the observed special regioselectivities.

4.2 Optimization of Reaction Conditions

In preliminary experiments, we have investigated the regioselective zincation of pyrimidine (**160a**) at position 2 with the TMP-zinc bases **162a** or **162b** leading to the zincated pyrimidine **162a** or **162b** (see Table 6). Thus, treatment of a 0.2 M solution of pyrimidine (**160a**) with TMPZnCl·LiCl (**162a,** 1.05 equiv) led to a highly regioselective zincation at 2-position (>99:1) in 34% ^{1}H-NMR yield as determined after deuterolysis (entry 1).[142] This conversion was improved by increasing the amount of base **162a**. Thus, using 1.25 equiv of **162a** provided, after deuterolysis, the deuterated pyrimidine **164a** in 74% yield with the same excellent regioselectivity (entry 2). Further increase of TMPZnCl·LiCl (**162a**) to 1.50 equiv or 1.75 equiv led to yields of up to 98% (entries 3 and 4). Using 2.0 equiv of **162a** gave a quantitative conversion, showing that **160a** may complex to **162a** (entry 5). Performing the metalation with the alternative bromide base TMPZnBr·LiBr (**162b**, 2.0 equiv) gave the same result after deuterolysis (entry 6). Despite the excess of base, no evidence of dizincation of **160a** was found.

Table 6. Zincation of pyrimidine (**160a**) with TMP-bases **162a** or **162b** furnishing 2-pyrimidylzinc halides (**163a** or **163b**) and subsequent deuterolysis using MeOD leading to the deuterated pyrimidine **164a**.



160a | **163a:** X = Cl, **163b:** X = Br | **164a**

Entry	TMP-base	Equiv	Yield[a]
1	TMPZnCl·LiCl (**162a**)	1.05	34%
2	**162a**	1.25	74%
3	**162a**	1.50	90%
4	**162a**	1.75	98%
5	**162a**	2.0	99%
6	TMPZnBr·LiBr (**162b**)	2.0	99%

[a] Yields are ^{1}H-NMR-yields using trichloroethylene as internal standard.

[142] An aliquot of the zincation experiment was quenched with MeOD and analyzed by ^{1}H-NMR using trichloroethylene as internal standard. For details see Supporting Information.

The regioselectivity, high yield and mild conditions observed for these reactions contrast with the inefficiency of TMPLi to metalate **160a,** yielding only dimer 6,6'-bipyrimidine even when working under extreme cryogenic temperatures (−100 °C).[141a] Furthermore, these conditions are also superior to that reported using TMPLi in combination with $Ga(CH_2SiMe_3)_3$. By using a trans-metal trapping (*TMT*) approach,[143] C4-gallation was observed in 59% yield, leaving the C2 position untouched.[144] Interestingly, the same C4-regioselectivity was found by Mongin for zincation of **160a** using an *in situ* mixture of $ZnCl_2$·TMEDA (0.5 equiv) and LiTMP (1.5 equiv).[138b] Also, when **160a** reacted with TMPMgCl·LiCl at −20 °C, formation of C4-magnesiated pyrimidine was observed in modest 28% yield, demonstrating the key role of zinc in favoring the C2-metalation.

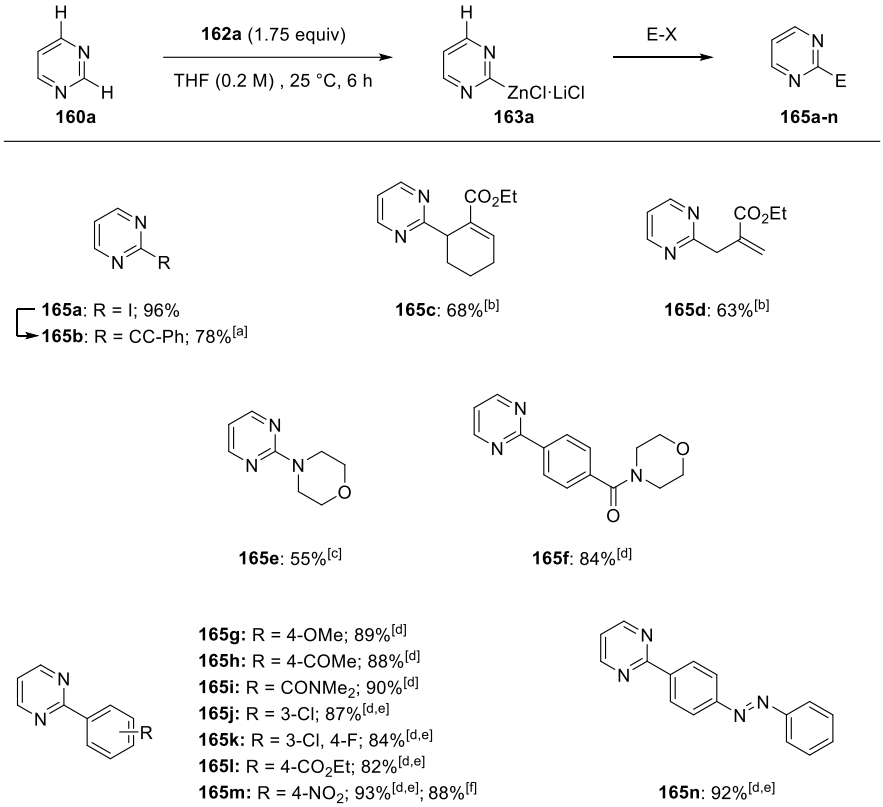
[143] a) M. Uzelac, R. E. Mulvey, *Chem. Eur. J,* **2018**, *24*, 7786–7793; b) M. Uzelac, A. R. Kennedy, E. Hevia, *Inorg. Chem.* **2017**, *56*, 8615–8626.

[144] M. Uzelac, A. R. Kennedy, E. Hevia, R. E. Mulvey, *Angew. Chem. Int. Ed.* **2016**, *55*, 13147–13150.

4.3 Zincations of Pyrimidines

With these results in hand, we have performed the metalation of pyrimidine (**160a**) with **162a** (1.75 equiv) and have examined the scope of the trapping of resulting 2-pyrimidylzinc chloride (**163a**; Scheme 52). Therefore, quenching **163a** with iodine (1.8 equiv) led to 2-iodopyrimidine (**165a**) in 96% yield. This useful iodide[145] further reacted with phenylacetylene in a copper-catalyzed Sonogashira cross-coupling providing the alkyne **165b** in 78% yield. Transmetalation of **165a** with CuCN·2LiCl (1.0 equiv) followed by addition of allylic bromides such as ethyl 2-(bromomethyl)acrylate or ethyl 6-bromocyclohex-1-ene-1-carboxylate[146] furnished the corresponding enoates **165c-d** in 63-68% yield. Furthermore, a copper-catalyzed electrophilic amination[110] with morpholino benzoate yielded the tertiary amine **165e** in 55% yield. Several palladium-catalyzed cross-coupling reactions were performed with 6 mol% of tri(2-furyl)phosphine (tfp)[147] in the presence of 3 mol% $Pd(dba)_2$ (dba = bis(dibenzylidenacetone) affording the arylated products **165f-n** in 82-93% yield. A range of electron-rich and electron-poor aryl iodides containing sensitive functionalities including an ester, an amide and a nitro group were well tolerated in these reactions. Whereas the Negishi cross-coupling was typically complete within 12-36 h (**165f-i**), we noticed that very long reaction times (up to 96 h) were required for very electron-poor aryl iodides. Therefore, we have examined the separate addition of $ZnCl_2$ and $MgBr_2$ salts, after the metalation, in order to modify the constitution of the organometallic intermediate and provide a species more amenable to transmetalation to ArPdX that would enhance the cross-coupling rate.[148] To our delight, the addition of $ZnCl_2$ (1.0 equiv) allowed to reach full conversion within 12 h in the case of these aryl iodides leading to the pyrimidines **165j-n**.

[145] a) G. Vlád, I. T. Horvath, *J. Org. Chem.* **2002**, *67*, 6550–6552; b) N. Weidmann, R. H. Nishimura, J. H. Harenberg, P. Knochel, *Synthesis* **2021**, *53*, 557–568.
[146] J-B. Langlois, A. Alexakis, *Adv. Synth. Catal*. **2010**, *352*, 447–457.
[147] V. Farina, e-EROS: *Encyclopedia for Reagents in Organic Synthesis* **2002**, doi: 10.1002/047084289X.rn00126.
[148] a) P. Eckert, M. G. Organ, *Chem. Eur. J.* **2019**, *25*, 15751–15754; b) P. Eckert, S. Sharif, M. G. Organ, *Angew. Chem. Int. Ed.* **2021**, *60*, 12224–12241.



Scheme 52. Zincation of pyrimidine (**160a**) and quenching with various electrophiles. [a] **165a**, phenylacetylene (1.3 equiv), CuI (4 mol%), NEt_3 (1.0 mL), 25 °C, 2 h; [b] CuCN·2LiCl (1.0 equiv), allyl bromides (1.5 equiv), 0 °C to 25 °C, 14 h; [c] $BzONR_2$ (NR_2 = *N*-morpholino; 0.8 equiv), $CuCl_2$ (5 mol%), 25 °C, 14 h; [d] Aryl iodide (0.8 equiv), $Pd(dba)_2$ (3 mol%), tfp (6 mol%), 25 °C, 14-30 h; [e] Extra 1.0 equiv of $ZnCl_2$ added; [f] Reaction was performed on 5.0 mmol scale.

Next, we extended the scope of this zincation to the functionalized pyrimidines **160b-f** (Scheme 53). Thus, 5-*p*-tolyl-substituted pyrimidine (**160b**)[149] or 5-methylpyrimidine (**160c**) were smoothly zincated under related conditions (1.75 equiv of TMPZnCl·LiCl (**162a**); 50 °C, 3 h in case of **160b** and 1.75 equiv of **162a**; 25 °C, 6 h for **160c**) providing **163c-d** in up to *ca.* 90% yield. Quenching with iodine or palladium-catalyzed cross-couplings with functionalized aryl iodides furnished the 2,5-disubstituted pyrimidines **166a-j** in 70-93% yield. Performing a cobalt-catalyzed electrophilic amination[109e-f] gave the aminated pyrimidine **166k** in 61% yield. Similarly, ethyl pyrimidine-5-carboxylate (**160c**) was metalated using **162a** (1.75 equiv) for 1 h at 60 °C with a regioselectivity of *ca.* 96:4. Iodolysis or palladium-catalyzed cross-coupling reactions with aryl iodides provided the desired functionalized pyrimidines **166l-o** in 64-69% yield, which were isolated as single regioisomers. Using the standard conditions (**162a**, 1.75 equiv, 25 °C, 6 h) developed for pyrimidine (**160a**), we have zincated the silyl-protected fenarimol[150] derivative **160e**. Quenching with iodine or performing a copper-catalyzed allylation gave the corresponding pyrimidines **166p** and **166q** in 61-74% yield. Also, 5-(1,3-dioxolan-2-yl)pyrimidine[151] (**160f**) was zincated using **162a** (1.75 equiv, 50 °C, 2h) in *ca.* 80% yield and a regioselectivity of 93:7. Iodination, Pd-catalyzed arylations and Co-catalyzed amination provided **166r-u** in up to 72% yield, which were isolated as single regioisomers.

[149] P. S. Gribanov, Y. D. Golenko, M. A. Topchiy, L. I. Minaeva, A. F. Asachenko, M. S. Nechaev, *Eur. J. Org. Chem.* **2018**, 120–125

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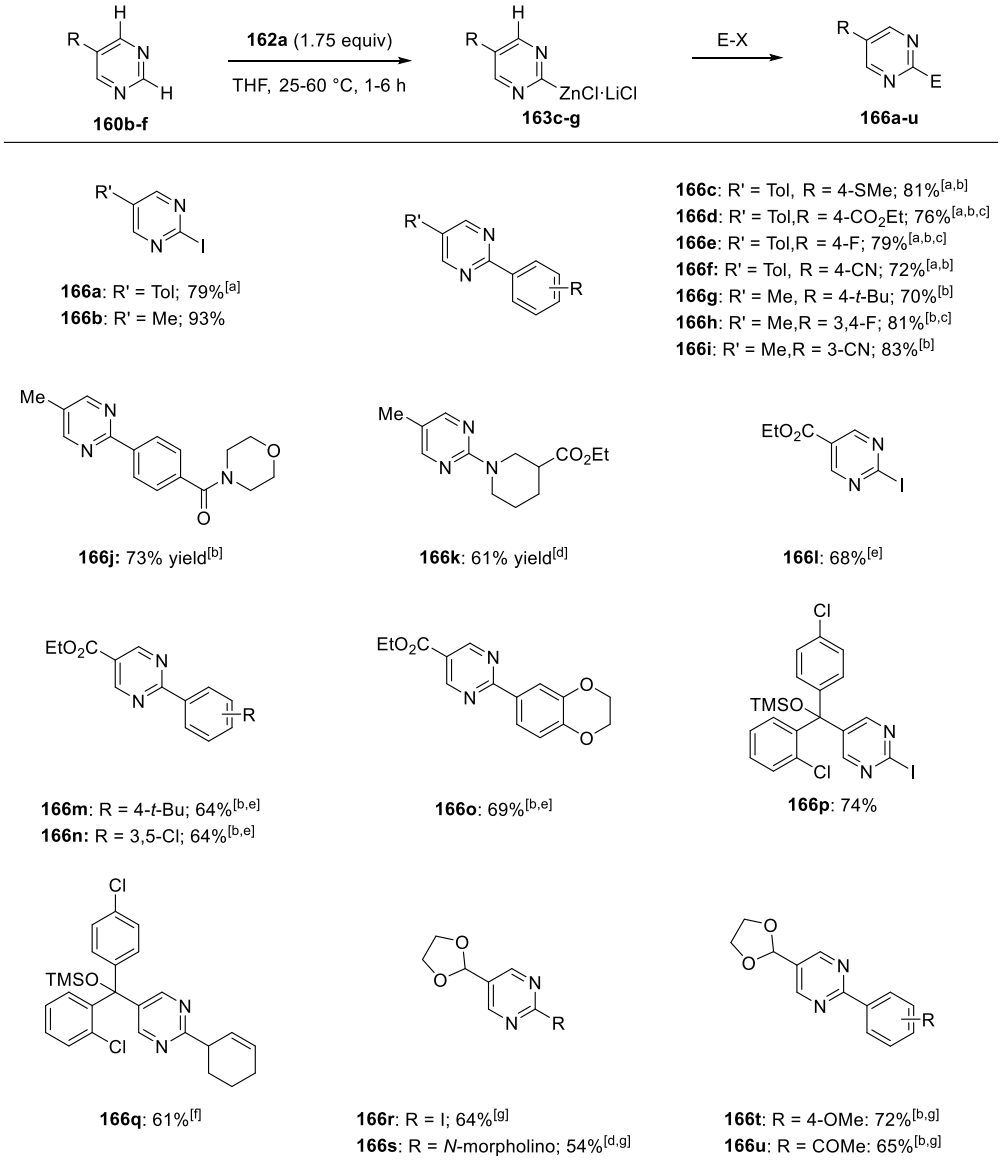
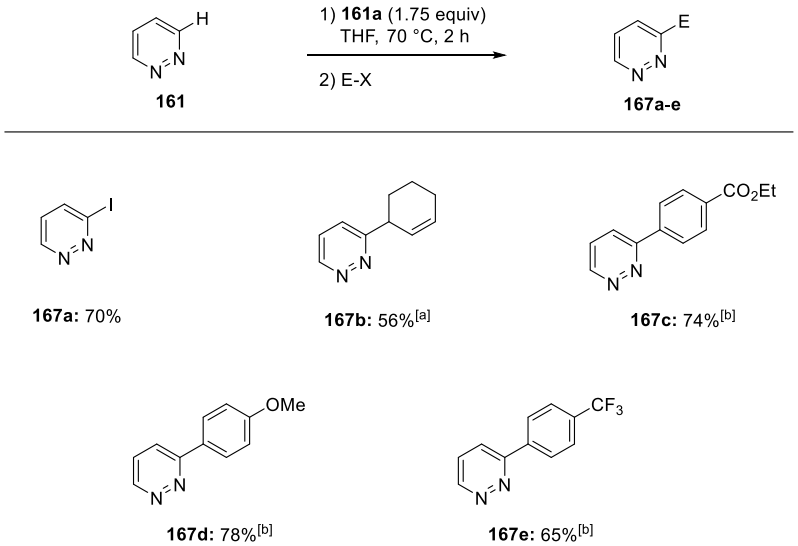
[151] O. V. Maltsev, R. Rausch, Z-J. Quan, L. Hintermann, *Eur. J. Org. Chem.* **2014**, 7426–7432.



Scheme 53. Zincation of pyrimidines **160b-f** and subsequent quenching with various electrophiles. [a] The metalation was performed at 50 °C for 3 h; [b] Aryl iodide (0.8 equiv), $Pd(dba)_2$ (3 mol%), tfp (6 mol%), 25 °C, 18 h; [c] Extra 1.0 equiv of $ZnCl_2$ was added; [d] *O*-hydroxylamine benzoate (0.8 equiv), $CoCl_2$ (5 mol%), TMEDA (10 mol%), 25 °C, 14 h; [e] Metalation was performed at 60 °C for 1 h; [f] CuCN·2LiCl (1.0 equiv), 3-bromocyclohex-1-ene (1.5 equiv), 0 °C to 25 °C, 14 h; [g] Metalation was performed at 60 °C for 2 h.

4.4 Zincations of Pyridazine

Next, we focused on the functionalization of pyridazine (**161**, Scheme 54). Its metalation remains a challenging task and could only be achieved in moderate yield or regioselectivity using excess of additives like $BF_3 \cdot OEt_2$ or TMEDA.[138a, 152] After several screening experiments, we found that the zincation of **161** in 3-position proceeded at 70 °C within 2 h, providing 3-iodopyridazine (**167a**) with a regioselectivity of 94:6 and 70% yield after iodolysis. Various quenching reactions such as a copper-catalyzed allylation or palladium-catalyzed arylations were performed providing **167b-e** in 56-78% yield as single regioisomers after isolation (>99% purity).



Scheme 54. Zincation of pyridazine (**161**) and quenching with various electrophiles. [a] CuCN·2LiCl (1.0 equiv), 3-bromocyclohex-1-ene (1.5 equiv), 0 °C to 25 °C, 14 h; [b] Aryl iodide (0.8 equiv), $Pd(dba)_2$ (3 mol%), tfp (6 mol%), 25 °C, 18 h.

[152] M. Balkenhohl, H. Jangra, T. Lenz, M. Ebeling, H. Zipse, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58*, 9244–9247.

4.5 Structural Investigations

Pleased by these findings, we subsequently took a closer look at the constitution of the zincated intermediates involved in these transformations, using base **162b** and pyrimidine (**160a**) or 5-methylpyrimidine (**160c**) as model substrates. The bimetallic base TMPZnBr·LiBr, prepared *in situ* in d_8-THF by combining equimolar amounts of TMPLi and $ZnBr_2$, was characterized by multinuclear (^1H, ^{13}C, and ^7Li) and DOSY NMR spectroscopy (see Experimental Part for details). The results supported formation of a lithium zincate which in solution is most likely to exist as solvent separated ion pair species of formula $[\{Li(d_8\text{-THF})_x\}^+\{ZnBr_2(TMP)(d_8\text{-THF})\}^-]$ (**I**) (see Experimental Part for details). Next, we monitored the reaction of **162b** with **160a** (Figure 4a) under the optimized reaction conditions by ^1H NMR (25 °C, d_8-THF, 1.75 equiv of **162b**). While the reaction occured almost instantaneously with full consumption of **160a** and appearance of TMP(H), the aromatic region of the spectrum showed a complex mixture of products (Figure 4b). Its composition did not change significantly over the time but proved to be concentration dependent (Figure 4b, 4c and Experimental Part). Remarkably, when this mixture was quenched with iodine, 2-iodopyrimidine (**165a**) was obtained as single product in 88% yield consistent with the one obtained carrying out the reaction *in situ*.

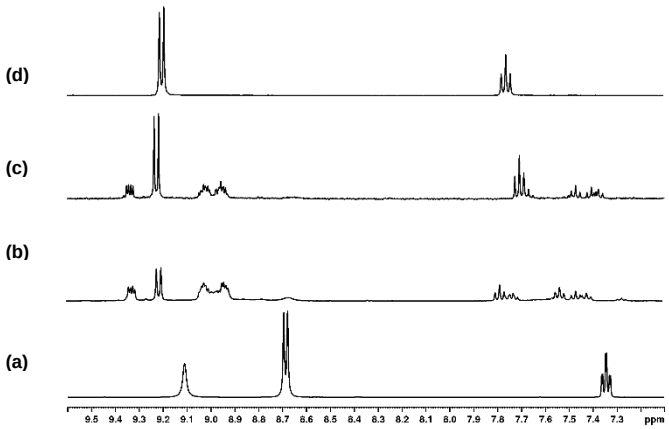
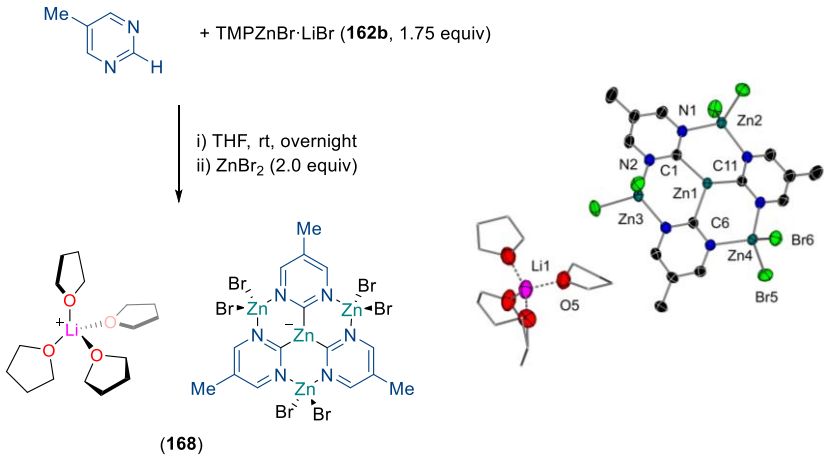


Figure 4. Aromatic region of ^1H NMR spectrum in d_8-THF of (a) pyrimidine; (b) pyrimidine + 1.75 equiv TMPZnBr·LiBr (0.13 M); (c) pyrimidine + 1.75 equiv TMPZnBr·LiBr (0.013 M); and d) pyrimidine + 1.75 equiv TMPZnBr·LiBr + 2 equiv $ZnBr_2$.

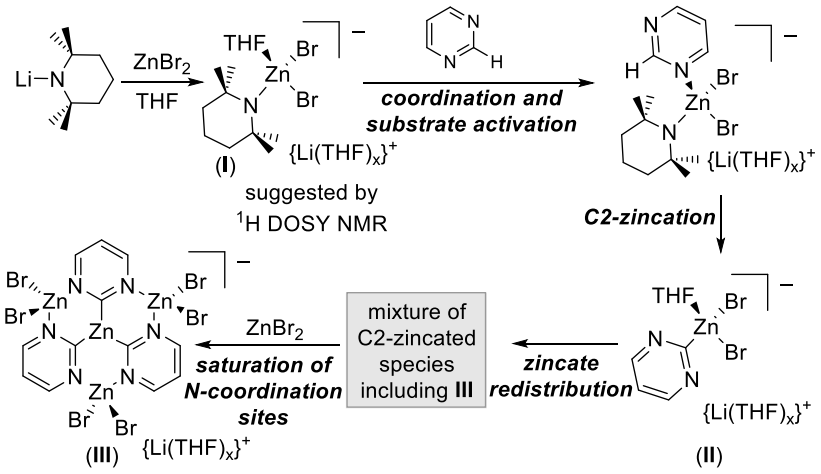
These findings are consistent with formation of several C2-zincated species present in solution and could be attributed to redistribution of initially formed heteroleptic zincate [{Li(THF)$_x$}$^+${ZnBr$_2$(HetAr)(THF)}$^-$] (**II**) into different species. While the composition of this mixture could not be confidently assigned, the possible formation of different mixed aggregates facilitated by the coordination of the strongly Lewis acidic zinc center to the *N* atoms of a pyrimidyl fragment of a neighboring unit[28] should be considered as a contributing factor to this solution complexity. Interestingly, when assessing the effect of inorganic salts to this complex mixture, we found that introducing stoichiometric amounts of LiBr or MgBr$_2$ did not have any significant effect. However, dosing increasing amounts of ZnBr$_2$ (up to 2 molar equivalents) influenced the constitution of this mixture showing eventual convergence of all species into a single C2-zincated product, displaying a doublet and a triplet at δ 9.20 and δ 7.77 ppm respectively (Figure 1d and Figure S14 in SI). The ^{13}C NMR spectrum is also consistent with the presence of a single species in solution, displaying a distinct signal at δ 209.5 ppm for the Zn-C2 unit. It should be noted that this species is present in solution in the reaction mixture from the beginning as a major product, especially under dilute reaction conditions (Figures 1b and 1c). The same behavior in solution was observed for 5-methylpyrimidine (see SI) and in this case the final product after addition of ZnBr$_2$ was isolated as the crystalline solid **168**, which was structurally authenticated (Scheme 55).



Scheme 55. Synthesis of [{Li(THF)$_4^+${Zn(Me-C$_4$H$_2$N$_2$)$_3$(ZnBr$_2$)$_3$}$^-$] (**168**). Molecular structure of **168** with displacement ellipsoids at 30% probability, all H atoms omitted and C-atoms in THF shown as wires for clarity. One THF molecule present in the unit cell has been removed for clarity.

Complex **168** is a solvent-separated ion pair. The lithium cation sits in a distorted tetrahedron of THF ligands. More significantly, the anion has a tetranuclear arrangement of zinc centers. Demonstrating that these reactions are genuine zincations, this anion comprises a central Zn center bonded to three C2-metallated 5-methylpyrimidyl fragments (mean Zn-C bond distance, 2.029 Å). Three equivalents of $ZnBr_2$ are also incorporated within the structure, each coordinated to two pyrimidyl nitrogen atoms closing three 6-membered {ZnCNZnNC} rings, which are fused by sharing a central Zn vertex (Zn1 in Figure 2). Collectively, this gives an eye-catching motif composed of six fused 6-membered rings. These findings also correlate with the reactivity studies assessing the ability of these systems in cross-coupling processes where significantly shorter reactions times were observed when using an excess of $ZnCl_2$ as an additive (*vide supra*). This can be attributed to the formation of a kinetically activated monomeric tris(aryl) zincate similar to **168**.

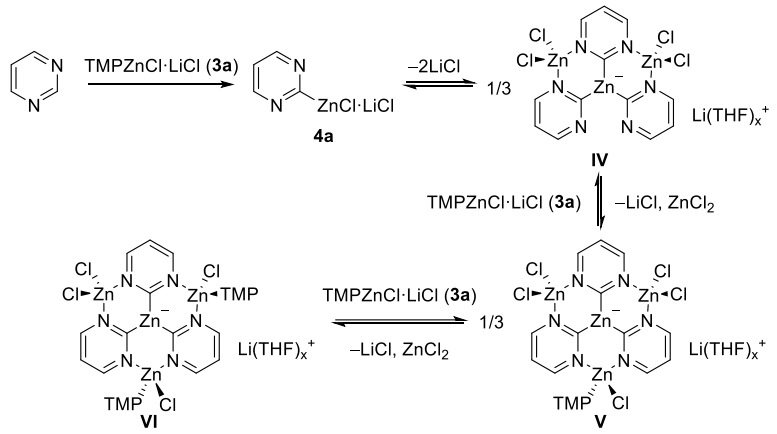
The notable effect of $ZnBr_2$ on favoring the formation of a single species by blocking the *N*-coordinating sites of the pyrimidyl fragments can also inform on the special regioselective control observed in these metalation processes. Thus, we envisoned initial coordination of **160a** to Zn in $[\{Li(THF)_x\}^+\{ZnBr_2(TMP)(THF)\}^-]$ (**I**) (Scheme 56) to be a key factor for activating the substrate and also directing the metalation regioselectively towards the C2 position. Furthermore, the fact that full conversion only occurs when an excess of base is employed led us to suspect that perhaps one equivalent of **162b** coordinates to each of the *N*s of **160a**, enhancing even more the acidity of the C2-position compared to the other positions (C4 and C6). These positions should be less acidified since only one adjacent Lewis acid coordinates. A proposed metalation intermediate $[\{Li(THF)_x\}^+\{ZnBr_2(C_4H_3N_2)(THF)\}^-]$ (**II**) may form, which in turn undergoes fast redistribution forming an intricate mixture of C2-zincated species including co-complex $[\{Li(THF)_4^+\{Zn(C_4H_3N_2)_3(ZnBr_2)_3\}^-]$ (**III**) (see Figure 1). Adding excess $ZnBr_2$ to these mixtures blocks the *N*-coordination sites on the pyrimidyl rings leading to the selective formation of **III** which was isolated and spectroscopically characterized.



Scheme 56. Metalation of pyrimidine triggered by substrate coordination to TMPZnBr·LiBr (**162b**).

Demonstrating the importance of substrate precoordination to the zinc base, $Zn(TMP)_2$ on its own was found to be incapable of metalating **160a**, which we attributed to the large steric encumbrance (as demonstrated by ^1H DOSY NMR studies, see SI). In contrast, reducing the steric space and increasing the Lewis acidity of the zinc center, we found that TMPZnBr allowed the effective C2 metalation of **160a** affording a white solid which was insoluble in THF (iodolysis of this suspension afforded 2-iodo pyrimidine in 92% yield). We also investigated the metalation of **160a** by forming first a coordination adduct with $ZnBr_2$ and reacting this complex with LiTMP (Scheme S2 in SI). Under these conditions, a mixture of 2 and 4-iodopyrimidine was observed (28% and 37% respectively) along with some other unidentified products. This illustrates the importance of using a zincating reagent to control the selectivity of the reaction and the stability of the relevant metalated intermediates.

Furthermore, the performance of metalations of pyrimidine (**160a**) with TMPZnCl·LiCl (**162a**) in the presence of bidentate ligands such as 2,2'-bipyridine led to a significant yield decrease of zincated pyrimidine **163a** (see Experimental Part). Therefore, an explanation for the requested excess of base **162a** to achieve complete metalation may be the consumption of one or two equivalents of **162a** in the reaction with complexes such as **IV,** leading to species such as **V** and **VI**. (Scheme 57). Concerning the origin of the regioselectivity of the zinaction of pyridazine (**161**), we propose that the precoordination to the nitrogen is key for a metalation at C3.

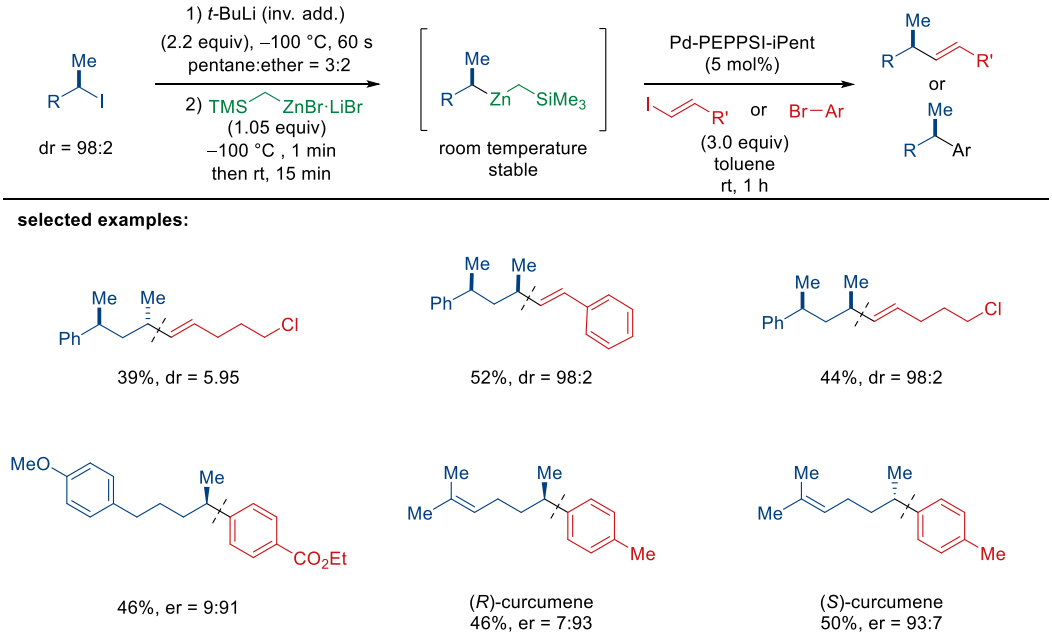


Scheme 57. Possible involved intermediates in the zincation of pyrimidine (**160a**) using 2 equiv of TMPZnCl·LiCl (**162a**)

5 Summary

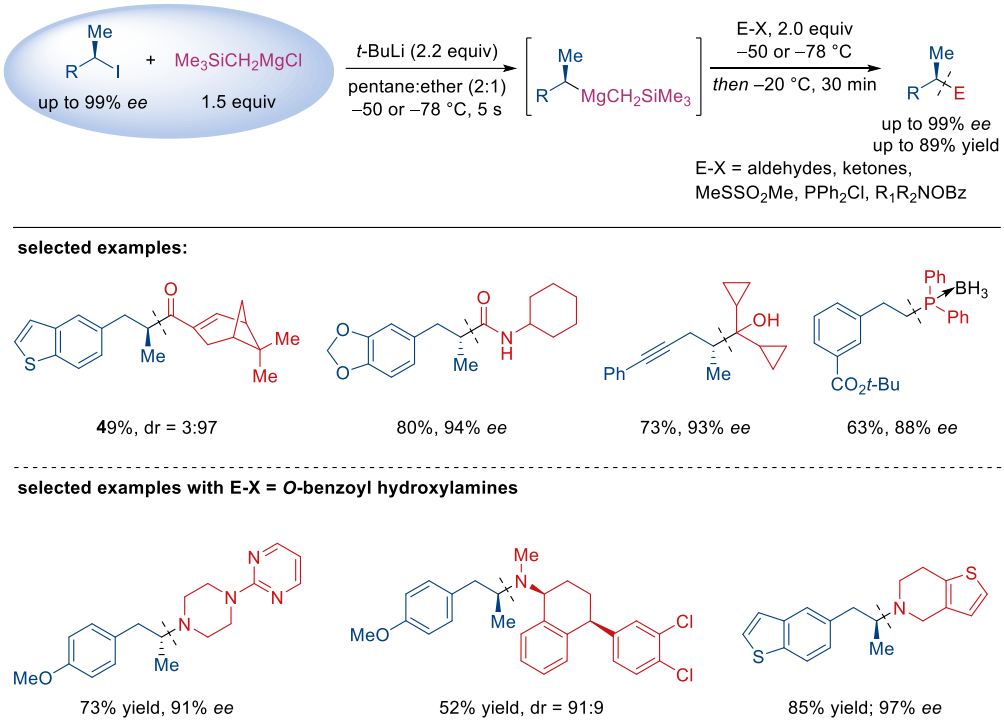
This thesis focused on expanding the scope of possible stereoretentive transmetalations of chiral secondary alkyllithium reagents. These new organometallics were used as key pre-cursors for the facile preparation of optically enriched molecules with high stereoretention.

Therefore, a stereoretentive transmetalation to optically enriched secondary alkylzinc reagents was developed. The ether soluble zinc reagent $Me_3SiCH_2ZnBr{\cdot}LiBr$ was found to be suitable and several diastereomerically or enantiomerically chrial secondary alkyllithium reagents were transmetalated to the desired chiral alkylzincs. A palladium-catalyst (Pd-PEPPSI-iPent) was found, which enabled highly stereoretentive cross-coupling reactions of these chiral secondary alkylzinc reagents with alkenyl iodides and aryl bromides providing optically enriched α-chiral alkenes and arenes in up to 76% yield (over three reaction steps) and up to er = 93:7 or dr = 98:2. The configurational stability of these optically enriched alkylzinc reagents was investigated and by using this method, the pheromones (*R*)- and (*S*)-curcumene were prepared in three steps from commercial precursors (see Scheme 58).



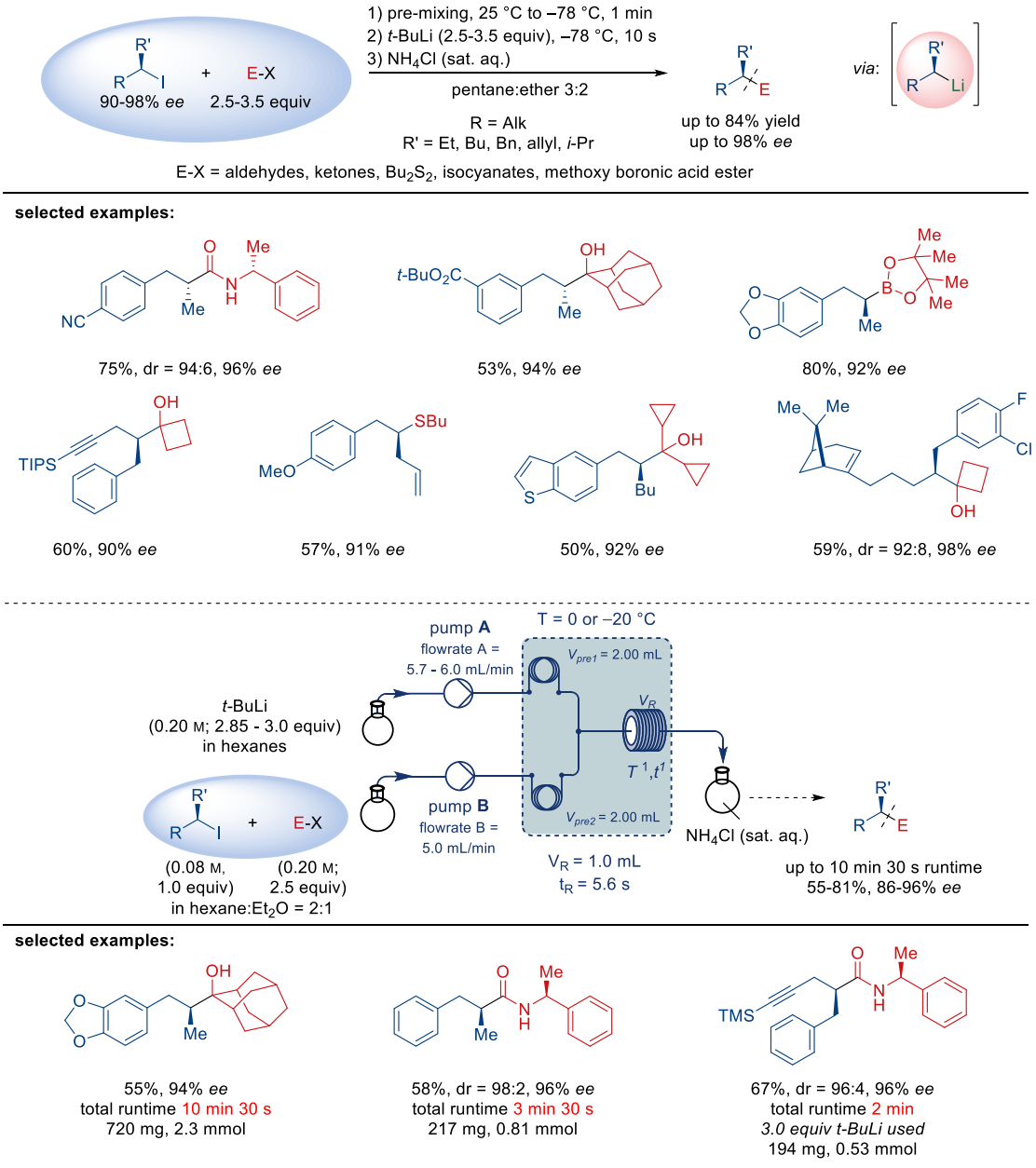
Scheme 58. Palladium-catalyzed stereoretentive cross-couplings of optically enriched secondary alkylzincs with alkenyl iodides and aryl bromides.

Furthermore, a stereoretentive transmetalation of chiral alkyllithiums to the corresponding chiral alkylmagnesium reagents was developed using commercially available Me_3SiCH_2MgCl. This process was realized in a Barbier-type procedure, in which the transmetalation reagent was added to the optically enriched iodide before the addition of *t*-BuLi. This approach allowed a general and convenient generation of several chiral Grignard reagents in high optical purity under previously impossible reaction conditions (up to −50 °C) drastically enhancing the generality and practicability of formerly reported approaches. These chiral Grignard reagents reacted with a range of electrophiles including non-enolizable ketones, aldehydes, acid chlorides, isocyanates, *S*-methyl methanethiosulfonate, chlorophosphines providing α-chiral tertiary alcohols, ketones, amides, thioethers, phosphines in up to 89% yield and up to 99% *ee*). Interestingly, the optically enriched secondary alkylmagnesiums reacted chemoselectively with *O*-benzoyl hydroxylamines in the absence of any transition-metal catalyst. Several optically enriched α-chiral tertiary amines were prepared (up to 85% yield and up to 97% *ee*) by this electrophilic amination (see Scheme 59).



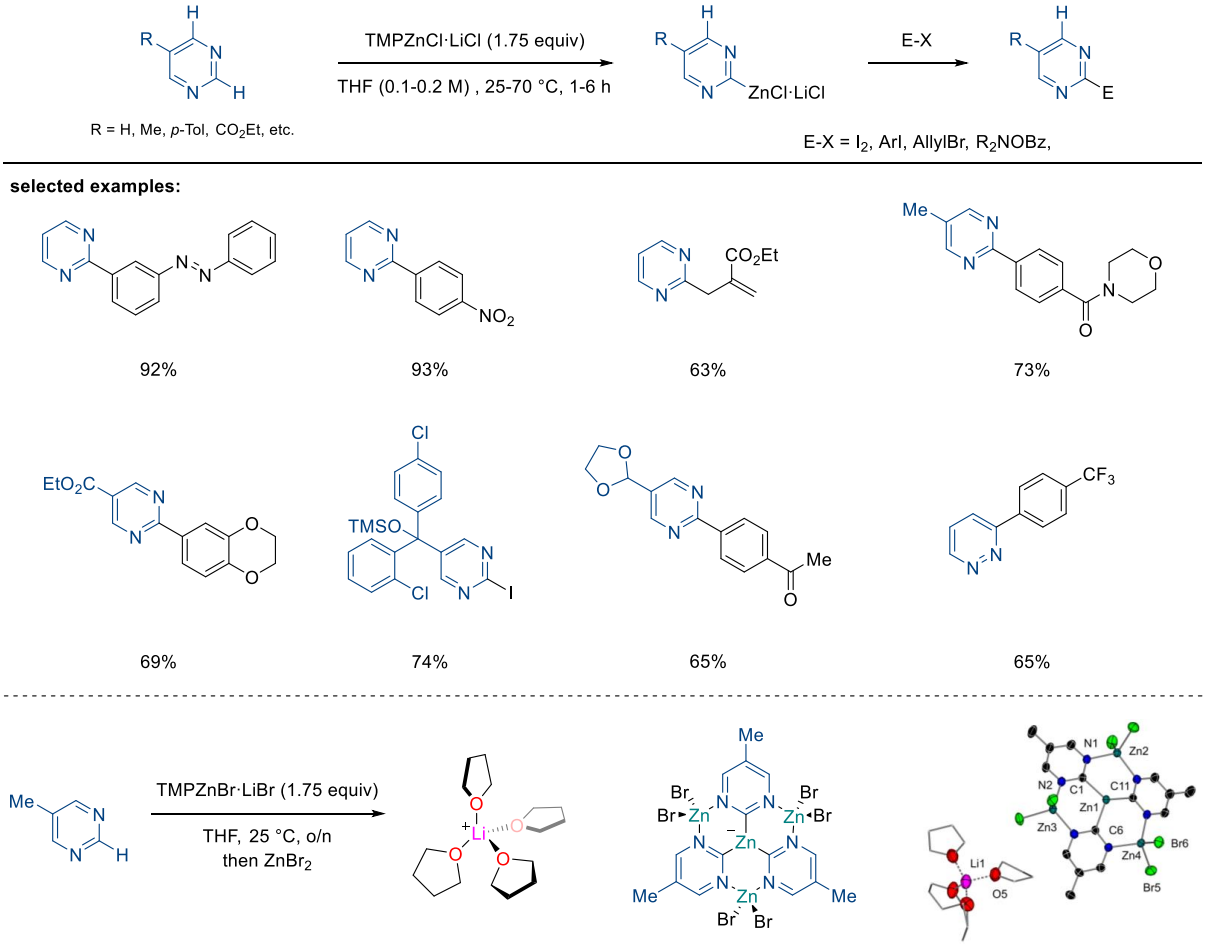
Scheme 59. Preparation of optically enriched secondary alkylmagnesium reagents *via* I/Li-exchange in the presence of Me_3SiCH_2MgCl and subsequent reaction with electrophiles.

In addition, an *in situ* quench (ISQ) reaction of chiral secondary alkyl iodides in the presence of electrophiles was developed. After dropwise addition of *t*-BuLi several optically enriched products were prepared. This method is complementary to the developed preparation of chiral Grignard reagents as several important electrophiles which did not react sufficiently were now compatible. A range of functionalized secondary alkyl iodides proved suitable under our reaction conditions and the reaction could be performed in batch at up to −40 °C. Furthermore, the reaction conditions were adapted into continuous flow, allowing an up to 40-fold scale-up compared to batch conditions (see Scheme 60).



Scheme 60. ISQ of chiral secondary alkyl iodides in the presence of electrophiles in batch and continuous flow.

Finally, the preparation of 2-zincated pyrimidines and 3-zincated pyridazine was investigated. These zincations occurred under very mild conditions (25–70 °C, using 1.75 equiv of base without additives), furnishing 2-zincated pyrimidines and 3-zincated pyridazine, which were trapped with a variety of electrophiles. Remarkably, the regioselective functionalization of these substrates represented a major challenge since they lack directing groups generally needed for regioselective control. Furthermore, combining spectroscopic and structural interrogations of the involved organometallic intermediates helped understand these unprecedented regioselectivities (see Scheme 61).



Scheme 61. Preparation of 2-zincated pyrimidines and 3-zincated pyridazine and their subsequent functionalization using arylations, allylations, aminations and iodinations.

C. Experimental Part

1 General

All reactions were carried out with magnetic stirring and under argon atmosphere in glassware dried with a heat gun. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon three times prior to use. Unless otherwise indicated, yields as stated are isolated yields of compounds and are estimated to be >95% pure as determined by 1H-NMR (25 °C) and capillary gas chromatography. The ratio of diastereoisomers was determined by ^{1}H-NMR and ^{13}C-NMR spectroscopy or GC-analysis. The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis

1.1 Solvents

All solvents were dried according to standard methods by distillation over drying agents as stated below and were stored under argon atmosphere. Solvents for column chromatography were distilled on a vacuum evaporator prior to use.

EtOH was treated with phthalic anhydride (25 g/L) and sodium, heated to reflux for 6 h and distilled.

Diethyl ether was predried over calcium hydride and dried with the solvent purification system SPS-400-2 from INNOVATIVE TECHNOLOGIES INC.

MeOH was heated to reflux over magnesium methoxide and distilled.

THF was continuously refluxed and distilled from sodium benzophenone ketyl under nitrogen.

D_8-THF was purchased from VWR, dried over NaK alloy for 16 h and then cycles through 3 rounds of degassing by employing a freeze-pump-thaw method. The solvent was then collected *via* vacuum transfer and store under Ar atmosphere, over 4 Å molecular sieves throughout its use.

1.2 Chromatography

Gas chromatography was performed with machines of *Agilent* Technologies 7890, using a column of type HP 5 (*Agilent* 5% phenylmethylpolysiloxane; length: 15 m; diameter: 0.25 mm; film thickness: 0.25 µm) or *Hewlett-Packard* 6890 or 5890 series II, using a column of type HP 5 (*Hewlett-Packard*, 5% phenylmethylpolysiloxane; length: 15 m; diameter: 0.25 mm; film thickness: 0.25 µm).

Chiral gas chromatography (**GC**) was performed on the following column: Chirasil-Dex CB, Varian, CP7502 (25.0 m x 250µm x 0.25µm), Average velocity 20, H_2-flux.

Flash column chromatography was performed using SiO_2 (0.040–0.063 mm, 230–400 mesh ASTM) from Merck if not specially indicated.

Thin layer chromatography (TLC) was performed using SiO_2 pre-coated aluminium plates (Merck 60, F-254). The chromatograms were examined by 254 nm UV irradiation or visualized by molybdatophosphoric acid stain and heating.

Preparative HPLC: For purification, an Agilent Technologies 1260 Infinity HPLC-System was used, consisting of two prep-pumps (acetonitrile/water, no additives), a MWD-detector (210 nm wavelength, 40 nm bandwidth, ref-wavelength 400 nm, ref-bandwidth 100 nm) and a fraction collector. Three different columns were used:

1) Kinetix EVO C18 5 µm column (length: 150 mm, diameter: 10 mm).

2) Kinetix EVO C18 5 µm column (length: 150 mm, diameter: 21.2 mm) and

3) Waters XBridge Prep C8 5 µm column (length: 150 mm, diameter: 30 mm).

1.3 Reagents

All reagents were obtained from commercial sources and used without further purification unless otherwise stated.

Mechanistic Investigations: TMP(H) (2,2',6,6'-tetramethylpiperidine) was purchased from VWR and purified by drying over CaH2 for 16 h, before collecting by vacuum distillation. The reagent was stored in an Ar-sealed ampule with 4 Å molecular sieves for at least 24 h prior to use. Pyrimidine and 5-methylpyrimidine were purchased from Fluorochem and Sigma-Aldrich – both reagents were stored and used within an Ar-purged glovebox throughout the entirety of this study. $ZnBr_2$, LiBr, $ZnCl_2$ and $MgBr_2$ were purchased from VWR and Sigma Aldrich. These reagents were dried at 200 °C under dynamic vacuum until such times that all residual moisture was removed (typically 3 days), and stored in an Ar-purged glovebox for use during this study.

1.4 Analytical Data

^{1}H-NMR and **^{13}C-NMR** spectra were recorded on BRUKER ARX 300, VARIAN VXR 300 S, Bruker Avance III HD spectrometer equipped with a CryoProbeTM (at 400 MHz and 100 MHz, respectively) and Bruker AMX 600 instruments. Chemical shifts are reported as δ-values in ppm relative to the solvent peak in $CDCl_3$ (residual chloroform: δ 7.26 ppm for ^{1}H-NMR, δ 77.0 ppm for ^{13}C-NMR). Abbreviations for signal coupling are as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet).

Mass spectroscopy (MS): High resolution (HRMS) and low resolution (LRMS) spectra were recorded on a FINNIGAN MAT 95Q instrument. Electron impact ionization (EI) was conducted with an ionization energy of 70 eV.

Infrared spectra (IR) were recorded from 4500 cm^{-1} to 650 cm^{-1} on a PERKIN ELMER Spectrum BX-59343 instrument. For detection a SMITHS DETECTION DuraSampl*IR* II Diamond ATR sensor was used and the absorption bands are reported in wavenumbers. The abbreviations for intensity are as

follows: vs (very strong; maximum intensity), s (strong; above 75% of max. intensity), m (medium; from 50% to 75% of max. intensity), w (weak; below 50% of max. intensity) as well as br (broad).

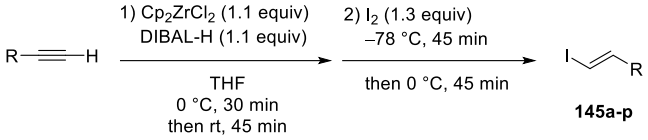
Optical rotation values were recorded in a Perkin Elmer 241 or anton Paar MCP 200 polarimeter. The specific rotation is calculated as follows:

$$[\alpha]_{\lambda}^{\varphi} = \frac{[\alpha] \cdot 100}{c \cdot d}$$

Thereby, the wavelength λ is reported in nm and the measuring temperature ϕ in °C. α represents the recorded optical rotation, c the concentration of the analyte in 10 mg/mL and d the length of the cuvette in dm. Thus, the specific rotation is given in $10^{-1} \cdot deg \cdot cm^2 \cdot g^{-1}$.Usage of the sodium D line (λ = 589 nm) is indicated by D instead of the wavelength in nm. The respective concentration as well as the solvent is reported at the relevant section of the experimental section.

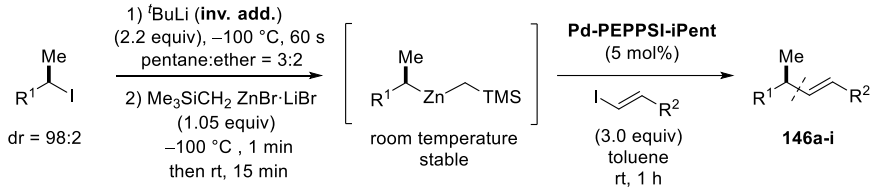
2 Typical Procedures

2.1 Preparation of Alkenyl Iodides (TP1)



According to a modified literature procedure,[153] a dry and Ar-flushed *Schlenk*-flask was charged with Cp_2ZrCl_2 (1.1 equiv) followed by THF (0.5 M) and cooled to 0 ºC. DIBAL-H (1.1 equiv, 1.0 M in *n*-hexane) was added dropwise. After stirring for 30 min at 0 ºC the corresponding alkyne (1.0 equiv) was added as a solution in THF (2.0 M). The reaction mixture was warmed to room temperature and stirred for 45 min, at which time the solution was homogenous. The reaction mixture was then cooled to –78 ºC and a solution of iodine (1.0 M in THF, 1.3 equiv) was added dropwise. The resulting brown solution was stirred at –78 ºC for 45 min before warming to 0 ºC within 45 min. A *Schlenk*-flask filled with *i*-hexanes (0.2 M) and HCl (2.8 equiv) was cooled to 0 °C and the reaction mixture was carefully transferred into it with vigorous stirring. The resulting biphasic solution was seperated and the aqueous layer was extracted with *i*-hexanes (3 × 100 mL). The combined organic layer was washed with HCl (1 M, 30 mL), $NaHCO_3$ (20% aq. sol., 30 mL), $Na_2S_2O_3$ (sat. aq. sol., 30 mL) and brine (30 mL). The combined organic phases were dried with Na_2SO_4 and filtered over a pad of Celite®. Solvents were removed and the crude product was purified by flash column chromatography on silica gel to afford the corresponding alkenyl iodides of type **145**.

2.2 Cross-Coupling Reactions of Chiral Secondary Alkylzincs and Alkenyl Iodides Using Pd-PEPPSI-iPent (TP2)

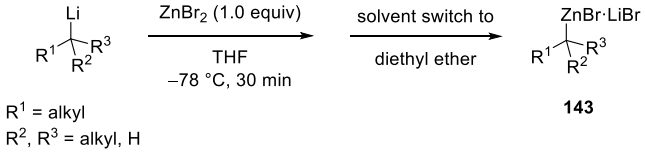


A dry and Ar-flushed *Schlenk*-tube was charged with *n*-pentane/diethyl ether (1.3 mL/0.9 mL) and cooled to −100 °C. *t*-BuLi (2.2 equiv) was added dropwise at −100 °C. A solution of the secondary alkyl iodide (1.0 equiv) in diethyl ether (0.4 mL) was added dropwise over a period of 60 s. Subsequently, a solution of $Me_3SiCH_2ZnBr{\cdot}LiBr$ (ca. 0.9 M, 1.05 equiv) was added dropwise and the reaction mixture was stirred for 1 min at −100 °C. The *Schlenk*-tube was then put to room temperature and the reaction mixture was let warm to ambient temperature. After 15 min, the reaction mixture was

[153] J. T. Edwards, R. R. Merchant, K. S. McClymont, K. W. Knouse, T. Qin, L. R. Malins, B. Vokits, S. A. Shaw, D. -H. Bao, F. –L. Wei, T. Zhou, M. D. Eastgate, P. S. Baran, *Nature* **2017**, **545**, 213–218.

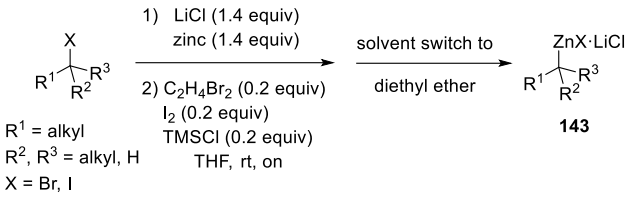
added dropwise to a premixed solution of Pd-PEPPSI-iPent (5 mol%) and the alkenyl iodide (3.0 equiv) in toluene (1.8 mL). The reaction mixture was stirred for 1 h at room temperature. After quenching with sat. aq. NH_4Cl solution, the reaction mixture was extracted with diethyl ether (3 × 10 mL). The combined organic phases were dried over $MgSO_4$ and the solvents were evaporated. The obtained crude product was purified by flash column chromatography on silica gel to afford alkenes of type **146**.

2.3 Preparation of Alkylzinc Reagents *via* Transmetalation (TP3)



A dry and Ar-flushed *Schlenk*-tube was charged with $ZnBr_2$ (1.0 equiv) and heated at 300 °C under vacuum for 5 min. After addition of THF (30 mL), the flask was cooled to −78°C. The alkyllithium species (1.0 equiv) was added dropwise to the reaction mixture and the reaction mixture was stirred at −78°C for 30 min. Solvents were evaporated under argon atmosphere at 0 °C and diethyl ether (5 mL) was added. Solvents were evaporated again and this process was repeated three times. Finally, the residue was dissolved in diethyl ether (20 mL) to obtain the desired ether solution.[154] The concentration was determined by titration of a small aliquot with iodine.[155]

2.4 Preparation of Alkylzinc Reagents *via* Oxidative Addition (TP4)

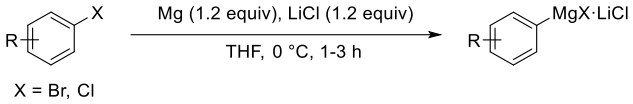


According to a modified literature procedure,[22] a dry and Ar-flushed *Schlenk*-flask was charged with zinc dust (1.4 equiv) and lithium chloride (1.4 equiv). After drying at 300 °C under vacuum for 5 min the reagents were dissolved in THF (ca. 0.5 M). 1,2-dibromoethane (0.1 mL) was added and the reaction mixture was carefully heated at 40 °C until gas evolution was observed. A piece of iodine and TMSCl (0.1 mL) were added to the reaction mixture and it was again heated to 40 °C. After cooling to room temperature the alkyl halide was added dropwise and the reaction mixture was stirred at ambient temperature overnight. Solvents were evaporated under argon atmosphere and then diethyl ether (5 mL) was added. Solvents were evaporated again and this process was repeated three times. Finally, the

[154] M. Westerhausen, B. Rademacher, W. Schwarz, J. Weidlein, *J. Organomet. Chem.* **1994**, *469*, 135–149.
[155] A. Krasovskiy, P. Knochel, *Synthesis* **2006**, 890–891.

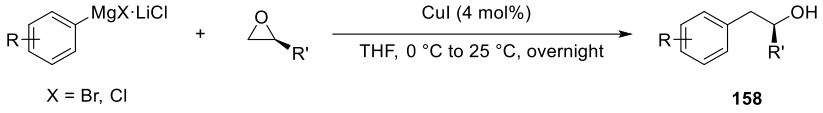
residue was dissolved in diethyl ether (20 mL) leading to the desired ether solution. The concentration was determined by titration of a small aliquot with iodine.

2.5 Preparation of Arylmagnesium Reagents (TP5)



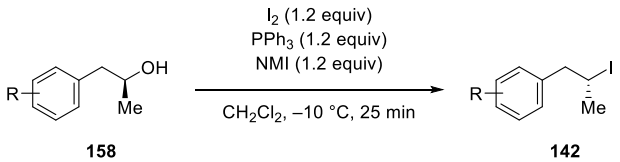
According to a modified literature procedure,[156] a dry and argon-flushed *Schlenk*-flask was charged with magnesium turnings (1.2 equiv) and anhydrous lithium chloride (1.2 equiv) in THF (1.0 M solution) and cooled to 0 °C. The aryl halide (1.0 equiv) was added and the reaction mixture was stirred for 1-3 h at 0 °C. The concentration of the obtained arylmagnesium species was determined *via* titration with iodine in THF.

2.6 Preparation of Chiral Secondary Alkyl Alcohols (TP6)



According to a modified literature procedure,[120] a dry and argon-flushed *Schlenk*-flask was charged with a solution of an aryl magnesium reagent (1.2 equiv) and diluted with THF to afford a ca. 0.5 M solution. The mixture was cooled to 0 °C and CuI (4 mol%) was added to the reaction mixture. Then, the chiral epoxide (1.0 equiv, 0.5 M in THF) was added dropwise to the reaction mixture at 0 °C and allowed to warm to room temperature overnight. Thereafter, the mixture was quenched with a sat. aq. NH_4Cl solution. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The remaining crude product was purified by flash column chromatography on silica gel to afford the corresponding alkyl alcohol of type **158**.

2.7 Preparation of Chiral Secondary Alkyl Iodides (TP7)

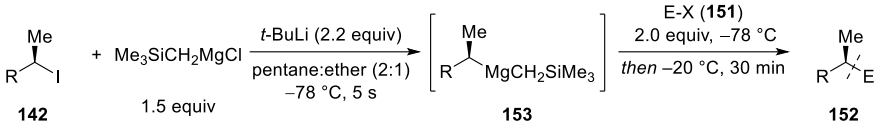


A dry and argon-flushed *Schlenk*-flask was charged with a solution of iodine (1.2 equiv) in CH_2Cl_2 (ca. 0.3 M solution) and cooled to −10 °C. Triphenylphosphine (1.2 equiv) was added in one portion and the resulting yellow suspension was stirred for 1 h at −10 °C. Then *N*-methylimidazole (1.2 equiv) was

[156] F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 6802–6806.

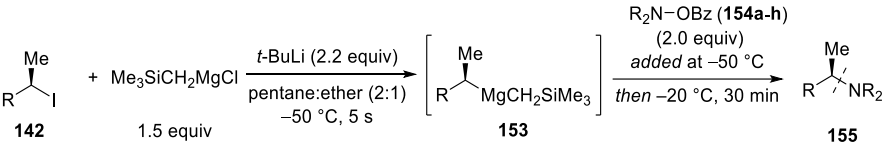
added dropwise. The reaction mixture was further stirred for 10 min after which the corresponding alcohol (**7**, 1.0 equiv, dissolved to 0.5 M in CH_2Cl_2) was added over a period of 15 min. The reaction was further stirred for 10 min at −10 °C and then quenched with freshly prepared sat. aq. $NaHSO_3{\cdot}Na_2S_2O_5$. The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure at 30 °C. The resulting oil was triturated with a mixture of *n*-pentane/diethyl ether. The precipitate was filtered off and the filtrate was concentrated under reduced pressure at 30 °C. The remaining crude product was purified by flash column chromatography on silica gel to afford the corresponding chiral secondary alkyl iodide of type **142**.

2.8 Preparation of Chiral Secondary Alkylmagnesium Reagents and Subsequent Trapping with Electrophiles (TP8)



A dry and argon-flushed *Schlenk*-flask was charged with the secondary alkyl iodide (**1**, 1.0 equiv) in *n*-pentane/diethyl ether (0.125 M/0.40 M) and cooled to −78 °C. A solution of Me_3SiCH_2MgCl (ca. 1.0 M in diethyl ether, 1.5 equiv) was added to the reaction mixture. Subsequently, *t*-BuLi (2.2 equiv, ca. 2.0 M in pentane) was quickly added dropwise at −78 °C. After 30 s, the electrophile (2.0 equiv, neat or in 0.5 mL of diethyl ether) was added directly to the reaction mixture at −78 °C. After addition of the electrophile, the reaction mixture was stirred for 30 min at −20 °C. After quenching with sat. aq. NH_4Cl solution, the reaction mixture was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford products of type **152**.

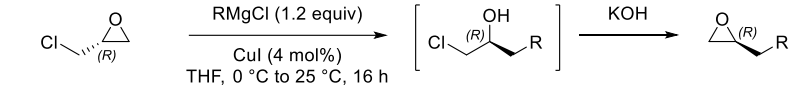
2.9 Preparation of Chiral Secondary Alkylmagnesium Reagents and Subsequent Trapping with *O*-Benzoyl Hydroxylamines (TP9)



A dry and argon-flushed *Schlenk*-flask was charged with the secondary alkyl iodide (**1**, 1.0 equiv) in *n*-pentane/diethyl ether (0.125 M/0.40 M) and cooled to −50 °C. A solution of Me_3SiCH_2MgCl (ca. 1.0 M in diethyl ether, 1.5 equiv) was added to the reaction mixture. Subsequently, *t*-BuLi (2.2 equiv, ca. 2.0 M in pentane) was quickly added dropwise at −50 °C. After 30 s, the *O*-hydroxylamine benzoate (**7**, 2.0 equiv, in 0.5 mL of dichloro methane) was added directly to the reaction mixture at −50 °C. After addition of the electrophile, the reaction mixture was stirred for 30 min at −20 °C. After quenching

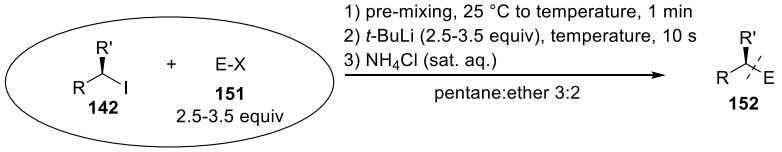
with sat. aq. $NaHCO_3$ solution, the reaction mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford products of type **155**.

2.10 Preparation of Chiral Epoxides from (*R*)-Epichlorohydrin (TP10)



According to a modified literature procedure,[119] a dry and Ar-flushed flask was charged with the desired magnesium reagent (1.2 equiv) in THF (0.5 M). Then, CuI (4 mol%) was added and the reaction was cooled to 0 °C. (*R*)-epichlorohydrin (*R*-**5**, 1.0 equiv) in THF (0.5 M) was added dropwise over a period of 15 minutes and the reaction was allowed to warm to ambient temperature overnight. A sat. aq. NH_4Cl solution was added, the phases were separated and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was **carefully** removed under reduced pressure. The remaining crude product was treated with powdered KOH (2.2 equiv based on starting material) in a round-bottom flask. For volatile epoxides, a distillation head was attached and the respective epoxide was distilled off. Higher molecular weight epoxides were treated with KOH (2.2 equiv. based on starting material) in a 1:1 mixture of Et_2O/water. The aqueous phase was extracted with Et_2O (2 × 20 mL), the combined organic layers were dried with $MgSO_4$, filtered and the solvent was removed. Epoxides were used without further purification.

2.11 *In Situ* Trapping of Chiral Secondary Alkyl Iodides in the Presence of Electrophiles (TP11)



The secondary alkyl iodide (0.1 mmol, 1.0 equiv) was dissolved in dry diethyl ether (0.16 M) and transferred into a dry and Ar-flushed Schlenk-finger. Then, *n*-pentane (0.125 M) was added and the electrophile (**3**, 2.5-3.5 equiv). The Schlenk finger was put into a dry ice/acetone bath at −78 °C or −40 °C and stirred for 1 min at this temperature. Subsequently, *t*-BuLi (2.5-3.5 equiv, ca. 2.1 M in pentane) was added dropwise over 10 s at −78 °C or −40 °C. The reaction tube was immediately quenched with sat. aq. NH_4Cl solution, diluted with water (2 mL) and diethyl ether (2 mL) before warming to ambient temperature over 10 min. The phases were separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the

solvent was removed under reduced pressure. The remaining crude product was purified by flash column chromatography on silica gel to afford products of type **152**.

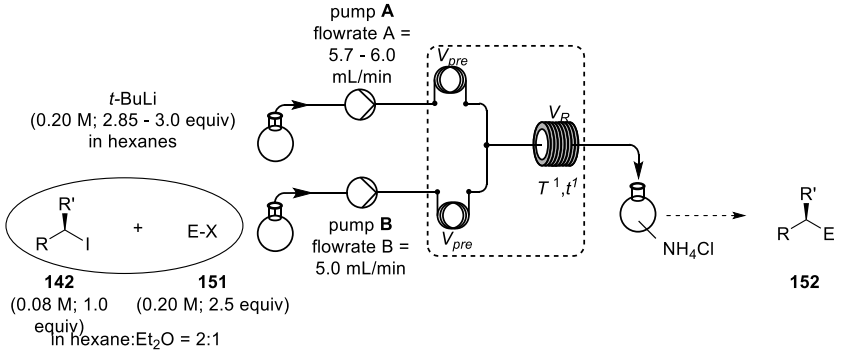
Note:

In the case of solid electrophiles or electrophiles, which proved to be insoluble at −78 °C, the reaction was performed at −40 °C in the presence of 3.0 equiv of electrophile.

In case of the products **4x**-**y** and **4aa** the reaction was performed using 3.5 equiv of *t*-BuLi in the presence of 3.5 equiv of electrophile to ensure full conversion of the iodide.

2.12 General Remarks on Flow and Subsequent Batch Quenching Reactions (TP12)

Tetradecane (nC$_{14}$H$_{30}$) was used as internal standard. All flasks were heat gun dried (650 °C) under vacuum and backfilled with argon after cooling. Syringes, which were used to transfer reagents and solvents, were purged with argon three times prior to use. Batch quenching reactions were carried out with magnetic stirring. Flow reactions were performed on the commercially available flow system (Vapourtec E-series Integrated Flow Chemistry System with 3rd Pump Kit). Hexane solutions of *t*-BuLi and hexane:Et$_2$O solutions of the corresponding reagents were kept in flasks with rubber septa under an argon atmosphere during the reactions. All reactions were performed in coiled tube reactors. Coiled reactors were made from PFA or PTFE Teflon (I.D. = 0.8 mm or 0.25 mm, O.D. = 1.6 mm) tubing and T-pieces (I.D. = 0.5 mm) were used as mixers. Prior to performing reactions, the systems were dried by flushing with dry hexane (flow rate of all pumps: 1.00 mL/min; run-time: 30 min).



A solution of alkyl iodide (**142**, 0.08 M, 1.00 equiv) and electrophile (**151**, 0.20 M, 2.50 equiv) in hexane:Et$_2$O (2:1) and a solution of *t*-BuLi (ca. 0.20 M in hexane, 2.85–3.00 equiv) were prepared. The solution of *t*-BuLi was pumped by pump A (flow rate A: 5.7–6.0 mL/min) into a precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The solution of the alkyl iodide **2** was pumped by pump B (flow rate B: 5.0 mL/min) into a second precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The precooled solutions were mixed in a T-shaped mixer and passed within a residence time of (t^1 = 5.5 to 5.6 s) through a coil reactor (V_R = 1.0 mL) at the corresponding temperature (T^1 = –20 to 25 °C). The stream was subsequently, upon reaching steady state, injected into a flask charged with sat. aq. NH$_4$Cl. The

aqueous phase was extracted three times with Et_2O (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was removed under reduced pressure and the remaining crude product was purified by flash column chromatography on silica gel to afford products of type **152**.

2.13 Metalation and Iodination of Pyrimidine in the C2-Position Using TMPZnCl·LiCl (TP13)

In a dry and argon flushed Schenk-flask, equipped with a magnetic stirring bar, pyrimidine (39 μL, 0.5 mmol, 1.0 equiv) was dissolved in THF (0.2 M, 2.5 mL). Next, TMPZnCl·LiCl (0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv) was added dropwise and the resulting reaction mixture was stirred at 25 °C for 6 h. The reaction mixture was quenched with a solution of I_2 (228 mg, 1.0 M in THF, 1.8 equiv). The crude product was concentrated and purified *via* flash column chromatography on silica gel.

2.14 Metalation and Iodination of Functionalized Pyrimidines in the C2-Position Using TMPZnCl·LiCl (TP14)

In a dry and argon flushed Schenk-flask, equipped with a magnetic stirring bar, the functionalized pyrimidine (0.5 mmol, 1.0 equiv) was dissolved in THF (0.1 or 0.2 M, 2.5-5 mL). Next, TMPZnCl·LiCl (0.36 M, 0.875 mmol, 1.75 equiv) was added dropwise and the resulting reaction mixture was stirred for 1-6 h at 25-60 °C. The reaction mixture was quenched with a solution of I_2 (228 mg, 1.0 M in THF, 1.8 equiv). The crude product was concentrated and purified *via* flash column chromatography on silica gel.

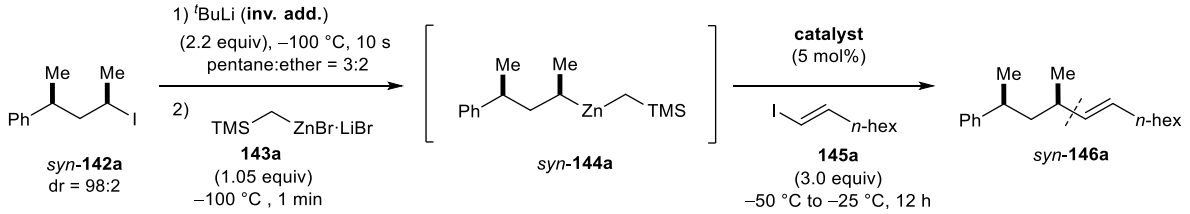
2.15 Metalation and Iodination of Pyridazine in the C3-Position Using TMPZnCl·LiCl (TP15)

In a dry and argon flushed pressure vessel, equipped with a magnetic stirring bar, pyridazine (36 μL, 0.5 mmol, 1.0 equiv) was dissolved in THF (0.1 M, 5.0 mL). Next, TMPZnCl·LiCl (0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv) was added dropwise and the resulting reaction mixture was stirred for 2 h at 70 °C. The reaction mixture was quenched with a solution of I_2 (228 mg, 1.0 M in THF, 1.8 equiv). The crude product was concentrated and purified *via* flash column chromatography on silica gel.

3 Optimization of Reaction Conditions

3.1 Various Optimizations for the Stereoretentive Cross-Coupling of Chiral Secondary Alkylzincs

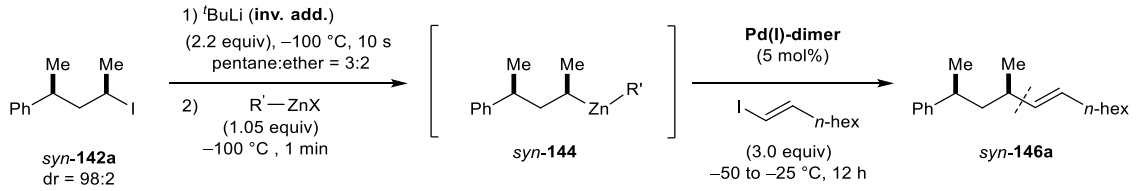
Table S1. Variation of the catalyst

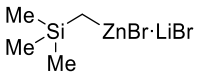
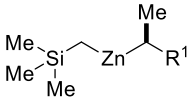
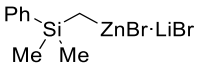
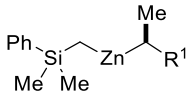
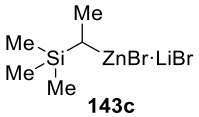
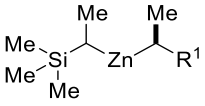
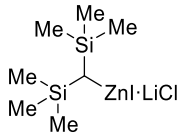
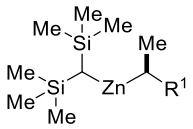
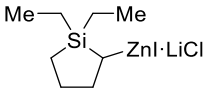
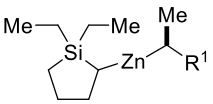
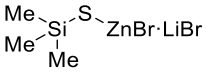
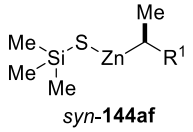
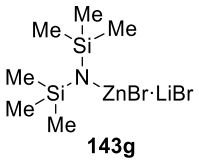
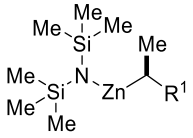
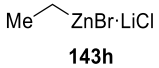
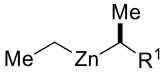


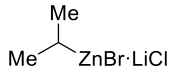
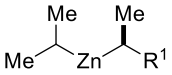
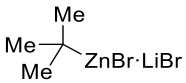
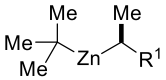
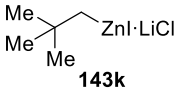
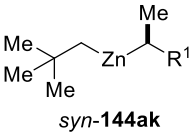
entry	catalyst	yield of *syn*-**146a**[a]	dr of *syn*-**146a**[a]	branched:linear
1	$Pd(PPh_3)_4$	39%	89:11	10:1
2	$Pd(OAc)_2$/CPhos	51%	92:8	1.5:1
3	Pd-PEPPSI-iPent	60%	96:4	25:1
4	Pd-PEPPSI-iPr	23%	91:9	2:1
5	$Pd_2I_2(Pt\text{-}Bu_3)_2$	58%	98:2	25:1
6	$PdCl_2(Amphos)_2$	0%	-	-
7	$NiCl_2(Pt\text{-}Bu_3)_2$	0%	-	-
6	$Ni(acac)_2$	0%	-	-
7	$NiCl_2$(dppp)	0%	-	-
8	$NiCl_2$/bipy	0%	-	-

[a] The yield and diastereoselectivity (dr: *syn*:*anti* ratio) was determined by GC-analysis using dodecane as internal standard.

Table S2. Variation of the zinc reagent

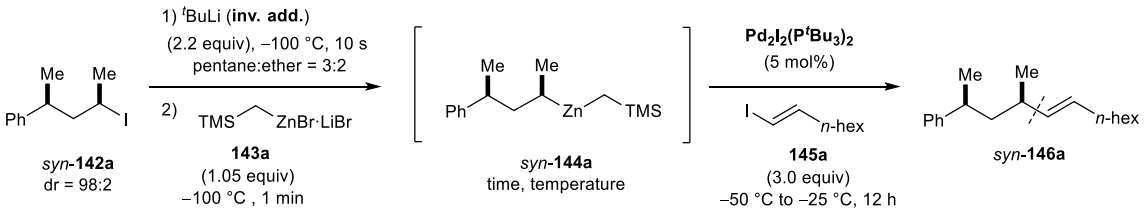


entry	zinc reagent	alkylzinc reagent	yield, dr of *syn*-**146a**[a]
1	 **143a**	 *syn*-**144a**	65% yield, dr = 98:2
2	 **143b**	 *syn*-**144ab**	59% yield, dr = 75:25
3	 **143c**	 *syn*-**144ac**	63% yield, dr = 80:20
4	 **143d**	 *syn*-**144ad**	55% yield, dr = 50:50
5	 **143e**	 *syn*-**144ae**	41% yield, dr = 60:40
6	 **143f**	 *syn*-**144af**	10% yield, dr = 50:50
7	 **143g**	 *syn*-**144ag**	21% yield, dr = 69:31
8	 **143h**	 *syn*-**144ah**	62% yield, dr = 90:10

9	 **143i**	 *syn*-**144ai**	31% yield, dr = 88:12
10	 **143j**	 *syn*-**144aj**	44% yield, dr = 91:9
11	 **143k**	 *syn*-**144ak**	62% yield, dr = 85:15

[a] The yield and diastereoselectivity (dr: *syn*:*anti* ratio) was determined by GC analysis using dodecane as internal standard.

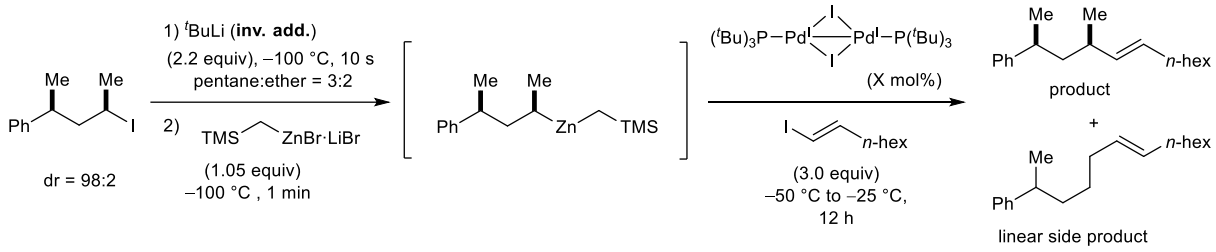
Table S3. Configurational stability of the zinc reagent.



entry	temperature	time	yield of *syn*-**146a**[a]	dr of *syn*-**146a**[a][b]
1	–50 °C	10 min	61%	97:3
2	–30 °C	10 min	58%	97:3
3	–10 °C	10 min	50%	97:3
4	25 °C	60 min	51%	96:4
5	25 °C	240 min	53%	89:11

[a] determined by capillary GC with dodecane as internal standard. [b] The branched:linear ratio was determined to be higher than 25:1.

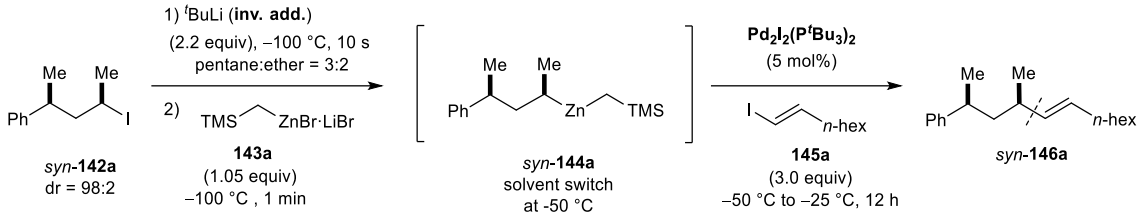
Table S4. Variation of the catalyst loading.



entry	catalyst loading	time	yield of *syn*-**146a**[a]	dr of *syn*-**146a**[a]	branched:linear
1	1 mol%	5 min	35%	98:2	-
2	1 mol%	60 min	52%	98:2	-
3	1 mol%	12 h	54%	97:3	4:1
4	5 mol%	5 min	37%	98:2	-
5	5 mol%	60 min	54%	98:2	-
6	5 mol%	12 h	58%	98:2	25:1
7	10 mol%	5 min	40%	98:2	-
8	10 mol%	60 min	54%	98:2	-
9	10 mol%	12 h	59%	96:4	30:1

[a] The yield and diastereoselectivity (dr: *syn*:*anti* ratio) was determined by GC-analysis using dodecane as internal standard.

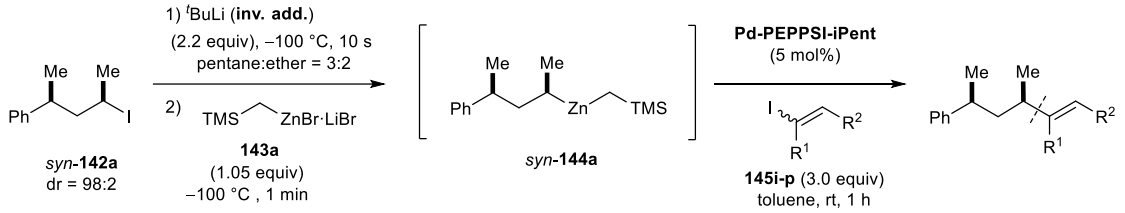
Table S5. Variation of the solvent.

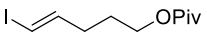
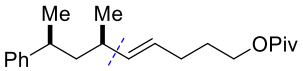
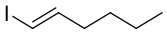
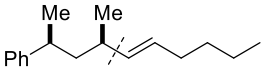
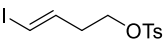
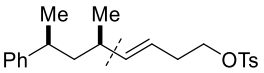
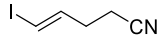
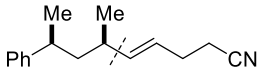
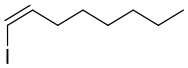
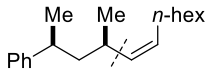
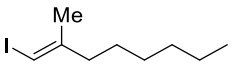
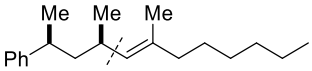
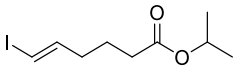
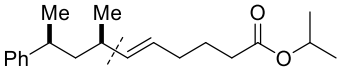
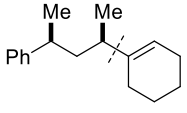
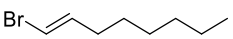
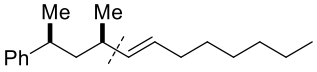


entry	solvent	time	yield of *syn*-**146a**[a]	dr of *syn*-**146a**[a][b]
1	THF	5 min	43%	98:2
2	THF	60 min	58%	98:2
3	THF	3 h	58%	98:2
4	THF	12 h	58%	98:2
5	toluene	5 min	40%	97:3
6	toluene	60 min	63%	95:5
7	toluene	3 h	63%	95:5
8	toluene	12 h	63%	95:5

[a] The yield and diastereoselectivity (dr: *syn*:*anti* ratio) was determined by GC-analysis using dodecane as internal standard. [b] The branched:linear ratio was determined to be higher than 25:1.

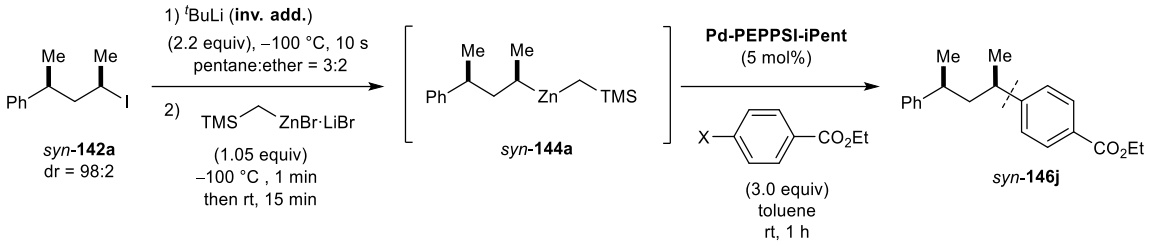
Table S6. Unsuccesful alkenyl iodides.



entry	zinc reagent	electrophile	yield, dr of product of type **146**[a]
1	*syn*-**142a**	 **145i**	 46% yield, dr = 90:10
2	*syn*-**142a**	 **145j**	 3% yield, dr = -
3	*syn*-**142a**	 **145k**	 54% yield, dr = 92:8
4	*syn*-**142a**	 **145l**	 17% yield, dr = 94:6
5	*syn*-**142a**	 **145m**	 15% yield, dr = 90:10
6	*syn*-**142a**	 **145n**	 18% yield, dr = 89:11
7	*syn*-**142a**	 **145o**	 40% yield, dr = 80:20
8	*syn*-**142a**	 **145p**	 11% yield, dr = 87:13
9	*syn*-**142a**	 **145q**	 23% yield, dr = 94:6

[a] The yield and diastereoselectivity (dr: *syn*:*anti* ratio) was determined by GC analysis using dodecane as internal standard.

Table S7. Variation of the leaving group.

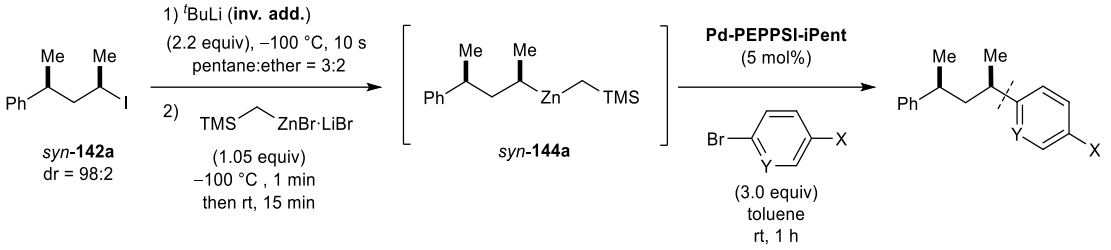


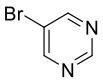
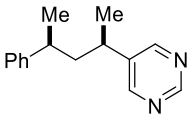
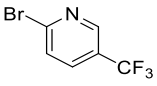
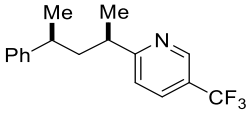
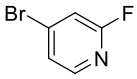
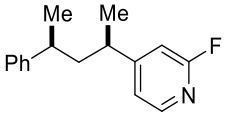
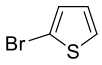
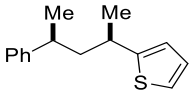
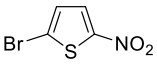
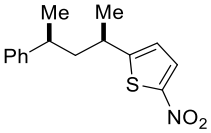
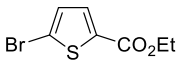
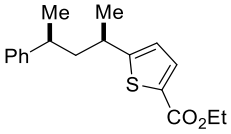
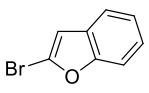
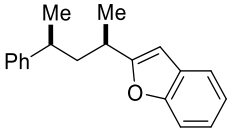
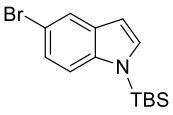
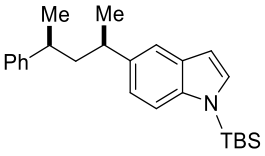
entry	X =	time	yield of *syn*-**146j**[a]	dr of *syn*-**146j**[a]
1	Cl	5 min	3%	-
2	Cl	30 min	17%	95:5
3	Cl	60 min	26%	94:6
4	Cl	12 h	34%	94:6
5	Br	5 min	12%	95:5
6	Br	30 min	34%	95:5
7	Br	60 min	40%	95:5
8	Br	12 h	48%	94:6
9	I	5 min	25%	95:5
10	I	30 min	25%	95:5
11	I	60 min	28%	91:9
12	I	12 h	29%	91:9
13	OTf	5 min	15%	94:6
14	OTf	30 min	17%	94:6

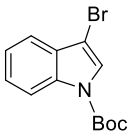
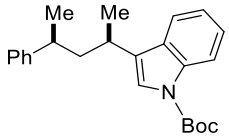
15	OTf	60 min	20%	92:8
16	OTf	12 h	24%	92:8
17	ONf	5 min	25%	94:6
18	ONf	30 min	27%	94:6
19	ONf	60 min	29%	94:6
20	ONf	12 h	29%	94:6

[a] The yield and diastereoselectivity (dr: *syn*:*anti* ratio) was determined by GC-analysis using dodecane as internal standard.

Table S8. Variation of the heteroaryl halides.



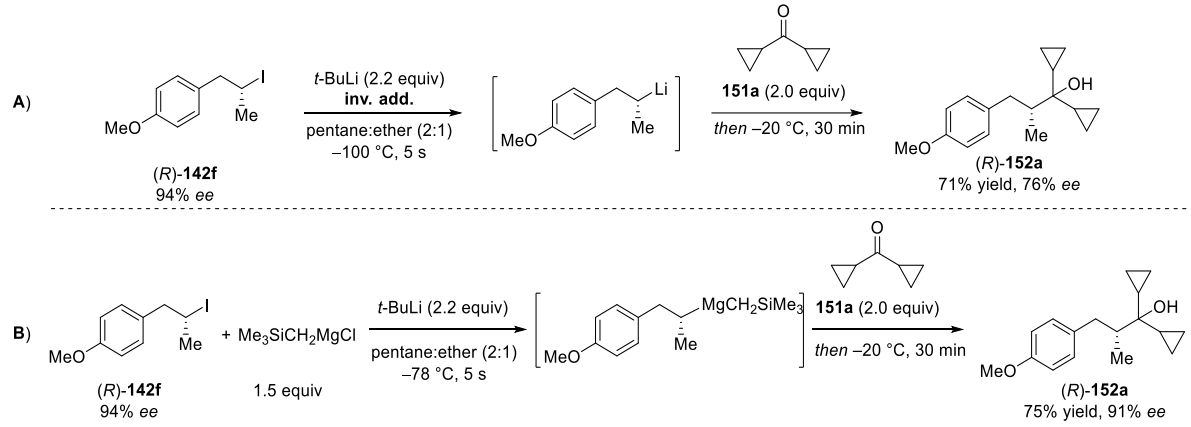
entry	electrophile	product	yield, dr of product[a]
1			0% yield, -
2			36% yield, dr = 80:20
3			0% yield, -
4			12% yield, dr = 91:9
5			traces
9			27% yield, dr = 74:26
10			traces
11			11% yield, -

12			0% yield

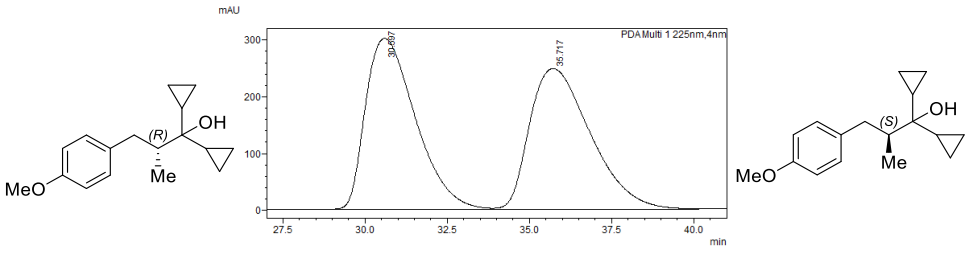
[a] The yield and diastereoselectivity (dr: *syn*:*anti* ratio) was determined by GC analysis using dodecane as internal standard.

3.2 Proof of Stereoretention for the Transmetalation of Secondary Alkyllithiums to the Corresponding Secondary Alkylmagnesiums

The reaction of the secondary alkyllithium species obtained after a stereoretentive I/Li-exchange from the enantiomerically enriched (*R*)-enantiomer of the secondary alkyl iodide (*R*)-**142f** with *t*-BuLi at −100 °C reacted with the electrophile **151a** affording (*R*)-**152a** in 76% *ee* (A). Experiment B shows that the transmetalation from lithium to magnesium proceeds with retention of configuration as in the presence of 1.5 equiv. of Me_3SiCH_2MgCl the same enantiomer of the tertiary alcohol (*R*)-**152a** was obtained in 91% *ee*.

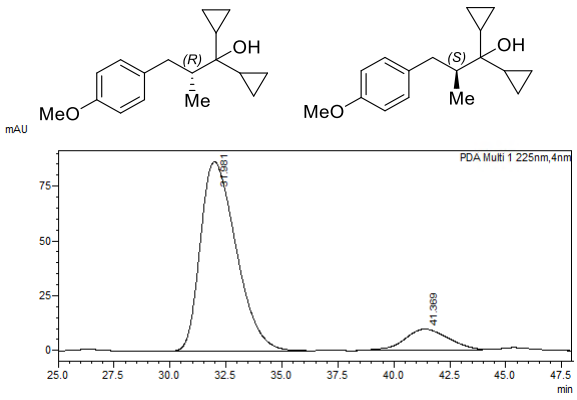


Racemate:



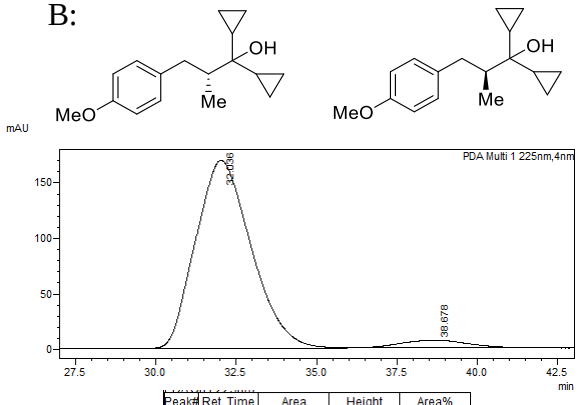
Peak#	Ret. Time	Area	Height	Area%
1	30.597	31717245	300745	49.856
2	35.717	31900167	247589	50.144
Total		63617412	548334	100.000

A:



Peak#	Ret. Time	Area	Height	Area%
1	31.981	9640135	86459	88.085
2	41.369	1304015	9624	11.915
Total		10944150	96084	100.000

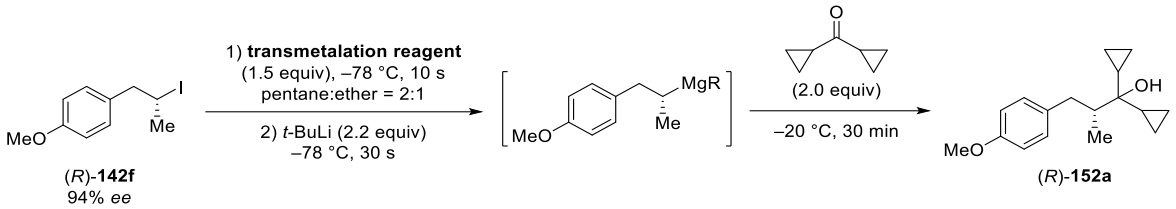
B:



Peak#	Ret. Time	Area	Height	Area%
1	32.036	20354365	169281	95.558
2	38.678	946215	6756	4.442
Total		21300581	176037	100.000

3.3 Test of Different Magnesium Derived Transmetalation Reagents

Table S9: Optimization of the transmetalation reaction to alkylmagnesiums

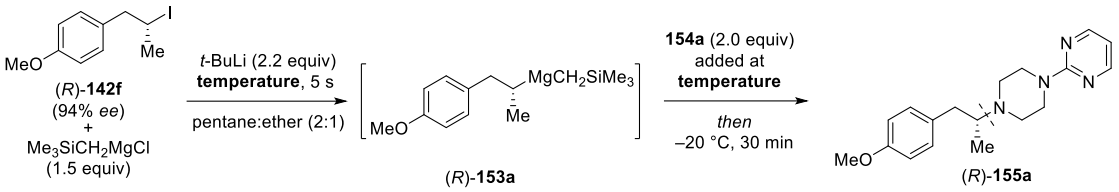


Entry	Transmetalation reagent	Yield of (*R*)-**152a**[a]	*ee* of (*R*)-**152a**[b]
1	–	*traces*	n.d
2	EtMgBr	35%	30%
3	PhMgBr	34%	34%
4	MeMgBr·LiBr	56%	12%
5	*t*-BuMgBr·LiBr	77%	76%
6	Me_3SiCH_2MgCl	80% (75%)	91%
7	$Me_3SiCH_2MgBr{\cdot}LiBr$	78%	86%
8	$Me_3SiCH_2MgBr{\cdot}LiBr$[c]	12%	2%
9	$MgBr_2$	29%	52%
10	$MgBr_2$[d]	28%	32%

[a] The yield was determined by GC-analysis. [b] The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis. [c] The transmetalation reagent was dissolved in THF instead of diethyl ether. [d] 0.6 Equiv. of transmetalation reagent were used.

3.4 Optimization of the Electrophilic Amination

Table S10: Temperature dependence of the electrophilic amination



Entry	Temperature	Yield of (*R*)-**155a**[a]	*ee* of (*R*)-**155a**[b]
1	–78 °C	30%	nd
3	–50 °C	78% (73%)	91%
4	–30 °C	52%	nd

[a] The yield was determined by GC-analysis. [b] The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis.

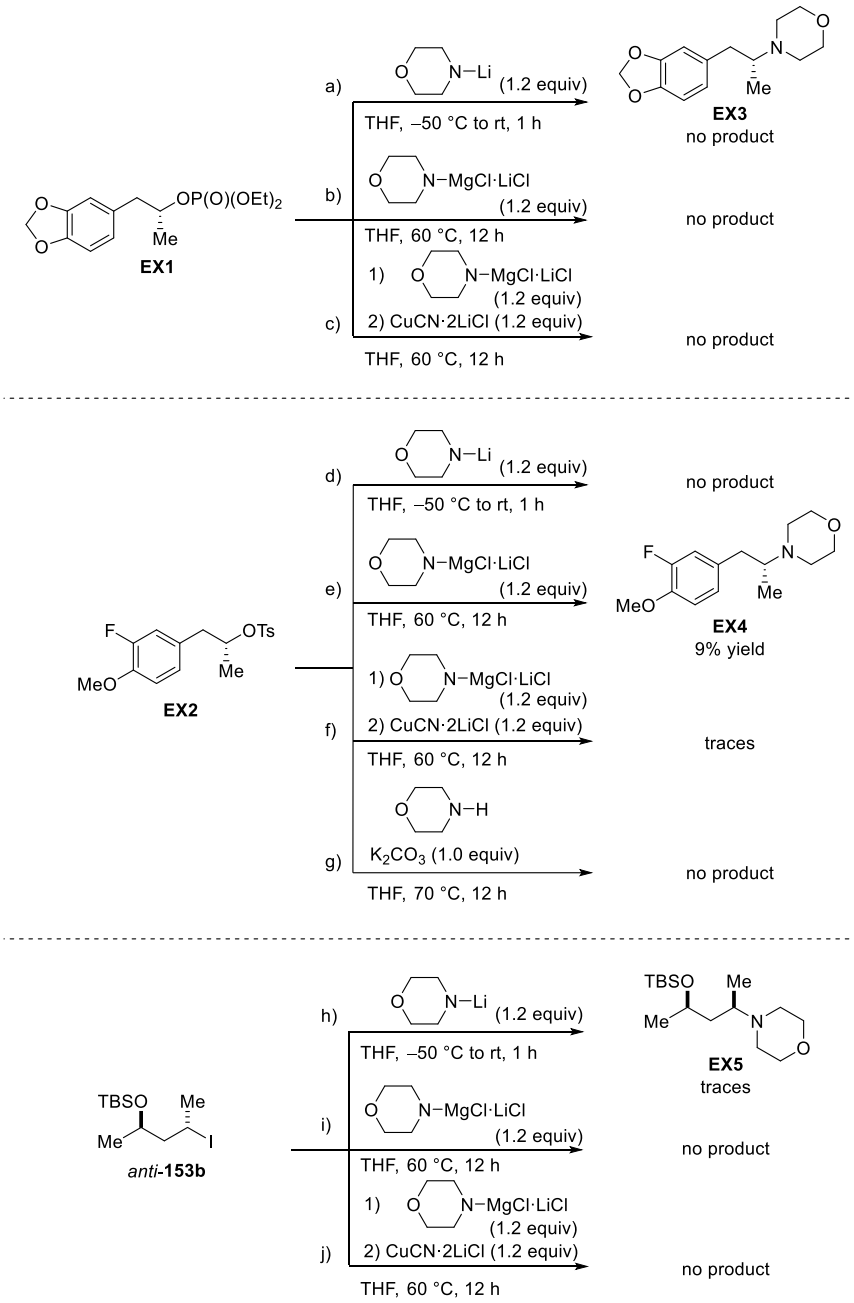
3.5 Comparison of Electrophilic and Nucleophilic Amination

To compare our method with a nucleophilic amination, we prepared three organometallic morpholino amides and reacted them with the optically enriched secondary alkyl phosphate **EX1**,[157] the tosylate **EX2**[158] and the secondary alkyl iodide *anti*-**153b**. When **EX1** was treated with lithium morpholino amide, the tertiary amine was not detected (reaction a). However, the corresponding alcohol was obtained in almost quantitative yield (96%). Treating **EX1** with the analogous magnesium or copper morpholino derivatives did not afford the expected tertiary amine **EX3** either (reactions b and c).

Analogously, **EX2** was treated with the organometallic morpholino amides (reactions d-f). Only magnesium morphplino amide provided the tertiary amine **EX4** in detectable yield, however harsh reaction conditions were required. Treating **EX2** with a mixture of morpholine and potassium carbonate[159] afforded the corresponding alcohol exclusively (reaction g).

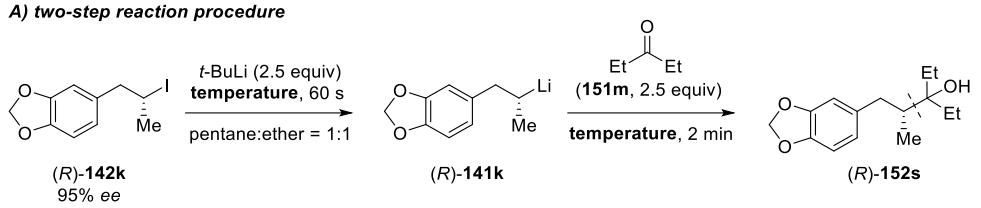
[157] S. Crook, N. J. Parr, J. Simmons, S. Jones, *Tetrahedron: Asymmetry* **2014**, *25*, 1298–1308.
[158] G. Hellmann, A. Hack, E. Thiemermann, O. Luche, G. Raabe, H.-J. Gais, *Chem. Eur. J.* **2013**, *19*, 3869–3897.
[159] T. Okutani, T. Kaneko, K. Masuda, *Chem. Pharm. Bull.* **1974**, *22*, 1490–1497.

Treating the diastereomerically enriched secondary alkyl iodide *anti*-**153b** with the organometallic amides led in all cases to complete epimerization of the starting material and only traces of **EX5** were detected (reactions h-j).

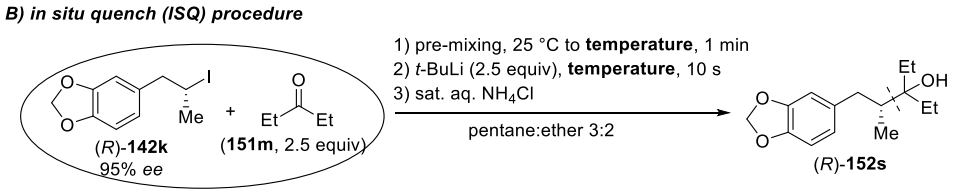


3.6 Optimization of the ISQ Reaction of Chiral Secondary Alkyllithiums

Table S11: Temperature dependence of two-step and ISQ reaction



Entry	Temperature [°C]	Yield of (*R*)-**152s**[a]	*ee* of (*R*)-**152s**[b]
1	−100	67%	92%
2	−78	61%	53%
3	−40	54%	0%



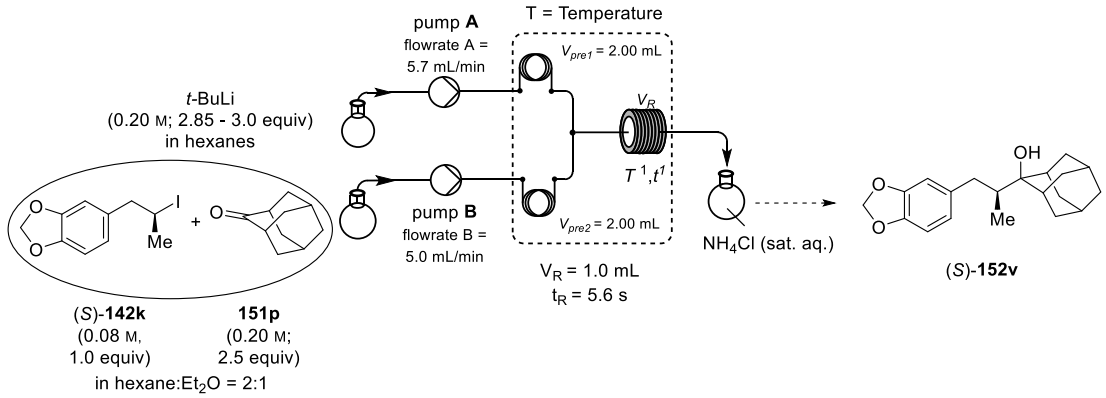
Entry	Temperature [°C]	Yield of (*R*)-**152s**[a]	*ee* of (*R*)-**152s**[b]
4	**−78**	**60%**[c]	**93%**
5	−60	52%	92%
6	−40	54%	90%
7	−20	44%	86%
8	0	41%	69%
9[d]	−78	28%	92%
10[e]	−78	48%	93%
11[f]	−78	31%	93%

[a] The yield was determined by GC-analysis; [b] The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis; [c] Yield of isolated analytically pure product; [d] 1.0 equiv of electrophile was used; [e] 2.0 equiv of electrophile was used; [f] 3.0 equiv of electrophile was used.

Low yields were attributed to low conversion of the iodide (entry 11) or to competitive reaction of excess *t*-BuLi on the electrophile (entries 9 and 10). In cases of incomplete conversion of the iodide (compounds **152ap-aq** and **152as**), the amount of *t*-BuLi and electrophile was raised to 3.5 equiv.

If a mixture of secondary alkyl iodide with electrophile was insoluble in pentane/ether at −78 °C, the reaction was performed at −40 °C.

Continuous Flow:



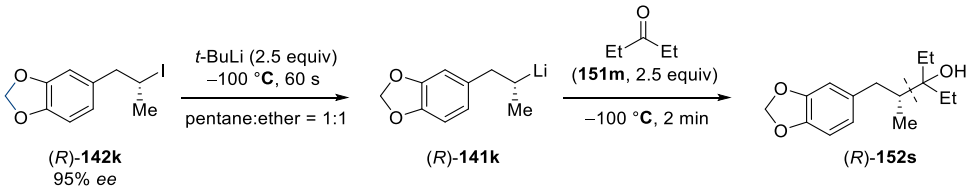
Entry	Temperature [°C]	Yield of (*S*)-**152v**[a]	*ee* of (*S*)-**152v**[b]
1	−40	-	-
2	−30	-	-
3	−20	59%[c]	94%

[a] The yield was determined by GC-analysis; [b] The enantiomeric excess (% *ee*) was determined by chiral HPLC-analysis; [c] Yield of isolated analytically pure product.

Performing the reaction at lower temperatures than −20 °C led to clogging of the tubes due to insoluble mixtures of the iodide and electrophile.

If remaining starting material was observed (see manuscript compounds **152w** and **152av**), the amount of *t*-BuLi was changed to 3.0 equiv instead of 2.85 equiv. Thus, the flow rate was changed to 6.0 mL/min.

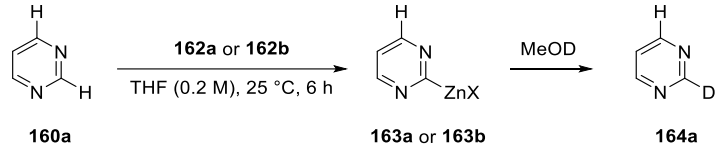
Procedure for the two-step reaction:



A dry and Ar-flushed Schlenk-tube was charged with *n*-pentane/diethyl ether (1.2 mL/0.8 mL) and cooled to −100 °C. *t*-BuLi (2.5 equiv) was added at −100 °C. A solution of the secondary alkyl iodide (*R*)-**142k** (0.1 mmol, 1.0 equiv) in diethyl ether (0.4 mL) was added dropwise over a period of 60 s. Subsequently, the electrophile **151m** (2.5 equiv) was added dropwise and the reaction mixture was stirred for 2 min at −100 °C. After quenching with sat. aq. NH_4Cl product (*R*)-**152s** was obtained.

3.7 Optimization of Zincation Conditions

Screening for pyrimidine (160a)

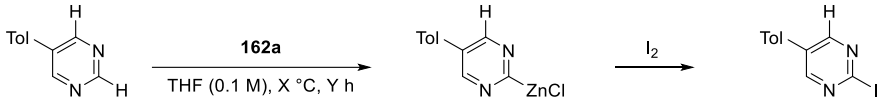


160a **163a** or **163b** **164a**

Entry	TMP-base	Equiv	Yield[a]
1	TMPZnCl·LiCl (**162a**)	1.05	70%
2	**162a**	1.25	74%
3	**162a**	1.50	90%
4	**162a**	1.75	98%
5	**162a**	2.00	99%
6	TMPZnBr·LiBr (**162b**)	2.00	99%
7	TMPMgCl·LiCl	1.1	28%[b]

[a] Yields are ^{1}H-NMR yields obtained by quenching an aliquot with MeOD using trichloroethylene as an internal standard. [b] The reaction was performed at −30 °C for 1 h.

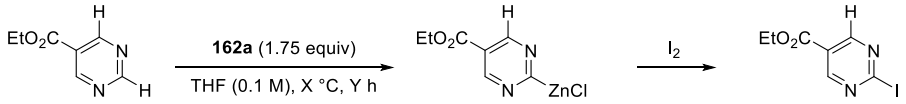
Screening for 5-(*p*-tolyl)pyrimidine (160b)



Entry	Temperature	Time	Yield[a]	Regiomeric ratio
1	50 °C	3 h	86%	97:3

[a] Yield was determined by GC-analysis using reaction aliquots quenched with I_2.

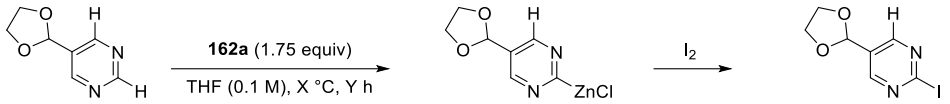
Screening for ethyl pyrimidine-5-carboxylate (160c)



Entry	Temperature	Time	Yield[a]	Regiomeric ratio
1	25 °C	1 h	53%	86:14
2	25 °C	2 h	64%	88:12
3	50 °C	2 h	62%	86:14
4	60 °C	1 h	72%	94:6

[a] Yields were determined by GC-analysis using reaction aliquots quenched with I_2.

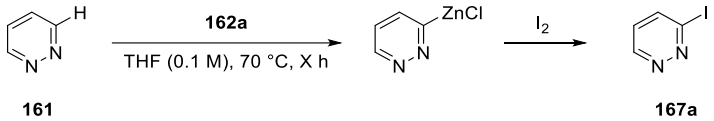
Screening for 5-(1,3-dioxolan-2-yl)pyrimidine (160f)



Entry	Temperature	Time	Yield[a]	Regiomeric ratio
1	25 °C	1 h	62%	91:9
2	25 °C	2 h	70%	90:10
3	40 °C	1 h	77%	91:9
4	60 °C	2 h	84%	92:8

[a] Yields were determined by GC-analysis using reaction aliquots quenched with I_2.

Screening for pyridazine (161)



161 **167a**

Entry	Temperature	Time	Yield[a]	Regiomeric ratio
1	70 °C	1 h	82%	94:6
2	70 °C	2 h	85%	94:6

[a] Yields were determined by ^{1}H-NMR analysis using reaction aliquots quenched with I_2 in THF-d8.

3.8 Metalation and Iodination of Pyrimidine in the C4-Position using TMPMgCl·LiCl

In a dry and argon flushed Schenk-flask, equipped with a magnetic stirring bar, pyrimidine (39 µL, 0.5 mmol, 1.0 equiv) was dissolved in THF (0.1 M, 5 mL). The mixture was cooled to −30 °C and TMPMg·LiCl (1.08 M, 510 µL, 0.55 mmol, 1.1 equiv) was added dropwise and the resulting reaction mixture was stirred for 2 h at −30 °C. The reaction mixture was quenched with a solution of I_2 (228 mg, 1.0 M in THF, 1.8 equiv). The crude product was concentrated and purified *via* flash column chromatography on silica gel with EtOAc/*i*-hexanes = 3:1 to afford 4-iodopyrimidine (**SI1,** 58 mg, 0.14 mmol, 28% yield) as a white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.89 (d, J = 1.3 Hz, 1H), 8.25 (d, J = 5.2 Hz, 1H), 7.80 (dd, J = 5.2, 1.3 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 158.8, 156.2, 133.2, 129.6.

The analytical data was in accordance with literature values.[138b]

3.9 Synthesis and Charcterization of LiTMP

LiTMP was prepared according to literature reports.[160] In an argon-flushed large Schlenk flask, 50 mL of hexane was added alongside 1.6 mL (10 mmoles) of TMP(H) and cooled to 0 °C. To this, an equimolar amount of *n*BuLi (6.3 mL, 10 mmoles, 1.6 M in hexanes) was added dropwise with constant stirring which resulted in the formation of a pale-yellow suspension. The mixture was allowed to slowly warm to ambient temperature and stirred for an additional one hour. The reaction mixture was then concentrated under reduced pressure to encourage further precipitation of LiTMP and then stored in a -30 °C freezer overnight. Following this, the remainder of the liquors were removed *via* cannula filtration and the resultant pale-yellow solid dried under vacuum. Due to the considerable solubility of LiTMP in even cold hexanes, the precipitate was not subjected to any displacement washes and was used without further purification.

^{1}H-NMR (D_8-THF, 400 MHz, 233 K): δ [ppm] = 1.61 (m, 2H, γ-CH_2), 1.19 (br. t, 4H, β-CH_2), 1.11 (s, 12H, CH_3).

^{7}Li-NMR (D_8-THF, 155.5 MHz, 233 K): δ [ppm] = 1.66, 1.31.

^{13}C-NMR (D_8-THF, 100.6 MHz, 233 K): δ [ppm] = 52.8 (α-C_q), 42.9 (β-CH$_2$), 35.9 (CH$_3$), 20.6 (γ-CH$_2$).

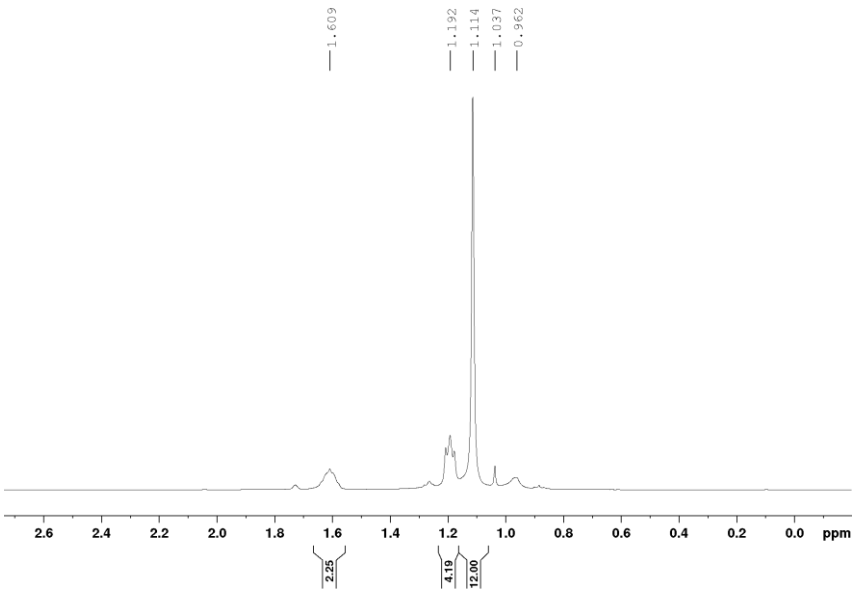


Figure S1. ^{1}H NMR spectrum of LiTMP in D_8-THF at 233 K.

[160] E. Hevia, A. R. Kennedy, R. E. Mulvey, D. L. Ramsay, S. D. Robertson, *Chem. Eur. J.*, **2013**, *19*, 14069–14075.

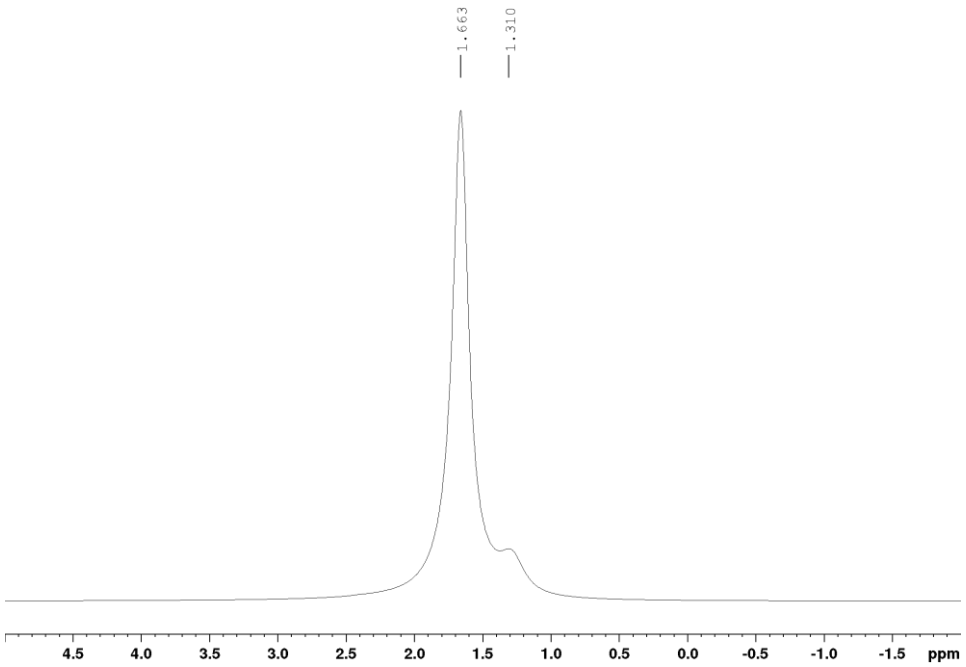


Figure S2. ^{7}Li NMR spectrum of LiTMP in D_8-THF at 233 K.

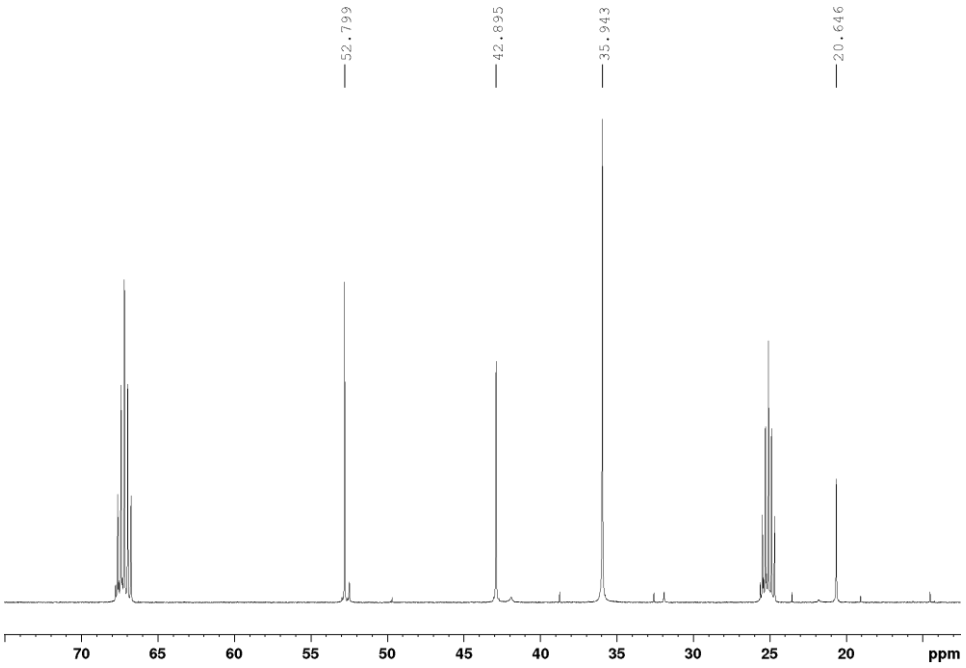


Figure S3. ^{13}C NMR spectrum of LiTMP in D_8-THF at 233 K.

3.10 Synthesis and Characterization of $Zn(TMP)_2$

$Zn(TMP)_2$ was prepared according to a modified literature procedure.[161] In an argon-flushed Schlenk flask, THF (15 mL) was added alongside 3.2 mL (20 mmoles) of TMP(H) and cooled to 0 °C. To this, an equimolar amount of *n*BuLi (12.6 mL, 20 mmoles, 1.6 M in hexanes) was added dropwise with constant stirring which resulted in the formation of a pale-yellow solution. 10 mmol of $ZnCl_2$ (1.36 g) was then added and the reaction stirred at ambient temperature overnight. The suspension was then filtered through dry celite and glaswool, collecting the yellow liquors. All volatiles were then reoved from the liquors, resulting in a pale yellow, waxy solid which was then suspended in 30 mL hexane. The suspension was filtered through a plug of dry celite and glasswool to furnish yellow liquors. The liquors were dried under reduced pressure to give crude $Zn(TMP)_2$ as a white solid, yield = 98 %. $Zn(TMP)_2$ can be purified by sublimation at 90 °C under dynamic vacuum to yield a white, crystalline solid.

^{1}H-NMR (D_8-THF, 400 MHz, 233 K): δ [ppm] = 1.75-1.62 (m, 4H, γ-CH_2), 1.36-1.29 (br. t, 8H, β-CH_2), 1.22 (s, 24H, CH_3).

^{13}C-NMR (D_8-THF, 100.6 MHz, 233 K): δ [ppm] = 53.3 (α-C_q), 39.8 (β-CH$_2$), 36.8 (CH$_3$), 19.7 (γ-CH$_2$).

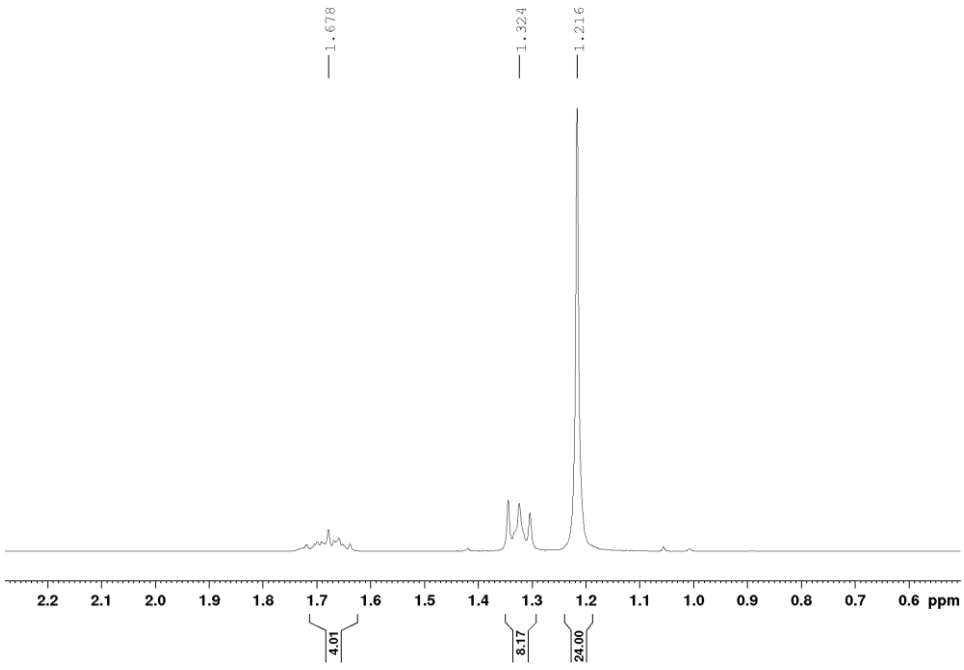


Figure S4. ^{1}H NMR spectrum of $Zn(TMP)_2$ in D_8-THF.

[161] a) D. R. Armstrong, A. R. Kennedy, R. E. Mulvey, J. A. Parkinson, S. D. Robertson, *Chem. Sci.* **2012**, *3*, 2700; b) W. S. Rees, O. Just, H. Schumann, R. Weimann, *Polyhedron*, **1998**, *17*, 1001–1004.

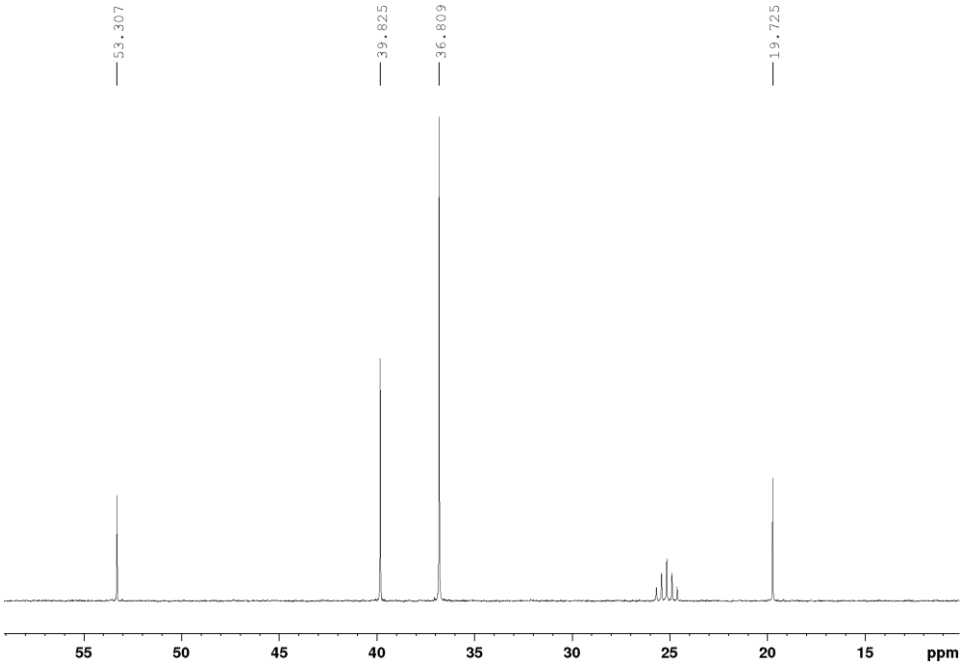


Figure S5. ^{13}C NMR spectrum of $Zn(TMP)_2$ in D_8-THF.

3.11 NMR Spectroscopic Characterization of TMPZnBr·LiBr (162b)

In a J. Young's tap NMR tube, equimolar amounts of LiTMP (25.7 g, 0.175 mmol) and $ZnBr_2$ (39.4 mg, 0.175 mmol) were added and subsequently dissolved in 0.77 mL of D_8-THF. Note that it was important to combine the solids prior to dissolution, in order to avoid competing reactivity of LiTMP with the D_8-THF solvent.

^{1}H-DOSY NMR was used to estimate the molecular weight and aggregation of TMPZnBr·LiBr in solution based on the diffusion coefficients obtained from this experiment using Stalke's external calibration method and heavy element correction against the normalized diffusion of tetraphenylnaphthalene as an internal standard.

^{1}H-NMR (D_8-THF, 400 MHz, 233 K): δ [ppm] = 1.69-1.58 (br. m, 2H, γ-CH_2), 1.29 (br. t, 2H, β-CH_2), 1.18 (s, 12H, CH_3).

^{7}Li-NMR (D_8-THF, 155.5 MHz, 233 K): δ [ppm] = 0.03.

^{13}C-NMR (D_8-THF, 100.6 MHz, 233 K): δ [ppm] = 53.1 (α-C_q), 39.6 (β-CH$_2$), 36.6 (CH$_3$), 19.5 (γ-CH$_2$).

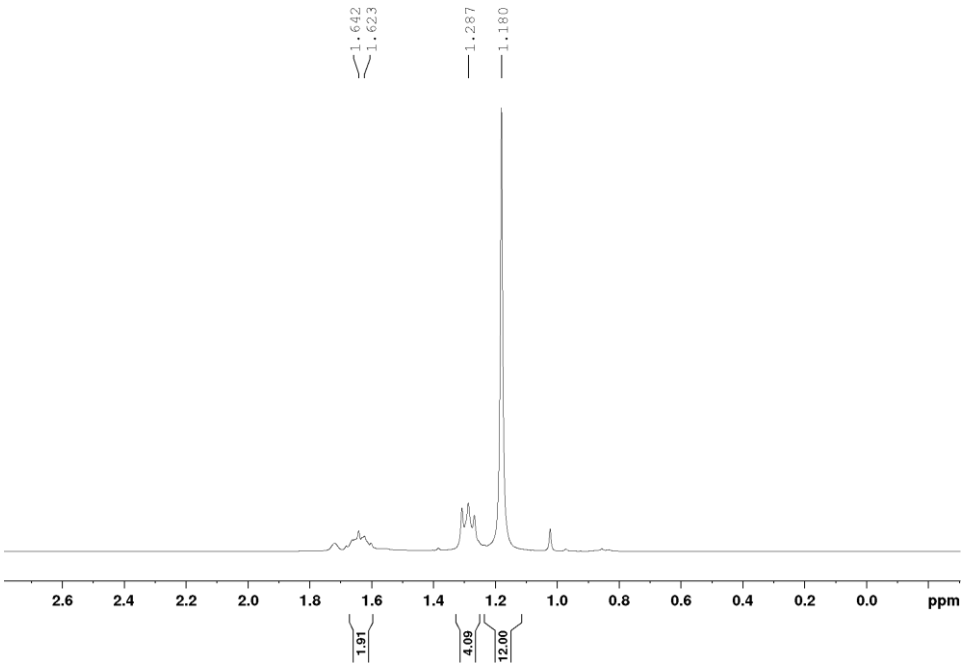


Figure S6. ^{1}H NMR spectrum of TMPZnBr·LiBr in D_8-THF.

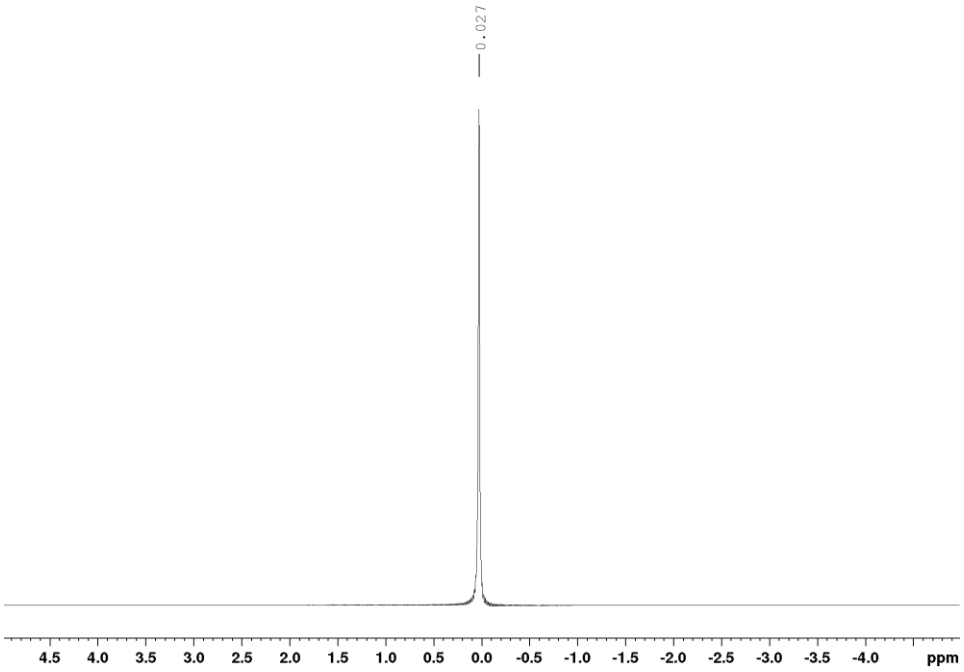


Figure S7. ^{7}Li NMR spectrum of TMPZnBr·LiBr in D_8-THF.

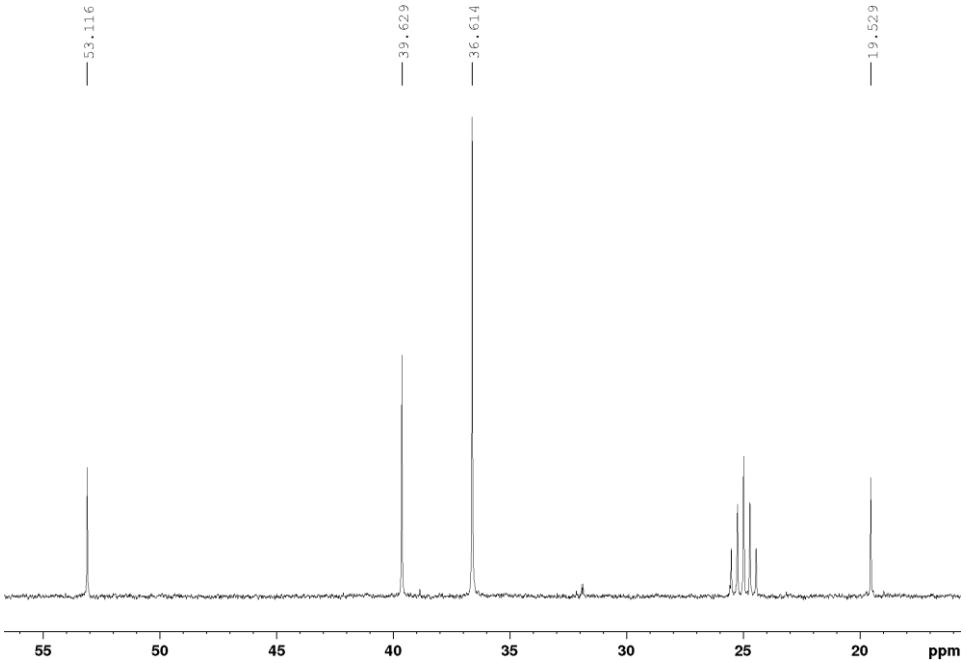


Figure S8. ^{13}C NMR spectrum of TMPZnBr·LiBr in D_8-THF.

3.12 Concentration Effect of Pyrimidine Metalation Using TMPZnBr·LiBr (162b)

The following experimental preparations were performed inside a glovebox.

In a J. Young's NMR tube, 0.1 mmol (7.9 μL) of pyrimidine was dissolved in 0.42 mL of D_8-THF, alongside 50 mol % (8.1 mg of C_6Me_6). In a glass sample vial, 25.7 mg (0.175 mmol) of LiTMP was charged alongside $ZnBr_2$ (39.4 mg, 0.175 mmol) and subsequently dissolved in 0.35 mL of D_8-THF, forming TMPZnBr·LiBr (3b). The solution of 3b was then added into the NMR tube containing the substrate and C_6Me_6. The reaction was mixed at ambient temperature for 6 h and analyzed by NMR spectroscopy.

Analysis of the reaction mixture by NMR spectroscopy showed complete consumption of pyrimidine, accompanied by formation of TMP(H). The aromatic region of the ^1H NMR spectrum shows a highly complex series of products (see Figure S and Figure 1b in the supporting manuscript). Further studies (*vide infra*) confirm that these are all representative of selective, C(2)-metalation of pyrimidine and not as a result of non-selective or poly-metalation. The ^7Li NMR spectrum shows a singular resonance at δ 0.33 ppm (Figure S).

Notably, a prominent set of signals at δ 9.22 ppm (d) and δ 7.79 ppm (t) are shown to increase in intensity under dilute conditions (0.013 M) – see Figure S and Figure 1c in the supporting manuscript for further insight. This lends weight to the fact that the complex aromatic region of the ^1H NMR spectrum is representative of different solution-state conformations of C(2)-metalated pyrimidine, clearly influenced by solvation state and aggregation.

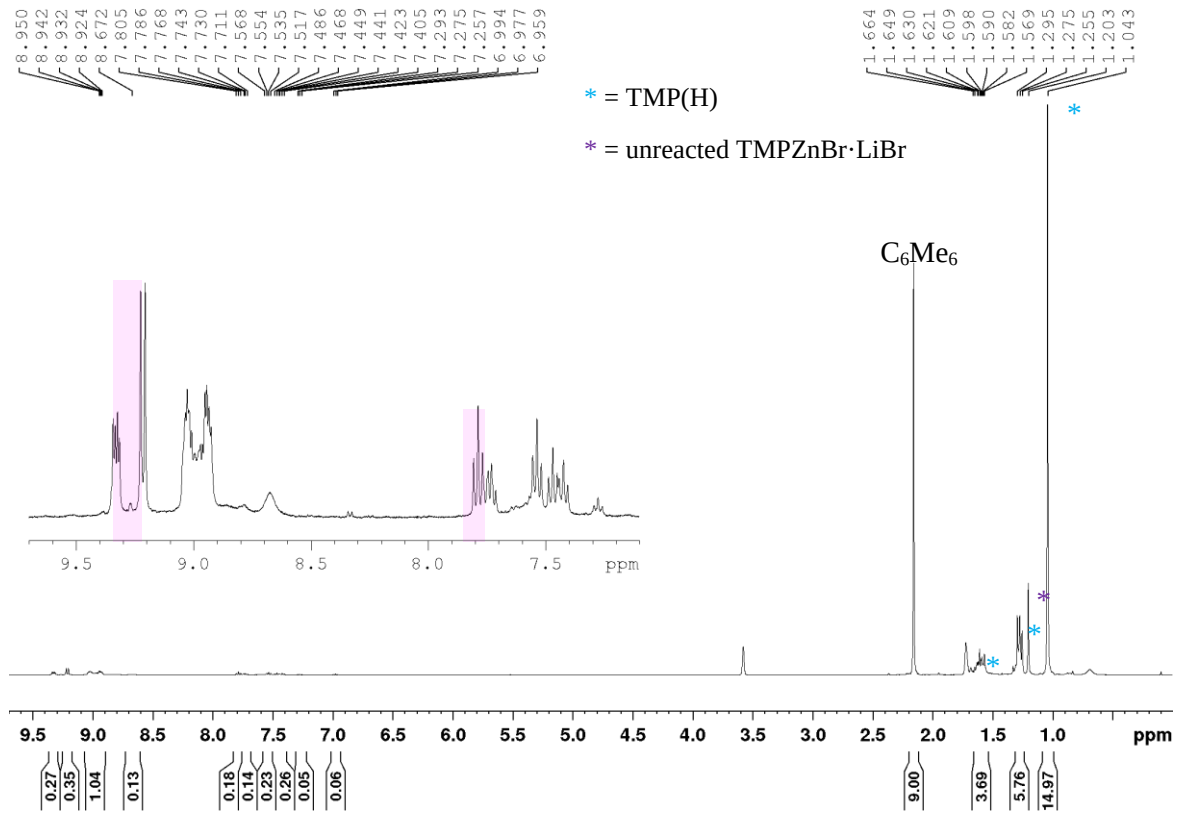


Figure S9. ^{1}H NMR spectrum of metalation of pyrimidine with **162b** in D_8-THF (0.13 M).

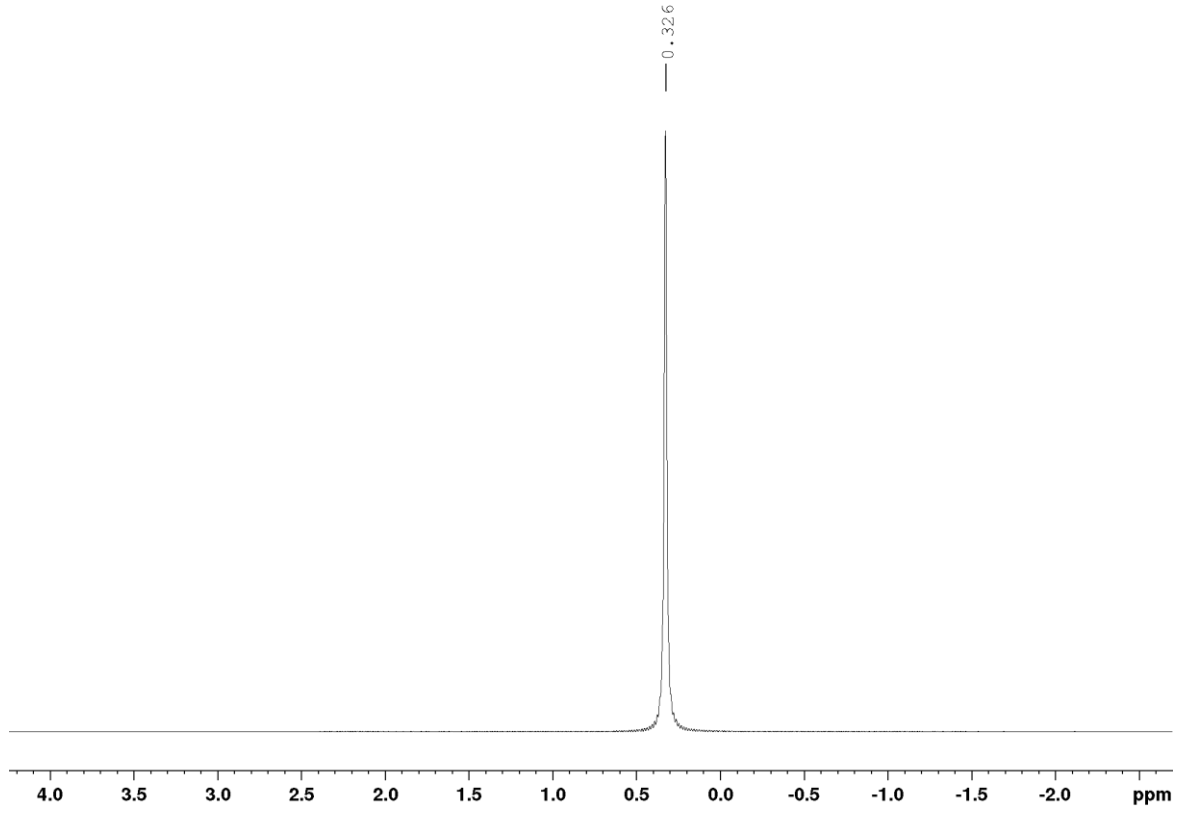


Figure S10. ^{7}Li NMR spectrum of metalation of pyrimidine with **162b** in D_8-THF (0.13 M).

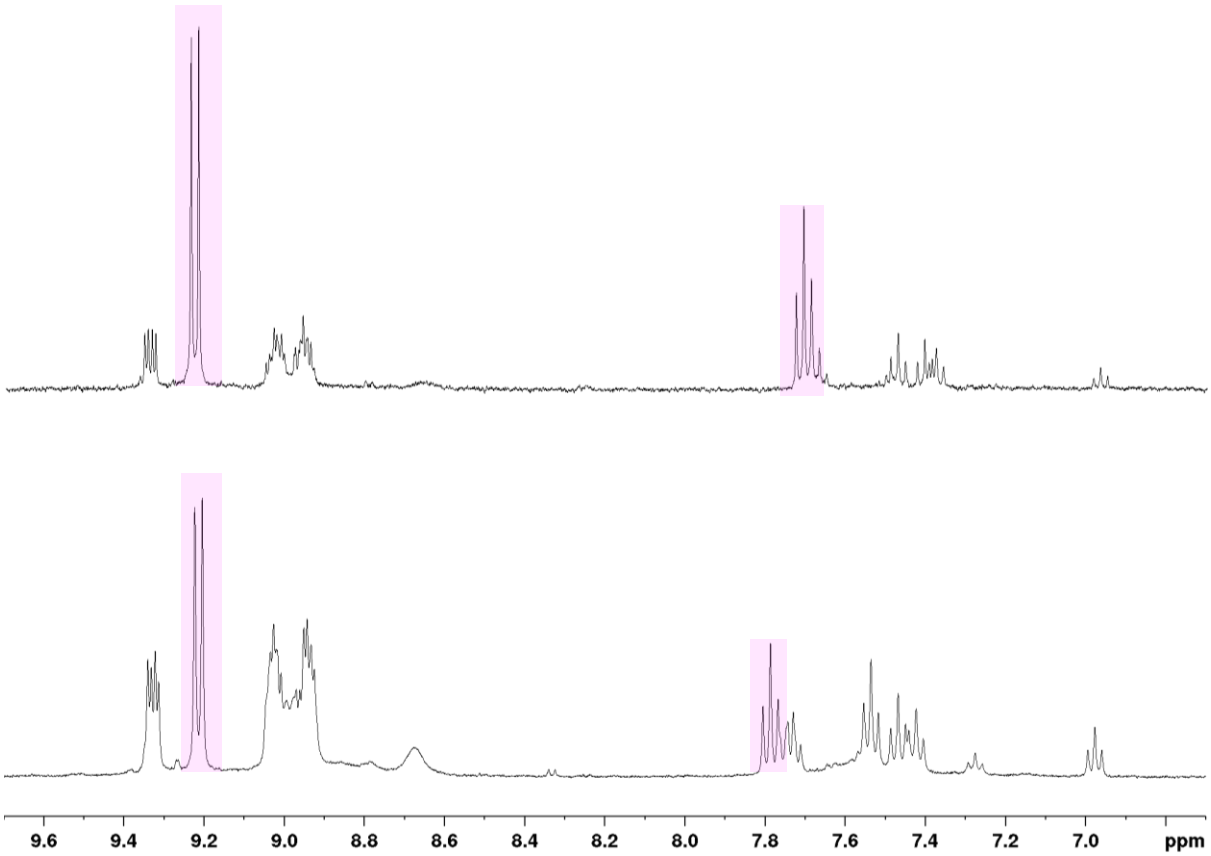


Figure S11. ^{1}H NMR spectrum of metalation of pyrimidine with **162b** in D_8-THF (top 0.013 M, bottom 0.13 M).

3.13 Salt Effects to the Metalation of Pyrimidine by TMPZnBr·LiBr (162b)

The following experimental preparations were performed inside a glovebox.

In a J. Young's NMR tube, 0.1 mmol (7.9 µL) of pyrimidine was dissolved in 0.42 mL of D_8-THF, alongside 50 mol % (8.1 mg of C_6Me_6). In a glass sample vial, 25.7 mg (0.175 mmol) of LiTMP was charged alongside $ZnBr_2$ (39.4 mg, 0.175 mmol) and subsequently dissolved in 0.35 mL of D_8-THF, forming TMPZnBr·LiBr (3b). The solution of 3b was then added into the NMR tube containing the substrate and C_6Me_6. The reaction was mixed at ambient temperature for 6 h, which was followed by the addition of either $ZnBr_2$ (0.2 mmol, 45 mg), LiBr (0.1 mmol, 8.6 mg) or $MgBr_2$ (0.2 mmol, 36.8 mg).

Neither LiBr (Figure S) nor $MgBr_2$ (Figure S) had an effect on the mixture of products observed in the complex aromatic region of the ^{1}H NMR spectrum. However, $ZnBr_2$ had a drastic effect and promoted complete convergence into a singular species with diagnostic signals at δ 9.20 ppm (d) and δ 7.77 ppm (t) (Figure S). This latter effect can also be seen with gradual increasing increments of $ZnBr_2$ (Figure S).

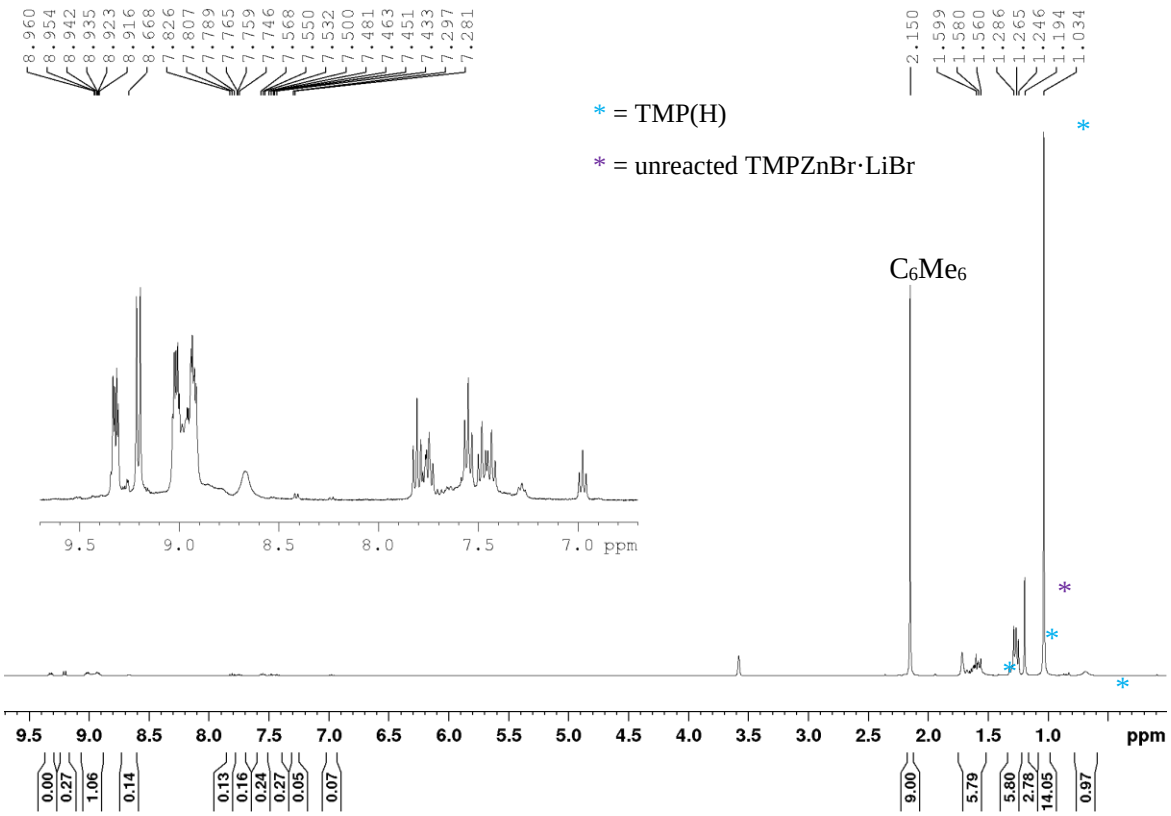


Figure S12. ^{1}H NMR spectrum of metalation of pyrimidine by **162b** in D_8-THF with added LiBr.

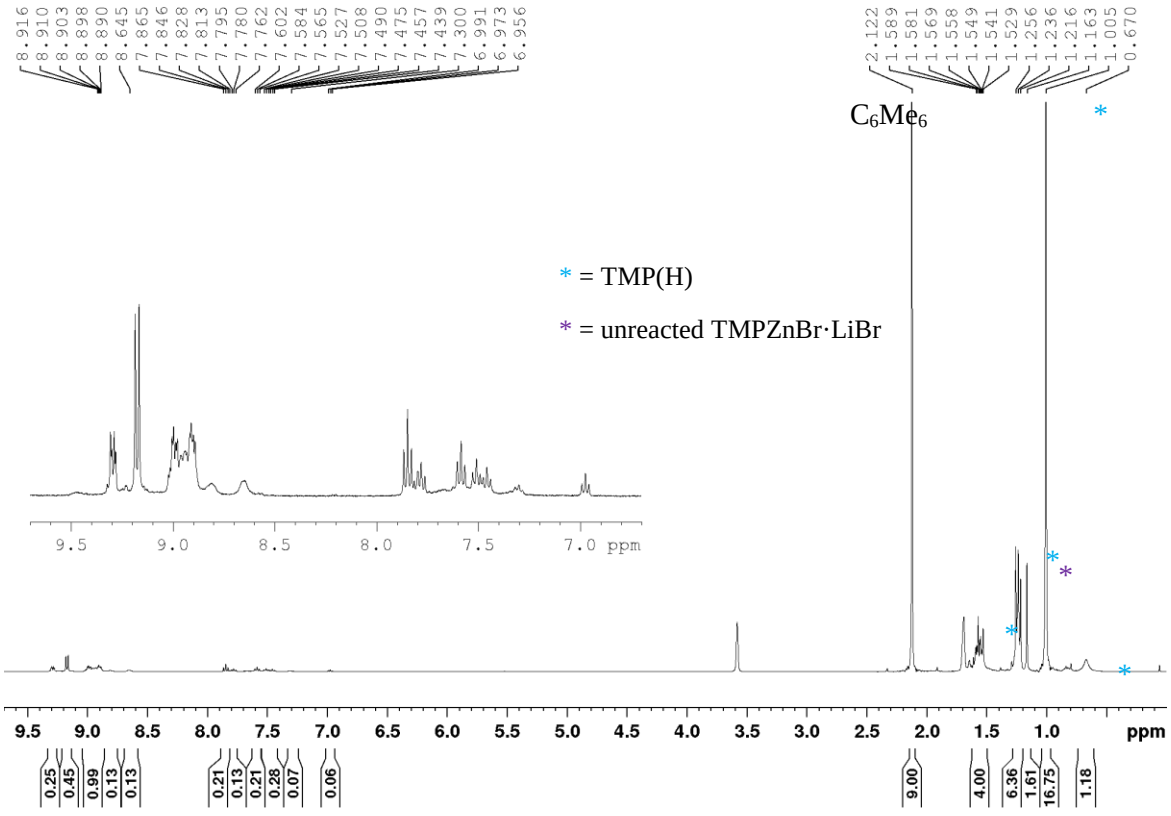


Figure S13. ^{1}H NMR spectrum of metalation of pyrimidine by **162b** in D_8-THF with added LiBr.

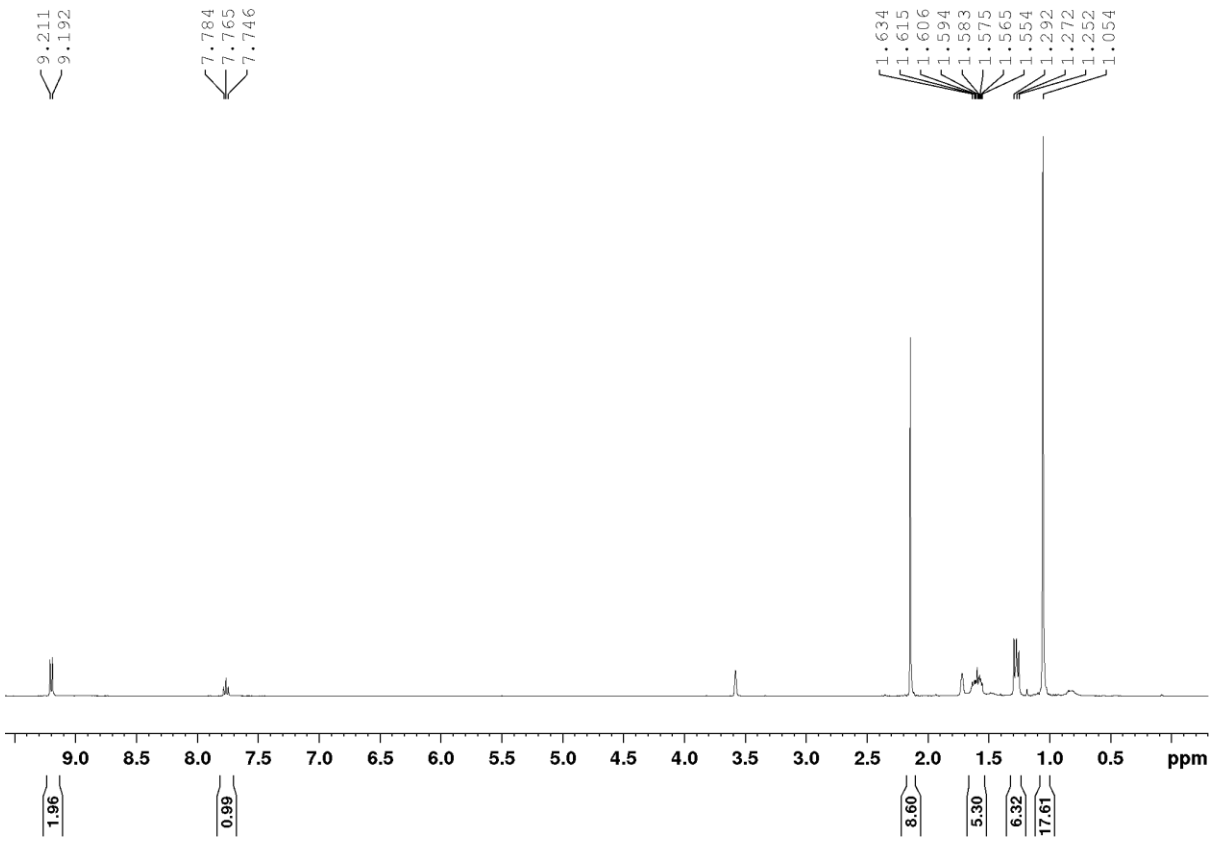


Figure S14. ^{1}H NMR spectrum of metalation of pyrimidine by **162b** in D_8-THF with added $ZnBr_2$.

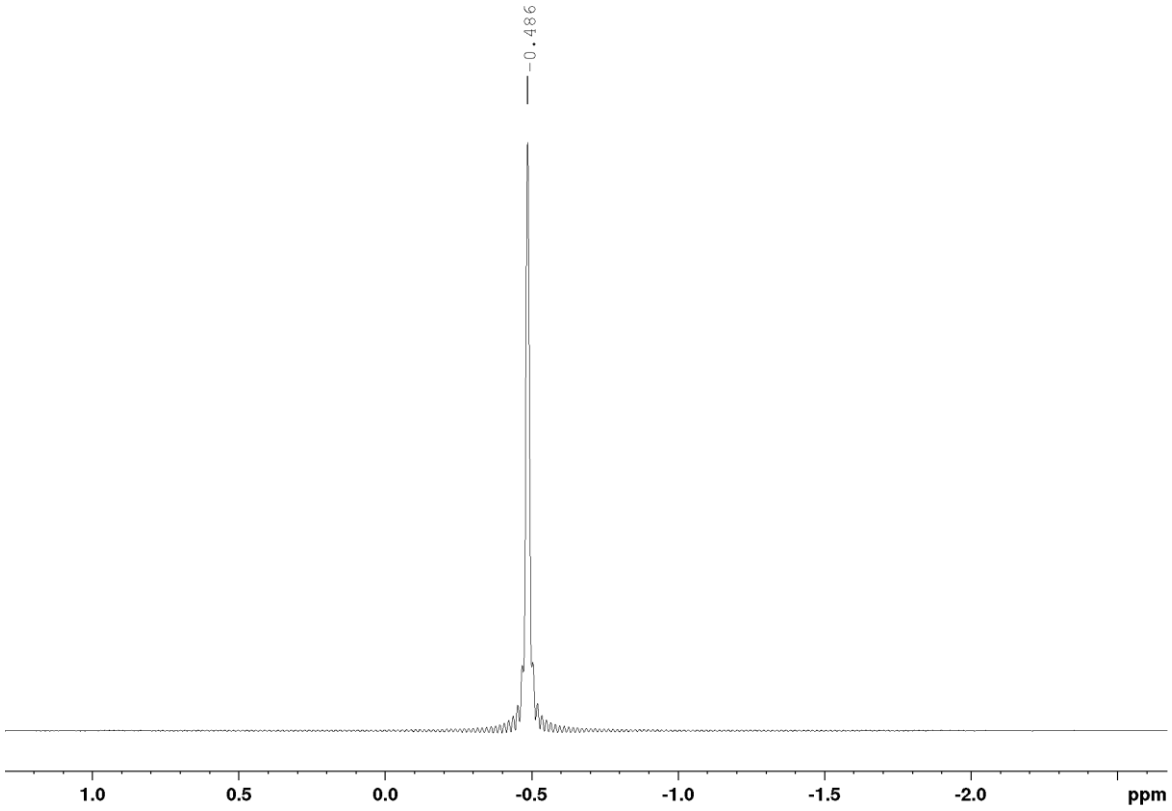


Figure S15. ^{1}Li NMR spectrum of metalation of pyrimidine by **162b** in D_8-THF with added $ZnBr_2$.

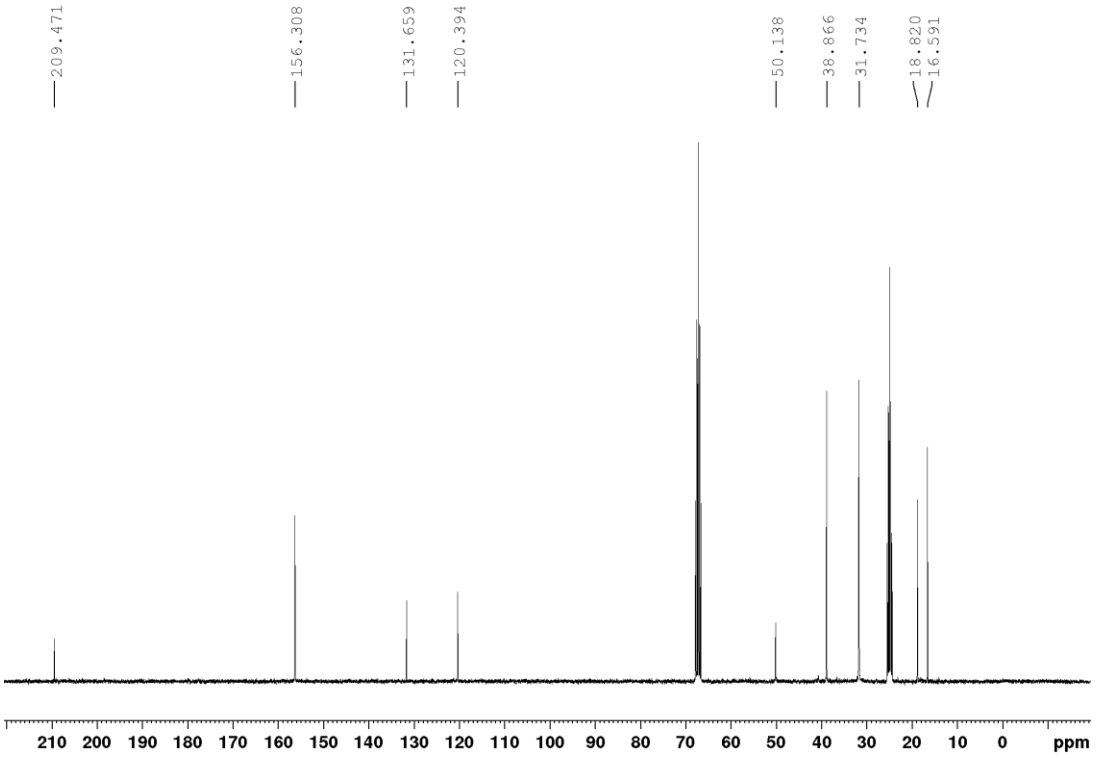


Figure S16. ^{13}C NMR spectrum of metalation of pyrimidine by **162b** in D_8-THF with added $ZnBr_2$.

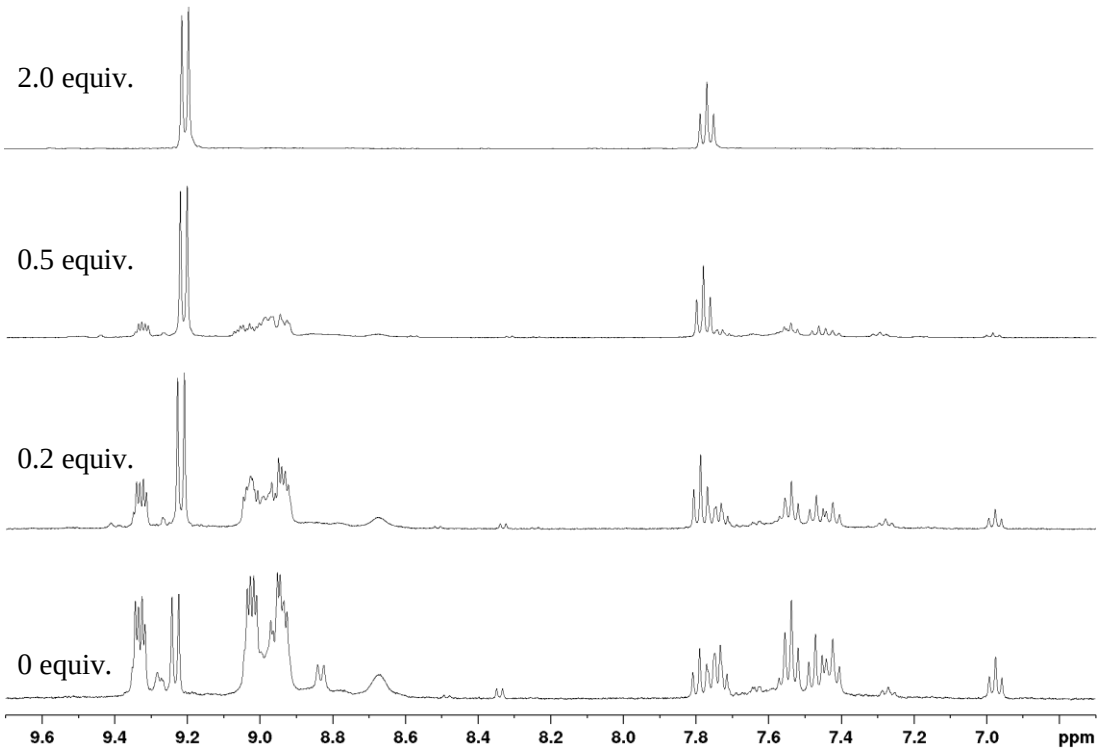
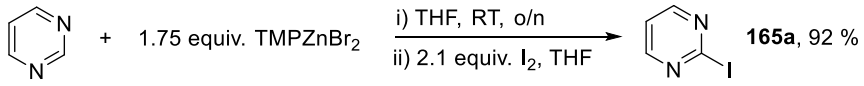


Figure S17. ^{1}H NMR spectrum of metalation of pyrimidine by **162b** in D_8-THF with increasing increments of $ZnBr_2$.

3.14 Reaction Between Pyrimidine and TMPZnBr



Scheme S1. Metalation and iodination of pyrimidine by TMPZnBr.

$ZnTMP_2$ (151 mg, 0.875 mmol), $ZnBr_2$ (99 mg, 0.875 mg) and C_6Me_6 (24.3 mg, 30 mol %) were weighted into a Schlenk flask and dissolved in 3.8 mL of dry THF under argon. Pyrimidine (39 µL, 0.5 mmol) was added to the solution, resulting in the formation of a yellow/green suspension which was stirred at ambient temperature overnight. A solution of I_2 (280 mg, 1.1 mmol) was prepared in 2 mL THF and then added to the reaction flask, followed by a stir period of 1.5 h. 6 mL of $Na_2SO_{3(sat.)}$ solution was added, and the mixture was extracted with 3 x 10 mL of EtOAc. The resultant organic fractions were dried over Na_2SO_4, filtered and an aliquot dried under reduced pressure for subsequent NMR spetroscopic analysis in $CDCl_3$.

The resultant spectrum showed 92 % of 2-iodopyrimidine. Spectroscopic signals are consistent with literature reports.[145a]

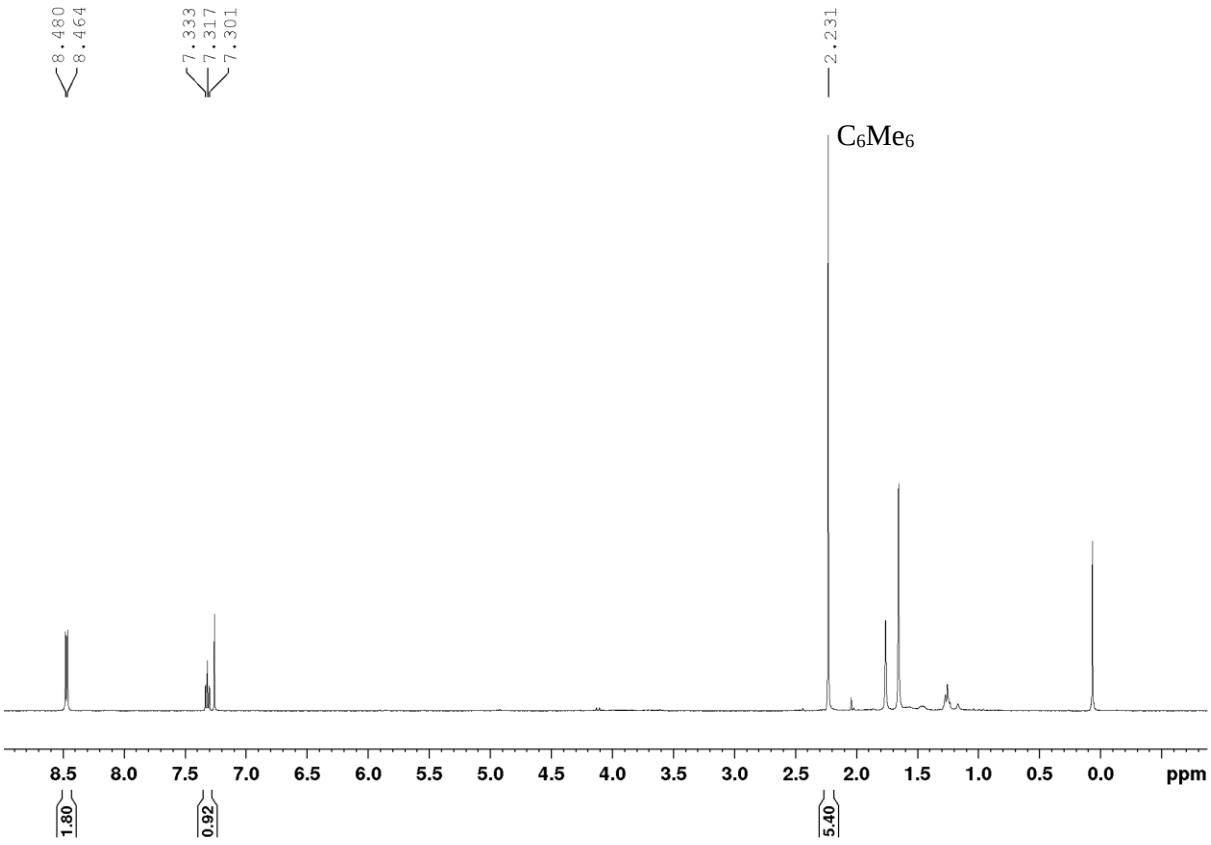
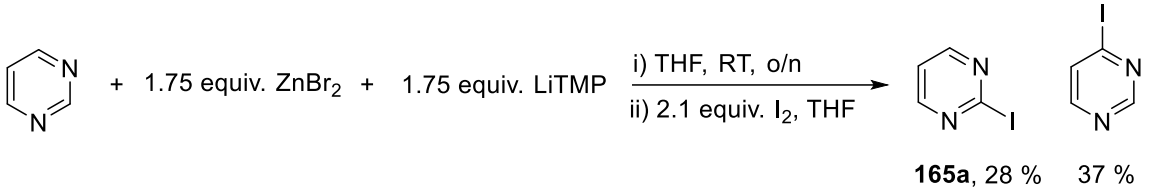


Figure S18. ^1H NMR spectrum of metalation of pyrimidine by TMPZnBr in $CDCl_3$.

3.15 Reaction Between Pyrimidine, $ZnBr_2$ and LiTMP



Scheme S2. Control reaction using $ZnBr_2$ as an additive, followed by metalation with LiTMP

Pyrimidine (39 µL, 0.5 mmol), C_6Me_6 (24.3 mg, 30 mol %) and $ZnBr_2$ (197 mg, 0.875 mmol) were dissolved in 3.8 mL of dry THF in a Schlenk flask under argon to give a pale yellow solution. To this, LiTMP (129 mg, 0.875 mmol) was added, resulting in a brown solution with a small amount of black precipitate. The mixture was stirred at ambient temperature overnight. A solution of I_2 (280 mg, 1.1 mmol) was prepared in 2 mL THF and then added to the reaction flask, followed by a stir period of 1.5 h. 6 mL of $Na_2SO_{3(sat.)}$ solution was added, and the mixture was extracted with 3 x 10 mL of EtOAc. The resultant organic fractions were dried over Na_2SO_4, filtered and an aliquot dried under reduced pressure for subsequent NMR spectroscopic analysis in $CDCl_3$.

The resultant NMR spectrum indicated a non-selective reaction, showing 28 % of 2-iodopyrimidine and 37 % of 3-iodopyrimidine,‡ as indicated by comparison to reference literature spectra.[145] It is postulated that a degree of polymetalation is also occurring, however the identity or quantity of such species could not be confidently commended upon.

‡ Confirmed by [^{1}H,^{1}H]-COSY NMR spectroscopy.

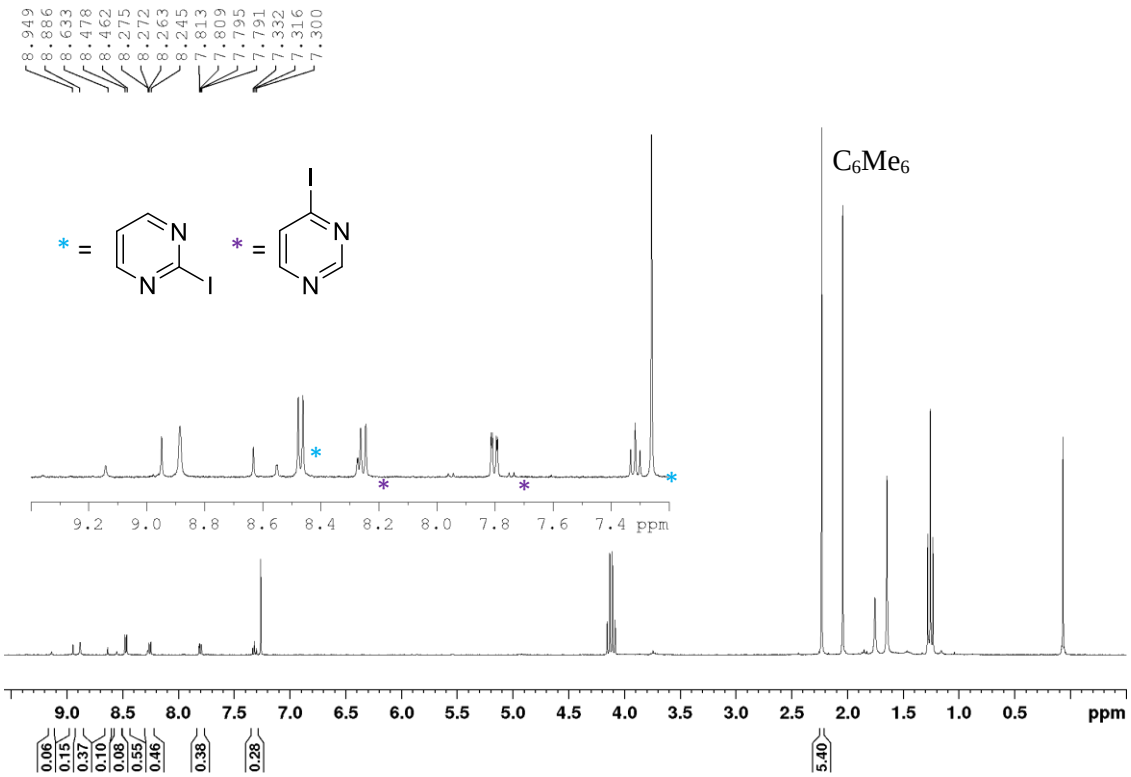


Figure S19. ^{1}H NMR spectrum of control reaction between pyrimidine, $ZnBr_2$ and LiTMP in $CDCl_3$.

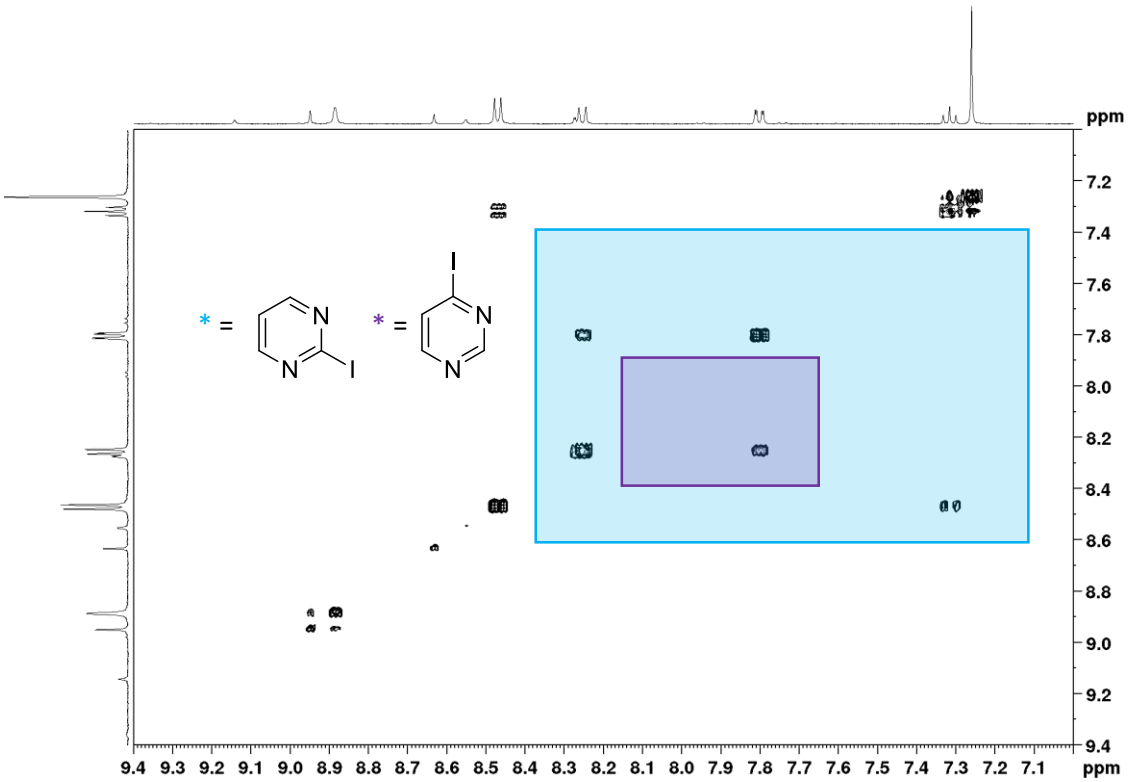


Figure S20. [^{1}H,^{1}H]-COSY NMR spectrum of control reaction between pyrimidine, $ZnBr_2$ and LiTMP in $CDCl_3$ highlighting correlations attributable to 2-iodo- and 3-iodopyrimidine^{1}H-DOSY NMR spectroscopic study of the reaction of pyrimidine and $Zn(TMP)_2$.

In a J. Young's tap NMR tube, equimolar amounts of $Zn(TMP)_2$ (35 mg, 0.1 mmol) and pyrimidine (8 µL, 0.1 mmol) were added and subsequently dissolved in 0.5 mL of D_8-THF.

Subsequent ^{1}H-DOSY NMR indicated there is no coordination of the pyrimidine substrate to the Zn centre in $Zn(TMP)_2$ based on two independent diffusion coefficients of the two compounds:

Pyrimidine (160a): D = 2.42 x10^{-9} m^{2}s^{-1}

Zn(TMP)$_2$: D = 9.28 x10^{-10} m^{2}s^{-1}

Note: No deprotonation of the substrate is observed in this reaction.

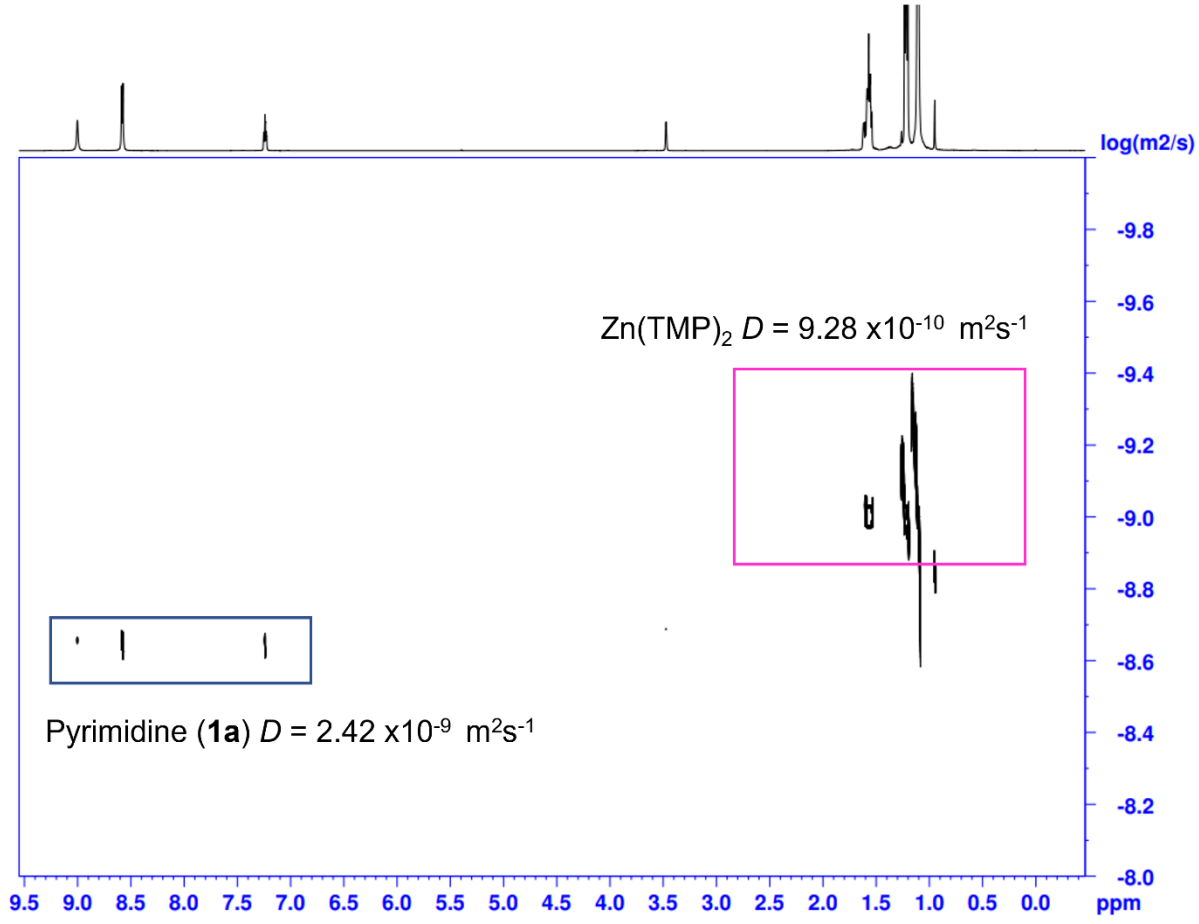


Figure S21. ^{1}H-DOSY NMR spectra of $Zn(TMP)_2$ and pyrimidine (**160a**) in D_8-THF.

^{1}H-DOSY NMR spectroscopic study of the reaction of TMPZnBr·LiBr

In a J. Young's tap NMR tube, equimolar amounts of LiTMP (1.1 mg, 0.0075 mmol) and $ZnBr_2$ (1.69 mg, 0.0075 mmol) were dissolved in d_8-THF (0.5 mL) and tetraphenylnaphthalene (3.24 mg, 0.0075 mmol) added to the mixture as an internal standard.

^{1}H-DOSY NMR was then used to estimate the molecular weight and aggregation of TMPZnBr·LiBr in solution. This is estimated based on the diffusion coefficients obtained from this experiment using Stalke's external calibration[162] method and heavy element correction[163] against the normalized diffusion coefficient of tetraphenylnaphthalene as an internal standard.

Determined molecular weight of "TMPZnBr·LiBr" based on diffusion coefficients = 449 g/mol. The expected molecular weight for a monomeric solvent separated ion pair system (SSIP) of formula $[\{Li(D_8\text{-}THF)_x\}^+\{ZnBr_2(TMP)(D_8\text{-}THF)\}^-]$ = 446 g/mol (1% difference). Contrastingly, the expected molecular weight for a monomeric contacted ion pair of formula $[LiZn(TMP)Br_2(d_8\text{-}THF)_2]$ = 533 (25% difference). These results suggest TMPZnBr·LiBr exist as a monomeric SSIP in THF solution; $[\{Li(D_8\text{-}THF)_x\}^+\{ZnBr_2(TMP)(D_8\text{-}THF)\}^-]$.

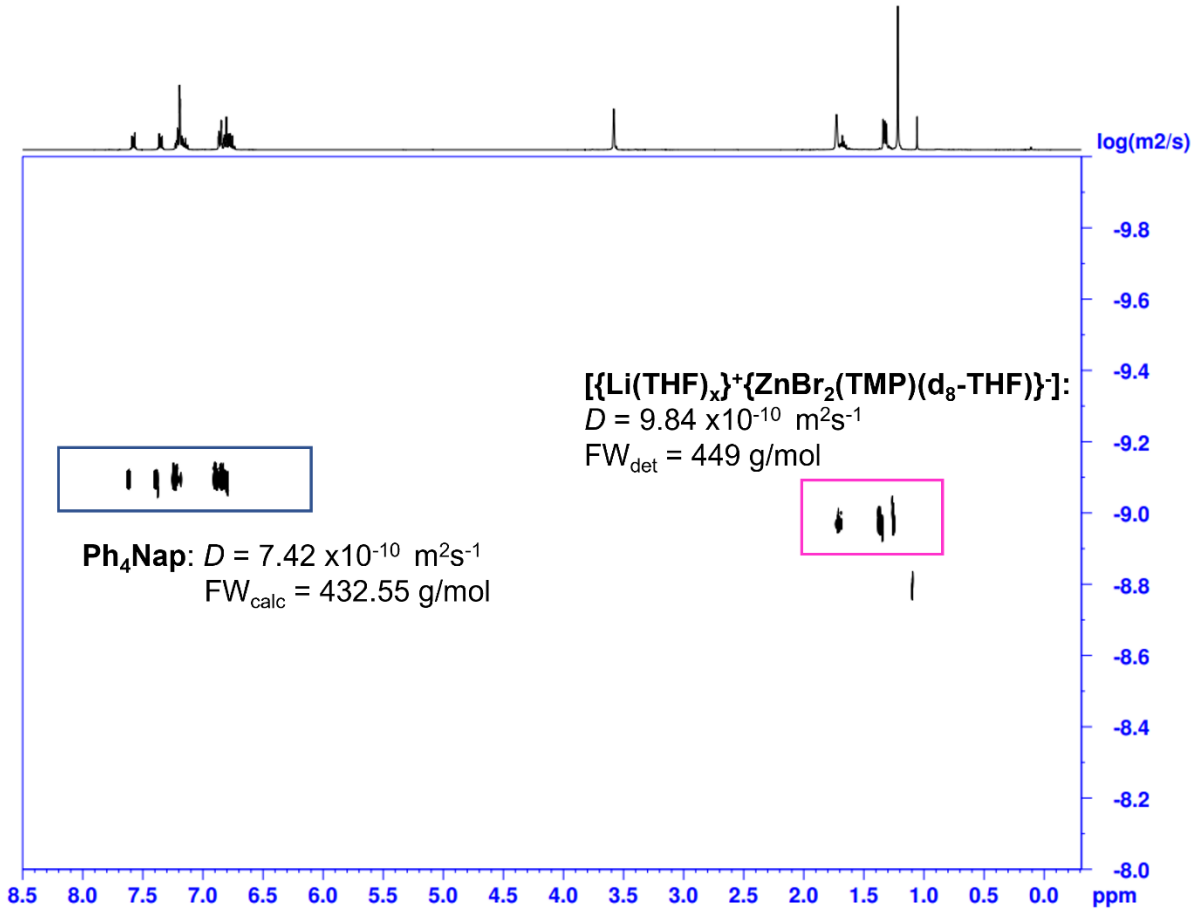


Figure S22. ^{1}H-DOSY NMR spectrum of TMPZnBr·LiBr in D_8-THF.

Synthesis of $[\{Li(THF)_4^+\{Zn(Me\text{-}C_4H_2N_2)_3(ZnBr_2)_3\}^-]$ (**168**)

[162] S. Bachmann, B. Gernert, D. Stalke, *Chem. Commun.* **2016**, *52*, 12861–12864.
[163] A. K. Kreyenschmidt, S. Bachmann, T. Niklas, D. Stalke, *ChemistrySelect*, **2017**, *2*, 6957–6960.

3.16 Synthesis and Characterisation of 168

In a Schlenk flask, 0.5 mmol (39 μL) of 5-methylpyrimidine was dissolved in 1 mL of dry THF. To this, a solution of TMPZnBr·LiBr in 2.8 mL THF (prepared by combining 129 mg LiTMP and 197 mg $ZnBr_2$ and dissolving in 2.8 mL THF) was added to the substrate, resulting in a yellow solution. The reaction mixture was stirred at ambient temperature overnight, at which point 1.75 equiv. of $ZnBr_2$ (197 mg, 0.88 mmol) was added and an orange solution afforded. The mixture was then concentrated under reduced pressure to a total volume of approximately 1 mL and then stored at -40 °C. After approximately 4 weeks at low temperature, a crop of colourless, block-shaped crystals had formed which were amenable for analysis by x-ray crystallography and confirmed to be [{$Li(THF)_4^+$}{$Zn(Me\text{-}C_4H_2N_2)_3(ZnBr_2)_3\}^-$] (9). A notably low yield of 100 mg (7 %) was obtained due to the high solubility of 9 in THF, rendering isolation difficult. However, NMR spectroscopic monitoring of the reaction showed quantitative conversion into the C2-metallated compound **168**; the spectral data of which is in accordance with that obtained for the isolated material (see section 6.2). Finally, despite repeated attempts, successful CHN analysis for this compound was unsuccessful.

^{1}H-NMR (D_8-THF, 400 MHz, 233 K): δ [ppm] = 9.08 (s, 6 H, C_{Ar}-*H*), 3.63-3.58 (m, THF), 2.42 (s, 9H, C*H*$_3$), 1.78-1.75 (m, THF).

^{7}Li-NMR (D_8-THF, 155.5 MHz, 233 K): δ [ppm] = -0.47.

^{13}C-NMR (D_8-THF, 100.6 MHz, 233 K): δ [ppm] = 205.3 (C_q-Zn), 156.4 (*C*$_{Ar}$-H), 130.4 (*C*$_q$-Me), 68.0 (THF), 26.1 (THF), 15.5 (*C*H$_3$).

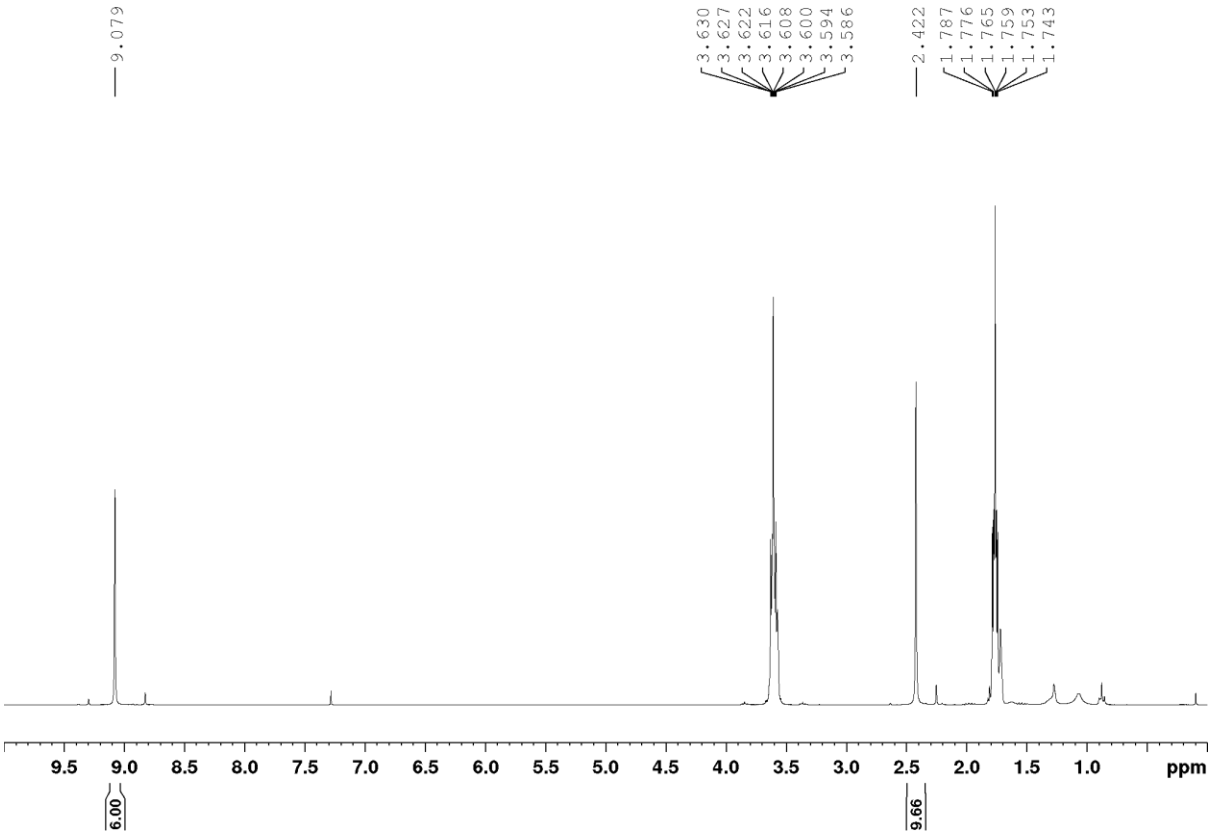


Figure S23. ^{1}H NMR spectrum of **168** in D_8-THF.

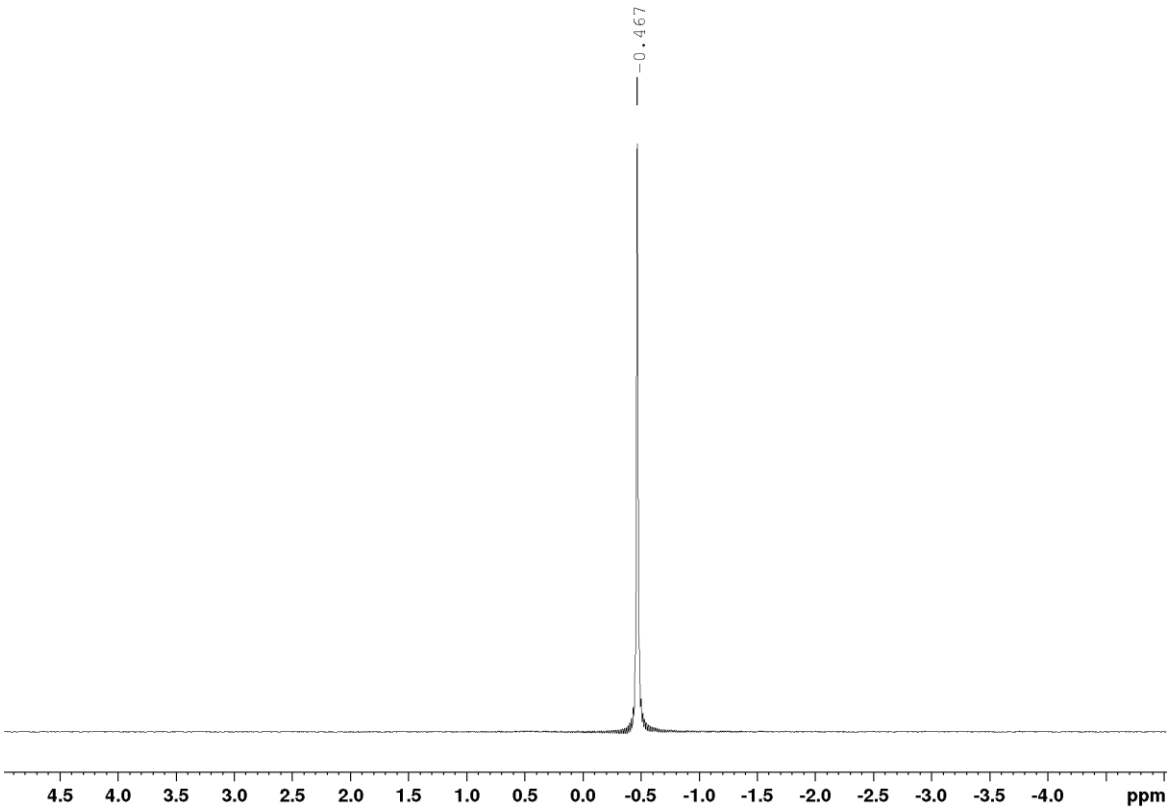


Figure S24. ^{7}Li NMR spectrum of **168** in D_8-THF.

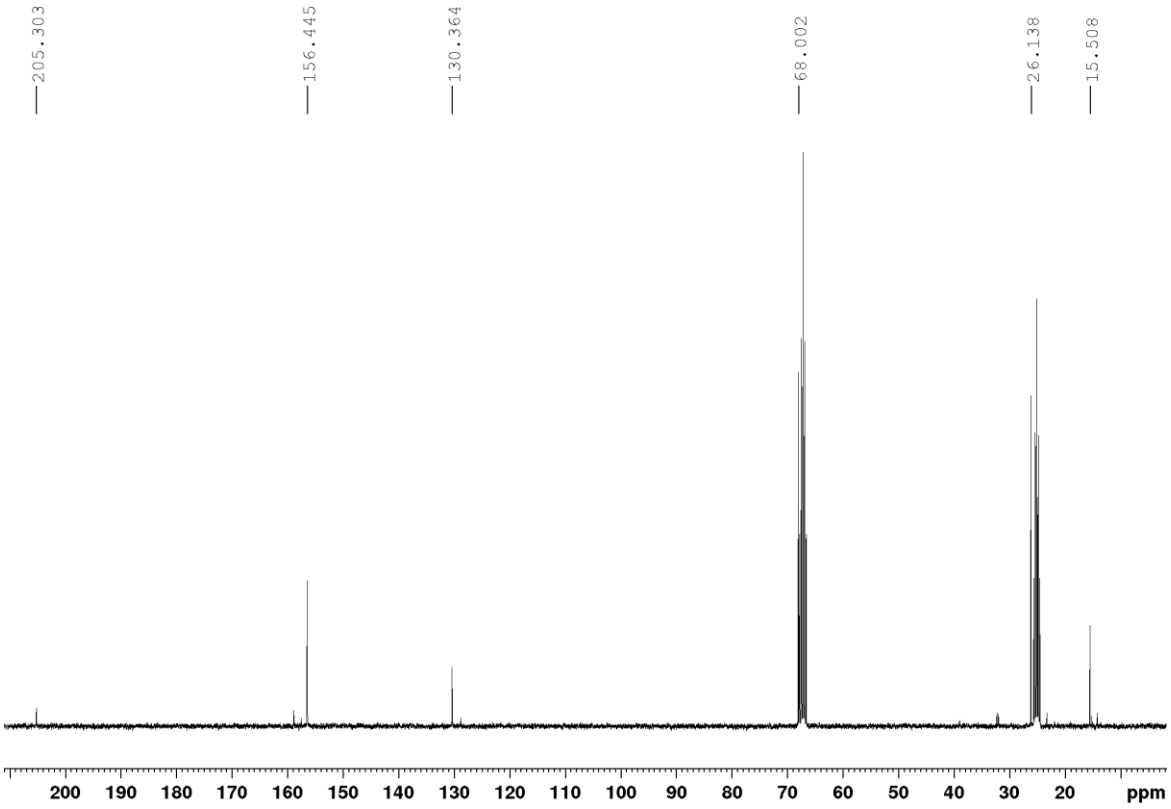


Figure S25. ^{13}C NMR spectrum of **16**8 in D_8-THF.

3.17 NMR Monitoring – Spectroscopically Tracking the Formation of 168

In a J. Young's NMR tube, 0.1 mmol (9.4 mg) of 5-methylpyrimidine was dissolved in 0.42 mL of D_8-THF, alongside 50 mol % (8.1 mg of C_6Me_6). In a glass sample vial, 25.7 mg (0.175 mmol) of LiTMP was charged alongside $ZnBr_2$ (39.4 mg, 0.175 mmol) and subsequently dissolved in 0.35 mL of D_8-THF, forming TMPZnBr·LiBr (3b). The solution of 3b was then added into the NMR tube containing the substrate and C_6Me_6. The reaction was mixed at ambient temperature for 12 h and analyzed by multinuclear NMR spectroscopy to reveal a complex mixture of species, which are all representative of the regioselective C2-metallation of the substrate – Figure S. Subsequent addition of an excess of $ZnBr_2$ (0.2 mmol, 45 mg) revealed quantitative convergence into a singular species by multinuclear NMR spectroscopy – the spectra of which are consistent with the in situ formation of **168** – Figure S.

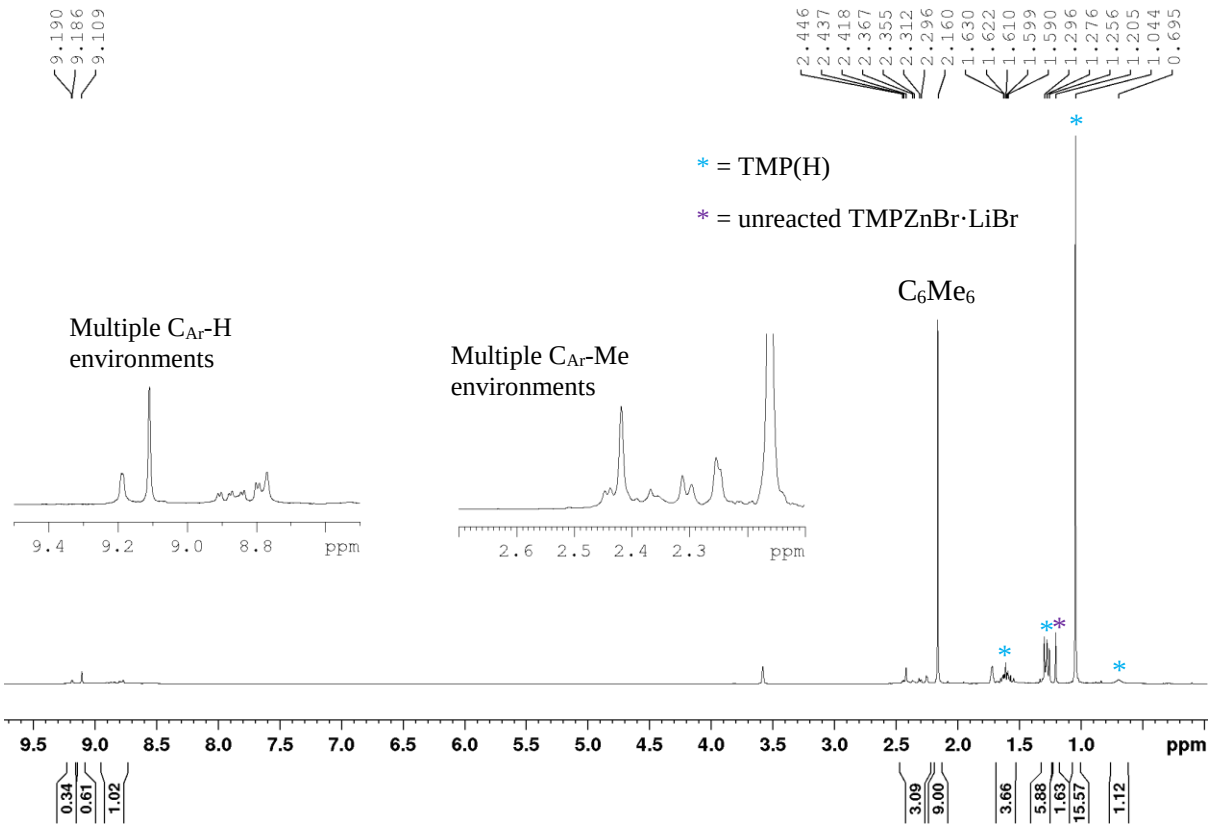


Figure S26. ^{1}H NMR spectrum of complex mixture of species formed from reaction between 5-methylpyrimidine and **162b** in D_8-THF.

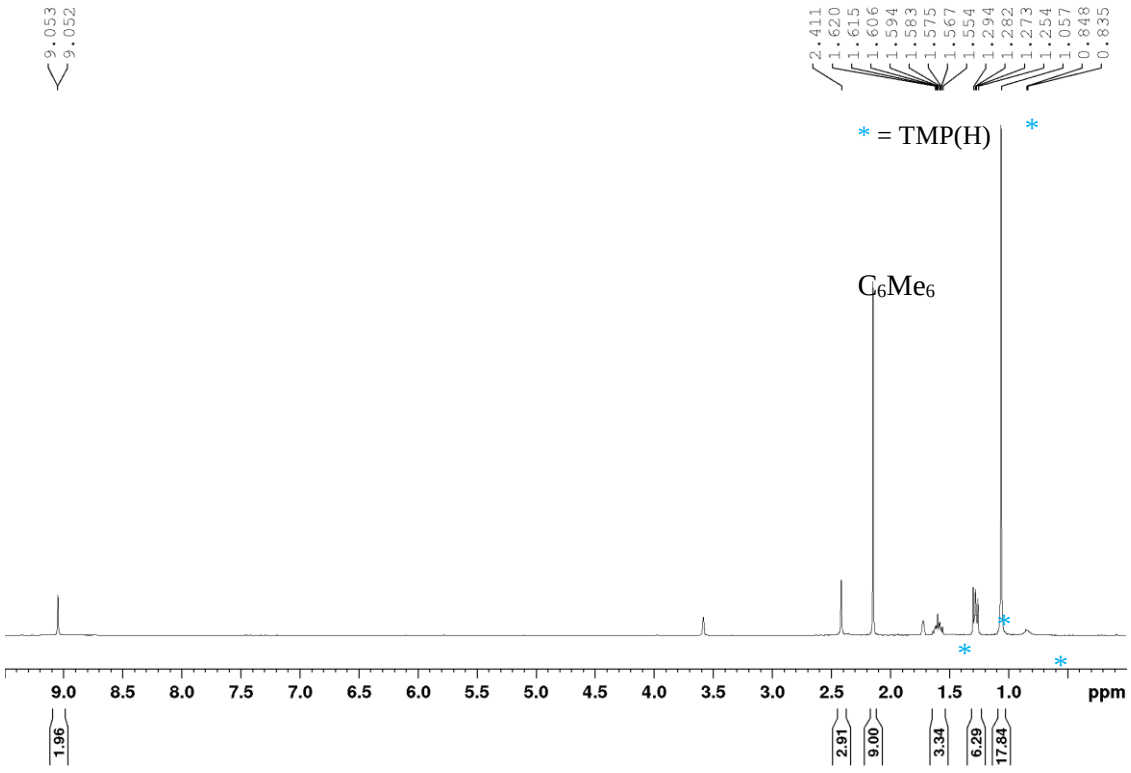


Figure S27. ^{1}H NMR spectrum of in situ formation of **168** from addition of 2 molar equivalents of $ZnBr_2$ to the reaction between 5-methylpyrimidine and **162b** in D_8-THF.

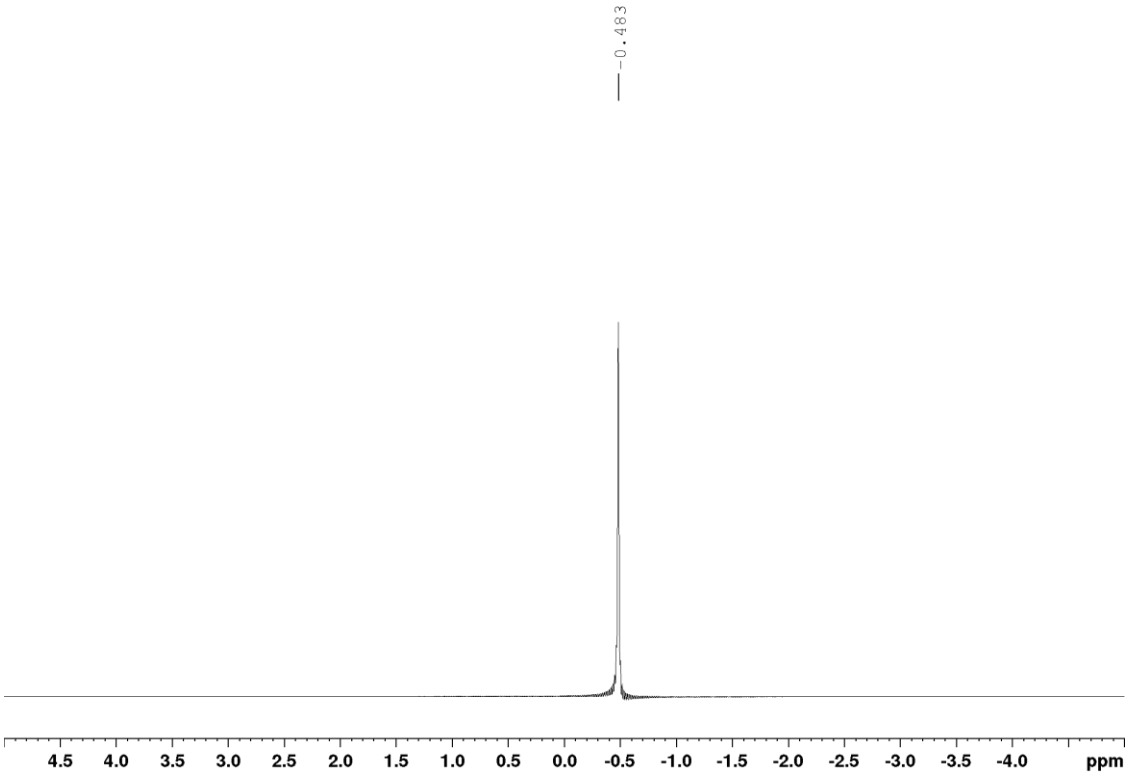
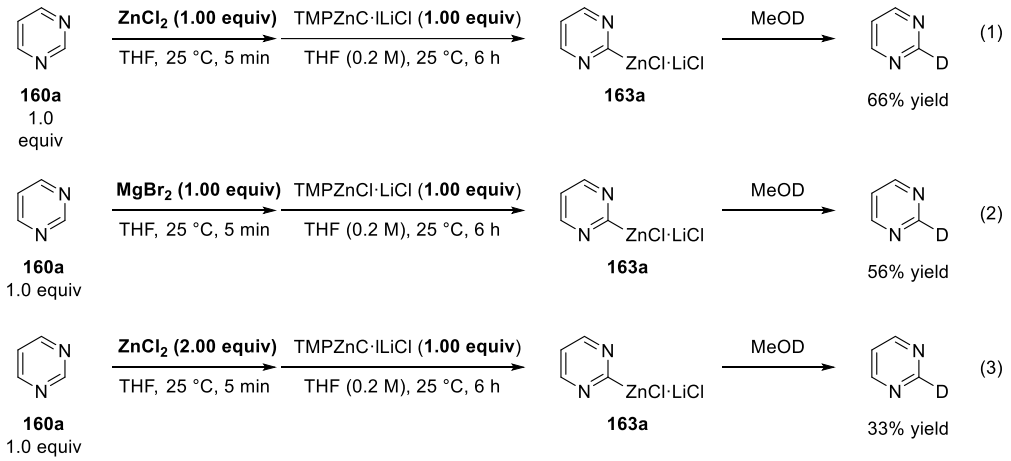


Figure S28. ^{7}Li NMR spectrum of in situ formation of **168** from addition of 2 molar equivalents of $ZnBr_2$ to the reaction between 5-methylpyrimidine and **162b** in D_8-THF.

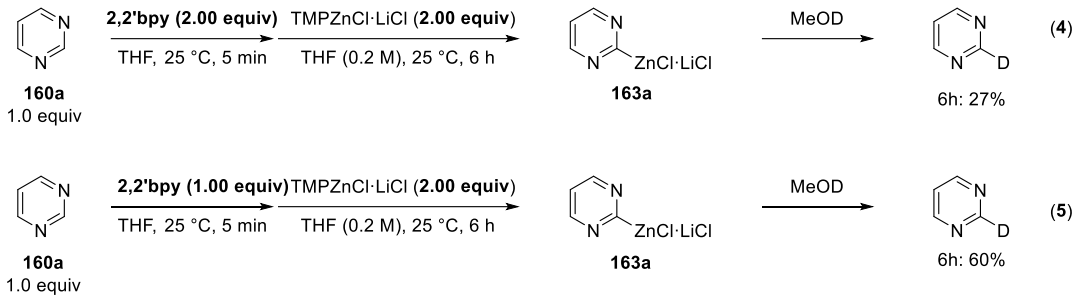
3.18 Additional Mechanistic Studies



Scheme S3. Metalation of **160a** in the presence of additional Lewis acids.

In some additional experiments (Scheme S3), we confirmed that complete zincation of **160a** can only be achieved using two equivalents of the base TMPZnCl·LiCl (**162a**, Figure S29). Thus, the addition of Lewis acids such as $ZnCl_2$ or $MgBr_2$ (1.0 equiv) improved the metalation using 1 equiv of **162a**

showing that an additional coordination facilitates the reaction (entries 1 and 2). Adding an excess of Lewis acid (2 equiv of $ZnCl_2$) shows a negative effect explained by unproductive complexation of **160a** with the Lewis acid (entry 3).



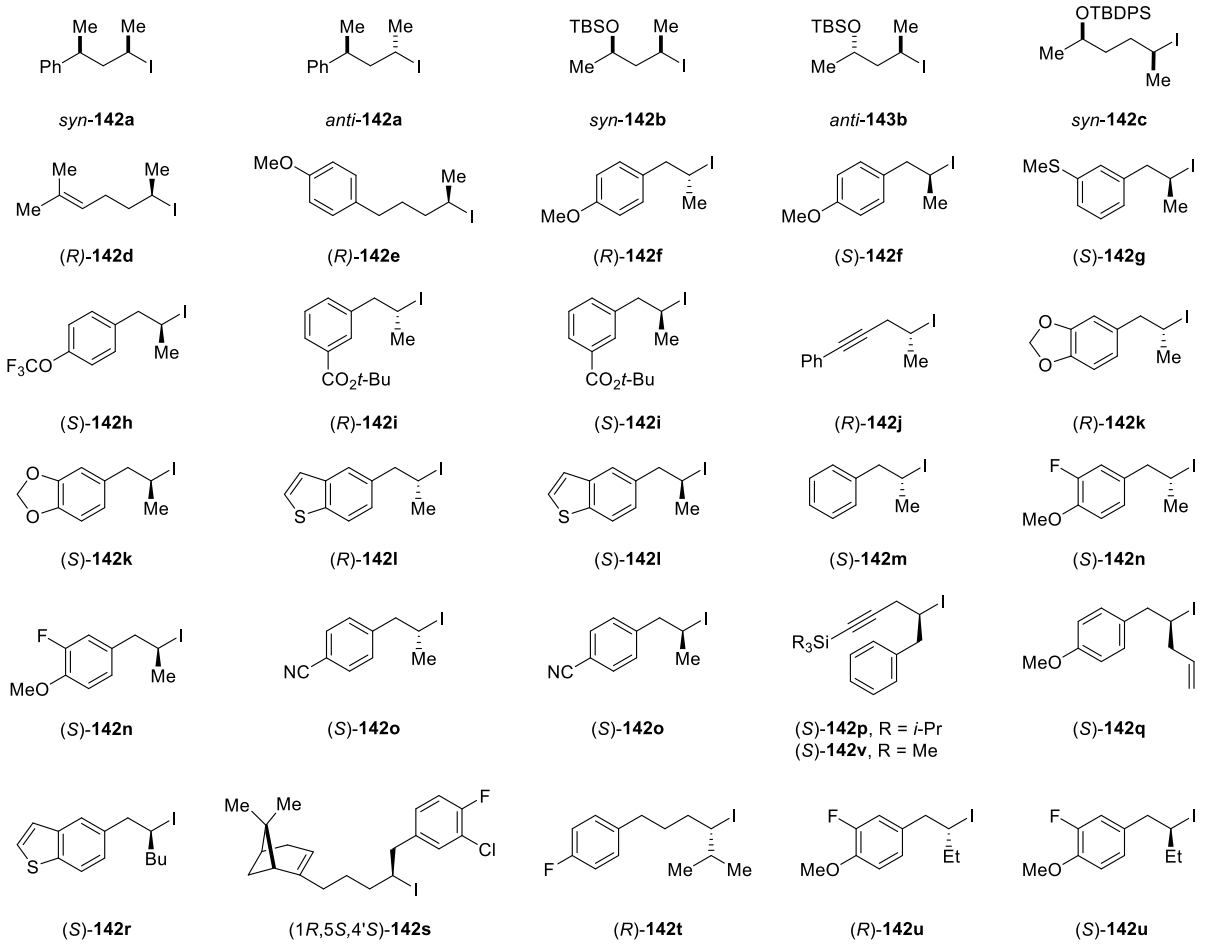
Scheme S4. Metalation of **160a** in the presence of additional 2,2'-bipyridine.

Furthermore, we have performed metalations of **160a** in the presence of the bidentate ligand such as 2,2'-bipyridine (Scheme S4). Using our optimized conditions (2.0 equiv of **162a**) for the metalation of **160a** in the presence of 2.0 equiv of the ligand led to a significant decrease in zincation (entry 4). Decreasing the amount of 2,2'-bipyridine to 1.0 equiv and using 2.0 equiv of **162a** led to 60% zincated **160a** (entry 5). In all cases, no zincation of 2,2'-bipyridine by **162a** was observed.

4 Synthesis of Starting Materials

4.1 Overview of Prepared Chiral Secondary Alkyl Iodides of Type 142

Several optically enriched secondary alkyl iodides (**142a-u**) have been prepared and used as starting materials for the stereoretentive I/Li exchange (Scheme S5). In all cases, the desired alkyl iodides could be prepared with high optical purity (>90% *ee*) from the corresponding optically enriched secondary alkyl alcohols (**158**). These alcohols were mainly prepared by copper-catalyzed expoxide opening of an arylmagnesium reagent with commercially available (*R*)- or (*S*)-propylene oxide.[120] In the course of this thesis, we have developed a method to prepare several other optically enriched epoxides (**157**) starting from (*R*)-epichlorohydrin (*R*-**156**) *via* copper-catalyzed epoxide opening and base mediated ring closing sequences.[122] These epoxides (**157**) were subsequently opened by magnesium or lithium reagents under copper catalysis. The obtained alcohols were subsequently stereoinverted under Appel conditions leading to the diversely functionalized secondary alkyl iodides **142p-s**.[121] Performing the I/Li-exchange reaction in the presence of a transmetalation reagents or in the presence of an electrophile allowed the tolerance of sensitive functional groups such as an ester (**142i**) or a nitrile (**142o**).



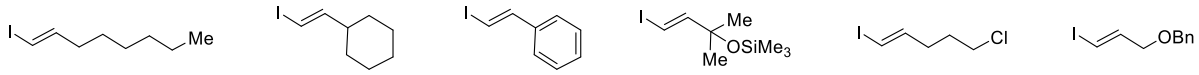
Scheme S5. Prepared optically enriched secondary alkyl iodides of type **142**.

4.2 Overview of Prepared and Used Electrophiles of Type 145, 149, 151 and 154

Alkenyl iodides of type **145** were prepared from the corresponding terminal alkynes *via* hydroalumination and subsequent iodination of the corresponding organoaluminum reagent (see Scheme S6a).[164] Aryl bromides of type **149** are commercially available and used as received from the supplier (see Scheme S6b). The electrophiles of type **151** are commercially available and have been used without further purification. The Weinreb amide **151r** was prepared from the corresponding acid chloride and *N*,*O*-dimethylhydroxylamine.[165] Furthermore, **151s** was prepared from *tert*-butyldimethylsilyl chloride and dihydroxyacetone (see Scheme S6c).[166] *O*-Benzoyl hydroxylamines (**154**) were prepared from commercial amines in two steps (Scheme S6d).[109f]

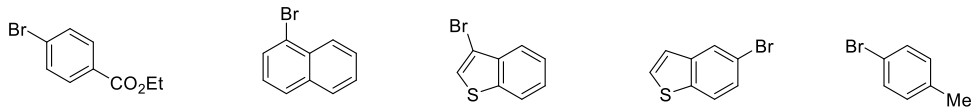
[164] B. M. Trost, M. T. Rudd, *Org. Lett.* **2003**, *5*, 4599-4602.
[165] H. J. A. Dale, C. Nottingham, C. Poree, G. C. Lloyd-Jones, *J. Am. Chem. Soc.* **2021**, *143*, 2097-2107.
[166] K. Ravindar, M. S. Reddy, P. Deslongchamps, *Org. Lett.* **2011**, *13*, 3178-3181.

a) used alkenyl iodides of type **145**



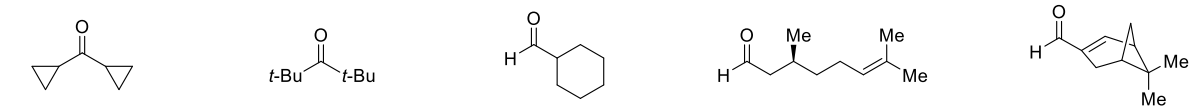
145a **145b** **145c** **145d** **145e** **145f**

b) used aryl bromides of type **149**

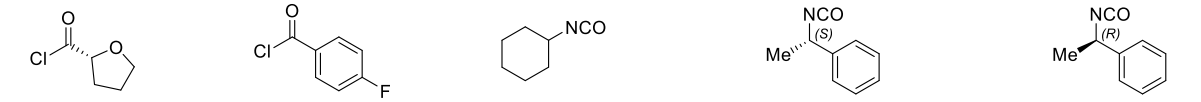


149a **149b** **149c** **149d** **149e**

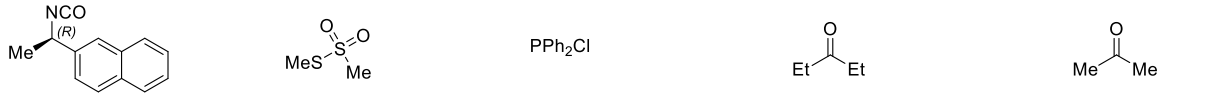
c) prepared and used electrophiles of type **151**



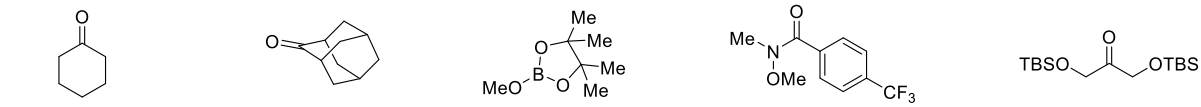
151a **151b** **151c** **151d** **151e**



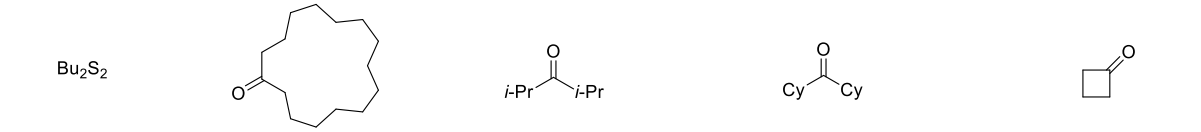
151f **151g** **151h** ***S*-151i** ***R*-151i**



***R*-151j** **151k** **151l** **151m** **151n**

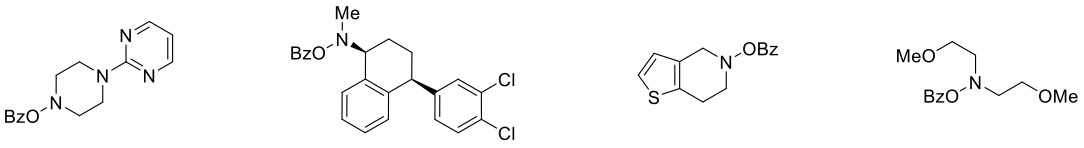


151o **151p** **151q** **151r** **151s**

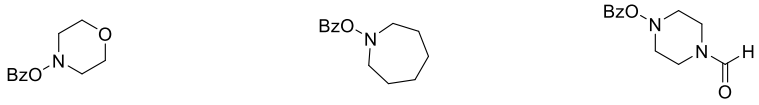


151t **151u** **151v** **151w** **151x**

d) prepared *O*-benzoyl hydroxylamines of type **154**



154a **154b** **154c** **154d**

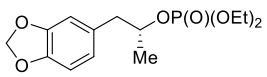


154e **154f** **154g**

Scheme S6. Prepared and used alkenyl iodides (**145**), aryl bromides (**149**), electrophiles of type **151** and *O*-benzoyl hydroxylamines (**154**).

4.3 Preparation of EX1, EX2 and EX4:

(*R*)-1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl diethyl phosphate (EX1):



EX1

A flask was charged with (*R*)-1-(benzo[*d*][1,3]dioxol-5-yl)propan-2-ol (180.1 mg, 1.0 mmol, 1.0 equiv) and THF (6 mL) and cooled to −78 °C. Then, a solution of *t*-BuLi (2.0 M in pentane, 0.55 mL, 1.1 mmol, 1.1 equiv) was added dropwise and the reaction mixture wasstirred for 30 min at this temperature. Diethyl chlorophosphate (189.8 mg, 1.1 mmol, 1.1 equiv) was added and the reaction mixture stirred for another 45 min at −78 °C before let warm to room temperature and stirred for 15 min at ambient temperature. The reaction mixture was quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phases were dried over MgSO4 and the solvent evaporated. The crude product was purified by flash column chromatography with diethyl ether to afford **EX1** (164.5 mg, 0.52 mmol, 52%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.76–6.62 (m, 3H), 5.91 (s, 2H), 4.71–4.53 (m, 1H), 4.16–3.86 (m, 4H), 2.89 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.79–2.65 (m, 1H), 1.37–1.20 (m, 9H).

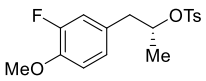
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.6, 146.3, 131.1, 122.7, 110.1, 108.2, 101.0, 76.4, 63.6, 43.6, 21.2, 16.3.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2982 (w), 2909 (w), 1609 (vw), 1504 (m), 1490 (m), 1460 (w), 1443 (m), 1392 (w), 1383 (w), 1369 (w), 1247 (s), 1212 (w), 1190 (w), 1166 (w), 1100 (w), 1028 (s), 991 (vs), 976 (vs), 940 (s), 928 (s), 859 (w), 808 (s), 774 (m), 742 (w), 726 (w), 714 (w).

MS (70 eV, EI): m/z (%): 122 (23), 105 (100), 77 (27).

HRMS (EI) for $C_{14}H_{21}PO_6$: calc. $[M-OEt]^{+\bullet}$: 271.0735, found: 271.0732.

(*R*)-1-(3-Fluoro-4-methoxyphenyl)propan-2-yl 4-methylbenzenesulfonate (EX2):



EX2

A flask was charged with TsCl (1.43 g, 7.5 mmol, 1.5 equiv), DMAP (1.22 g, 10.0 mmol, 2.0 equiv) and DCM (50 mL). Then, 1-(3-fluoro-4-methoxyphenyl)propan-2-ol (921 mg, 5.0 mmol, 1.0 equiv) dissolved in DCM (10 mL) was added in one portion. The reaction mixture was stirred overnight at ambient temperature and quenched with H_2O. The reaction mixture was extracted with DCM (3 x 100 mL) and the combined organic phases were dried over MgSO4 before concentration *in vacuo*.

The crude product was purified by flash column chromatography with *i*-hex/EtOAc (9:1) and 1% triethylamine to afford **EX2** (778 mg, 2.3 mmol, 46%) as a colorless solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.60–7.56 (m, 2H), 7.23–7.17 (m, 2H), 6.81–6.72 (m, 2H), 6.67–6.61 (m, 1H), 4.65 (dp, *J* = 7.4, 6.2 Hz, 1H), 3.85 (s, 3H), 2.79 (dd, *J* = 14.1, 7.4 Hz, 1H), 2.70 (dd, *J* = 14.2, 5.6 Hz, 1H), 2.42 (s, 3H), 1.34 (d, *J* = 6.3 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 153.3, 150.9, 146.6, 146.5, 144.6, 133.9, 129.7, 129.4, 129.3, 127.7, 125.3, 117.1, 116.9, 113.2, 80.6, 56.3, 42.0, 21.7, 21.0.

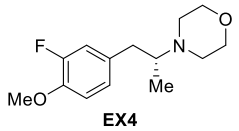
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2998 (w), 2939 (w), 1597 (w), 1585 (w), 1518 (m), 1516 (m), 1501 (m), 1492 (m), 1462 (m), 1454 (m), 1448 (m), 1432 (m), 1378 (m), 1369 (w), 1359 (s), 1343 (m), 1321 (m), 1303 (w), 1292 (w), 1279 (m), 1270 (m), 1228 (m), 1220 (m), 1208 (w), 1185 (s), 1172 (s), 1147 (m), 1132 (s), 1124 (m), 1118 (m), 1101 (m), 1094 (s), 1026 (s), 1017 (m), 961 (m), 936 (w), 914 (s), 906 (s), 888 (vs), 871 (vs), 844 (w), 832 (w), 819 (m), 807 (s), 799 (m), 762 (s), 746 (s), 714 (w), 703 (m), 663 (m).

MS (70 eV, EI): m/z (%): 166 (100), 155 (63), 139 (92), 91 (87).

HRMS (EI) for $C_{17}H_{19}SFO_4$: calc. $[M]^{+\bullet}$: 338.0988, found: 338.0983.

M.p. (°C): 93.

(*R*)-4-(1-(3-Fluoro-4-methoxyphenyl)propan-2-yl)morpholine (EX4):



EX4

EX2 (169.2 mg, 0.5 mmol, 1.0 equiv) was dissolved in THF (1 mL) and magnesium morpholino amide (1.0 M, 0.6 mL, 0.6 mmol, 1.2 equiv) was added dropwise. The reaction mixture was heated at 60 °C for 12 h. The reaction was quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc (3 x 10 mL). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography with EtOAc affording **EX4** (11.4 mg, 0.045 mmol, 9%) as a light brown oil.**^{1}H-NMR ($CDCl_3$, 400 MHz):** δ [ppm] = δ 6.95–6.84 (m, 3H), 3.87 (s, 3H), 3.72 (t, *J* = 4.6 Hz, 4H), 2.91 (dd, *J* = 13.3, 4.7 Hz, 1H), 2.60 (dd, *J* = 5.6, 3.7 Hz, 4H), 2.35 (dd, *J* = 13.3, 9.3 Hz, 1H), 0.95 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 153.5, 151.1, 145.9, 145.8, 133.6, 133.6, 124.9, 124.8, 117.0, 116.8, 113.4, 113.3, 67.5, 61.6, 56.5, 49.2, 38.5, 14.3.

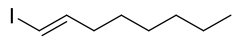
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2958 (w), 2926 (m), 2852 (m), 2812 (w), 1516 (s), 1460 (m), 1458 (m), 1443 (m), 1431 (w), 1376 (w), 1352 (w), 1272 (s), 1224 (m), 1208 (w), 1175 (w), 1115 (vs), 1067 (w), 1028 (m), 969 (m), 955 (m), 917 (w), 872 (w), 862 (m), 808 (m), 760 (m), 742 (w).

MS (70 eV, EI): m/z (%): 139 (8), 114 (100), 84 (8), 70 (9).

HRMS (EI) for $C_{14}H_{20}FNO_2$: calc. $[M–C_6H_{12}ON]^{+\bullet}$: 139.0559, found: 139.0553.

4.4 Preparation of the Alkenyl Iodides of Type 145

(*E*)-1-Iodooct-1-ene (145p):



(*E*)-**145a**

The alkenyl iodide **145a** was prepared from oct-1-yne (1.1 g, 10.0 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford (*E*)-**145a** (1.71 g, 7.2 mmol, 72 %) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.51 (dt, *J* = 14.3, 7.1 Hz, 1H), 5.97 (dt, *J* = 14.4, 1.5 Hz, 1H), 2.05 (qd, *J* = 7.2, 1.5 Hz, 2H), 1.43–1.34 (m, 2H), 1.34–1.22 (m, 6H), 0.91–0.85 (m, 3H).

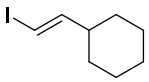
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.0, 74.4, 36.2, 31.7, 28.7, 28.5, 22.7, 14.2.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2956 (m), 2925 (vs), 2870 (m), 2855 (m), 1606 (w), 1466 (w), 1458 (w), 1437 (w), 1378 (w), 1227 (w), 1214 (w), 1202 (w), 1171 (w), 943 (m), 724 (w), 660 (w).

MS (EI, 70 eV): m/z (%): 238 (25), 183 (10), 167 (37), 154 (56), 69 (100).

HRMS (EI) for $C_8H_{15}I$: calc. $[M^+]$: 238.0218; found: 238.0210.

(*E*)-(2-Iodovinyl)cyclohexane (145b):



145b

The alkenyl iodide **145b** was prepared from ethynylcyclohexane (541 mg, 5.0 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with *i*-hexane to afford **145b** (921 mg, 3.9 mmol, 78%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.48 (dd, *J* = 14.4, 7.1 Hz, 1H), 5.95 (dd, *J* = 14.4, 1.2 Hz, 1H), 2.06–1.95 (m, 1H), 1.76–1.69 (m, 4H), 1.67–1.64 (m, 1H), 1.32–1.03 (m, 5H).

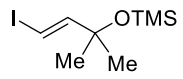
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.4, 73.4, 44.7, 32.1, 26.1, 25.9.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2922 (vs), 2850 (s), 1602 (w), 1448 (m), 1350 (w), 1296 (w), 1282 (w), 1260 (vw), 1240 (w), 1200 (w), 1174 (m), 1120 (w), 946 (vs), 920 (w), 892 (w), 842 (w), 758 (w), 742 (w), 710 (w), 664 (m).

MS (EI, 70 eV): m/z (%): 180 (13), 167 (14), 127 (17), 109 (100), 81 (12), 79 (14), 67 (74).

HRMS (EI) for $C_8H_{13}I$: calc. [M^+]: 236.0062; found: 236.0057.

(*E*)-((4-Iodo-2-methylbut-3-en-2-yl)oxy)trimethylsilane (145d):



145d

The alkenyl iodide **145d** was prepared from trimethyl((2-methylbut-3-yn-2-yl)oxy)silane (782 mg, 5.0 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with ethyl acetate/*i*-hexane = 1/20 to afford **145d** (966 mg, 3.4 mmol, 68%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.60 (d, J = 14.4 Hz, 1H), 6.22 (d, J = 14.4 Hz, 1H), 1.29 (s, 6H), 0.12 (s, 9H).

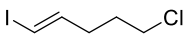
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 153.9, 76.4, 74.7, 30.0, 2.5.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2976 (w), 1610 (vw), 1456 (vw), 1378 (w), 1362 (w), 1288 (vw), 1250 (m), 1232 (m), 1192 (m), 1166 (m), 1136 (m), 1034 (s), 998 (w), 944 (m), 918 (w), 888 (m), 834 (vs), 752 (m), 714 (vw), 688 (w), 658 (w).

MS (EI, 70 eV): m/z (%): 269 (44), 185 (11), 157 (75), 127 (19), 75 (73), 73 (100), 47 (30), 45 (40), 43 (20), 41 (11).

HRMS (EI) for $C_8H_{17}IOSi$: calc. [$M-Me^+$]: 268.9859; found: 268.9855.

(*E*)-5-Chloro-1-iodopent-1-ene (145e):



145e

The alkenyl iodide **145e** was prepared from 5-chloropent-1-yne (513 mg, 5.0 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with ethyl acetate/*i*-hexane = 1/50 to afford **145e** (864 mg, 3.75 mmol, 75%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.48 (dt, J = 14.4, 7.2 Hz, 1H), 6.10 (dt, J = 14.4, 1.4 Hz, 1H), 3.54 (t, J = 6.4 Hz, 2H), 2.29–2.13 (m, 2H), 1.95–1.74 (m, 2H).

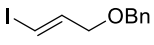
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 144.6, 76.3, 44.0, 33.1, 31.0.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3048 (vw), 2994 (vw), 2956 (w), 2912 (w), 2868 (vw), 2844 (w), 1606 (w), 1442 (m), 1352 (w), 1332 (vw), 1308 (w), 1294 (w), 1270 (m), 1218 (m), 1196 (m), 1144 (w), 1132 (w), 980 (w), 944 (vs), 860 (w), 780 (m), 728 (m), 660 (w).

MS (EI, 70 eV): m/z (%): 230 (75), 103 (39), 75 (29), 67 (94), 43 (23), 41 (100).

HRMS (EI) for C_5H_8ClI: calc. [M^+]: 229.9359; found: 229.9359.

(*E*)-(((3-Iodoallyl)oxy)methyl)benzene (145f):



145f

The alkenyl iodide **145f** was prepared from ((prop-2-yn-1-yloxy)methyl)benzene (219 mg, 1.5 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with ethyl acetate/*i*-hexane = 1/10 to afford **145f** (280 mg, 1.02 mmol, 68%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.39–7.28 (m, 5H), 6.66 (dt, *J* = 14.5, 5.7 Hz, 1H), 6.41 (dt, *J* = 14.5, 1.5 Hz, 1H), 4.52 (s, 2H), 3.96 (dd, *J* = 5.7, 1.5 Hz, 2H).

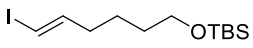
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 142.4, 137.7, 128.5, 127.9, 127.8, 78.9, 72.3, 71.8.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3086 (w), 3062 (w), 3030 (w), 2852 (m), 1680 (w), 1614 (m), 1496 (w), 1454 (m), 1404 (w), 1384 (w), 1354 (m), 1310 (w), 1278 (w), 1264 (w), 1242 (w), 1204 (w), 1186 (m), 1098 (vs), 1074 (s), 1028 (m), 1014 (m), 934 (m), 908 (w), 736 (s), 698 (vs), 666 (w).

MS (EI, 70 eV): m/z (%): 168 (6), 147 (7), 105 (6), 92 (31), 91 (100), 77 (7), 65 (7).

HRMS (EI) for $C_{10}H_{11}IO$: calc. [M^+]:273.9855; found: 273.9849.

(*E*)-*Tert*-butyl((6-iodohex-5-en-1-yl)oxy)dimethylsilane (145g):



145g

The alkenyl iodide **145g** was prepared from *tert*-butyl(hex-5-yn-1-yloxy)dimethylsilane (1.06 g, 5.0 mmol) according to **TP1**.The crude product was purified by flash column chromatography on silica gel with ethyl acetate/*i*-hexane = 1/50 to afford **145g** (1.23 g, 3.6 mmol, 72%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.51 (dt, *J* = 14.3, 7.1 Hz, 1H), 5.98 (dt, *J* = 14.4, 1.4 Hz, 1H), 3.60 (t, *J* = 6.2 Hz, 2H), 2.07 (qd, *J* = 7.2, 1.4 Hz, 2H), 1.54–1.37 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H).

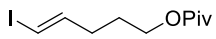
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 146.7, 74.7, 62.9, 36.0, 32.2, 26.1, 24.8, 18.5, –5.1.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2952 (m), 2928 (s), 2896 (m), 2858 (m), 2358 (w), 1472 (w), 1462 (w), 1388 (w), 1360 (w), 1254 (m), 1216 (w), 1204 (w), 1104 (s), 1006 (w), 978 (w), 940 (w), 836 (vs), 812 (w), 774 (s), 666 (w).

MS (EI, 70 eV): m/z (%): 283 (87), 241 (22), 185 (83), 155 (16), 81 (100), 75 (79), 73 (25).

HRMS (EI) for $C_{12}H_{25}IOSi$: calc. [M−Me$^+$]: 325.0485; found: 325.0481.

(*E*)-5-Iodopent-4-en-1-yl pivalate (145h):



145h

The alkenyl iodide **145h** was prepared from pent-4-yn-1-yl pivalate (841 mg, 5.0 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with ethyl acetate/*i*-hexane = 1/20 to afford **145h** (918 mg, 3.1 mmol, 62%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.51 (dt, *J* = 14.3, 7.1 Hz, 1H), 6.05 (dt, *J* = 14.4, 1.5 Hz, 1H), 4.05 (t, *J* = 6.4 Hz, 2H), 2.14 (qd, *J* = 7.3, 1.4 Hz, 2H), 1.79–1.67 (m, 2H), 1.19 (s, 9H).

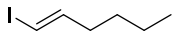
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 178.7, 145.3, 75.6, 63.4, 38.9, 32.7, 27.5, 27.3.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 658 (w), 718 (vw), 770 (w), 850 (vw), 872 (w), 888 (w), 914 (w), 946 (m), 992 (w), 1036 (m), 1148 (vs), 1218 (w), 1282 (m), 1366 (w), 1398 (w), 1460 (w), 1480 (m), 1538 (vw), 1608 (vw), 1724 (s), 2872 (vw), 2908 (w), 2936 (w), 2960 (w), 2970 (w), 3050 (vw).

MS (EI, 70 eV): m/z (%): 195 (5), 194 (100), 167 (11), 67 (35), 41 (23).

HRMS (EI) for $C_{10}H_{17}IO_2$: calc. [M−OPiv$^+$]: 194.9671; found: 194.9666.

(*E*)-1-Iodohex-1-ene (145i):



145i

The alkenyl iodide **145i** was prepared from hex-1-yne (411 mg, 5 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with *i*-hexane to afford **145i** (777 mg, 3.7 mmol, 74%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.58–6.39 (m, 1H), 5.97 (dt, *J* = 14.3, 1.4 Hz, 1H), 2.09–1.96 (m, 2H), 1.40–1.30 (m, 4H), 0.92–0.77 (m, 3H).

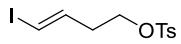
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 146.9, 74.4, 35.9, 30.6, 22.1, 14.0.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 656 (m), 668 (m), 1458 (m), 1466 (m), 1738 (m), 1748 (m), 1762 (m), 2340 (m), 2364 (m), 2858 (m), 2872 (m), 2930 (vs), 2958 (vs).

MS (EI, 70 eV): m/z (%): 210 (77), 168 (25), 167 (58), 154 (100), 127 (40), 83 (16), 41 (22).

HRMS (EI) for $C_6H_{11}I$: calc. [M$^+$]: 209.9905; found: 209.9900.

(*E*)-4-Iodobut-3-en-1-yl 4-methylbenzenesulfonate (145j):



145j

The alkenyl iodide **145j** was prepared from but-3-yn-1-yl 4-methylbenzenesulfonate (1.21 g, 5.0 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with ethyl acetate/*i*-hexane = 1/5 to afford **145j** (916 mg, 2.6 mmol, 52%) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.84–7.69 (m, 2H), 7.44–7.28 (m, 2H), 6.34 (dt, *J* = 14.3, 7.1 Hz, 1H), 6.13 (dt, *J* = 14.5, 1.3 Hz, 1H), 4.04 (t, *J* = 6.4 Hz, 2H), 2.46 (s, 3H), 2.39 (qd, *J* = 6.5, 1.3 Hz, 2H).

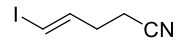
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 145.1, 140.1, 133.0, 130.1, 128.1, 78.9, 68.2, 35.4, 21.9.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 664 (m), 688 (vw), 704 (vw), 720 (vw), 778 (w), 816 (m), 834 (w), 914 (w), 944 (m), 978 (m), 1020 (w), 1040 (w), 1096 (w), 1120 (vw), 1176 (vs), 1190 (m), 1210 (vw), 1232 (w), 1262 (vw), 1292 (vw), 1306 (vw), 1358 (m), 1400 (vw), 1426 (vw), 1454 (vw), 1462 (vw), 1494 (vw), 1598 (w), 2850 (w), 2918 (w), 2956 (vw), 3050 (vw).

MS (EI, 70 eV): m/z (%): 225 (3), 180 (100), 167 (19), 155 (15), 91 (26).

HRMS (EI) for $C_{11}H_{13}IO_3S$: calc. [$M-I^+$]: 225.0585; found: 225.0578.

(*E*)-5-Iodopent-4-enenitrile (145k):



145k

The alkenyl iodide **145k** was prepared from pent-4-ynenitrile (396 mg, 5.0 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with ethyl acetate/*i*-hexane = 1/5 to afford **145k** (652 mg, 3.15 mmol, 63%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.60–6.45 (m, 1H), 6.31 (dt, *J* = 14.5, 1.2 Hz, 1H), 2.48–2.35 (m, 4H).

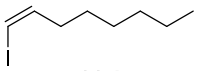
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 141.5, 118.6, 79.0, 31.8, 16.7.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 666 (m), 746 (w), 754 (w), 762 (w), 778 (w), 810 (w), 820 (w), 862 (w), 938 (vs), 974 (w), 988 (w), 1154 (m), 1198 (w), 1222 (m), 1424 (m), 1440 (w), 1608 (w), 2246 (w), 2340 (w), 2360 (w), 2924 (w), 3050 (w).

MS (EI, 70 eV): m/z (%): 207 (47), 167 (100), 127 (32), 80 (13).

HRMS (EI) for C_5H_6IN: calc. [M^+]: 206.9545; found: 206.9538.

(*Z*)-1-Iodooct-1-ene (145l):



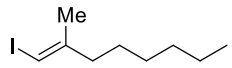
145l

The alkenyl iodide **145l** was prepared from oct-1-yne (1.1 g, 10.0 mmol) according to the literature.[167] The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford **145l** (1.33 mg, 5.6 mmol, 56%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.17 (s, 2H), 2.21–2.06 (m, 2H), 1.37–1.19 (m, 8H), 0.96–0.79 (m, 3H).

The analytical data were in accordance with literature values.

(*E*)-1-Iodo-2-methyloct-1-ene (145m):



145m

The alkenyl iodide **145m** was prepared from oct-1-yne (1.1 g, 10.0 mmol) according to the literature.[168]The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford **145m** (1.08 g, 4.3 mmol, 43%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 5.88–5.76 (m, 1H), 2.27–2.13 (m, 2H), 1.82 (d, J = 1.1 Hz, 3H), 1.50–1.37 (m, 2H), 1.34–1.20 (m, 6H), 0.94–0.82 (m, 3H).

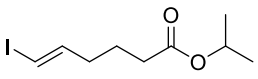
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.5, 74.5, 39.8, 31.7, 28.9, 27.8, 24.0, 22.7, 14.2.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 668 (w), 734 (m), 766 (w), 908 (w), 1142 (m), 1272 (m), 1376 (w), 1466 (w), 2334 (w), 2344 (w), 2362 (w), 2856 (m), 2870 (m), 2928 (vs), 2956 (m).

MS (EI, 70 eV): m/z (%): 252 (50), 182 (86), 181 (55), 168 (50), 127 (40), 83 (55), 79 (15), 69 (100), 67 (22), 57 (15) ,55 (100), 43 (29), 41 (77).

HRMS (EI) for $C_9H_{17}I$: calc. [M^+]: 252.0375; found: 252.0370.

Isopropyl (*E*)-6-iodohex-5-enoate (145n):



145n

[167] D. Yang, V. A. Cwynar, D. J. Hart, J. Madanmohan, J. Lee, J. Lyons, M. Caffrey, *Organic Synth.* **2012**, *89*, 183–201.

[168] M. Davoust, F. Cantagrel, P. Metzner, J. -F. Briere, *Org. Biomol. Chem.* **2008**, *6*, 1981–1993.

The alkenyl iodide **145n** was prepared from isopropyl hex-5-ynoate (771 mg, 5 mmol) according to **TP1**. The crude product was purified by flash column chromatography on silica gel with ethyl acetate/*i*-hexane = 1/20 to afford **145n** (1.07 g, 3.8 mmol, 76%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.49 (dt, *J* = 14.4, 7.2 Hz, 1H), 6.03 (dt, *J* = 14.4, 1.5 Hz, 1H), 5.08–4.89 (m, 1H), 2.27 (t, *J* = 7.4 Hz, 2H), 2.10 (qd, *J* = 7.3, 1.4 Hz, 2H), 1.72 (p, *J* = 7.4 Hz, 2H), 1.23 (d, *J* = 6.2 Hz, 6H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 172.9, 145.6, 75.6, 67.8, 35.4, 33.8, 23.7, 22.0.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 660 (w), 720 (vw), 748 (vw), 790 (vw), 822 (w), 866 (vw), 896 (w), 946 (m), 1014 (w), 1036 (vw), 1078 (w), 1106 (vs), 1144 (m), 1178 (s), 1226 (m), 1250 (m), 1288 (w), 1312 (w), 1328 (w), 1340 (w), 1374 (m), 1418 (w), 1438 (w), 1454 (w), 1468 (w), 1606 (w), 1726 (vs), 2936 (w), 2978 (w), 3050 (vw).

MS (EI, 70 eV): m/z (%): 239 (2), 223 (24), 197 (5), 223 (34), 180 (24), 155 (21), 113 (100), 71 (45), 67 (26), 42 (21).

HRMS (EI) for $C_9H_{15}IO_2$: calc. [$M-{}^iPr^+$]: 238.9569; found: 238.9563.

1-Iodocyclohex-1-ene (145o):

145o

A 250 mL flask was charged with a solution of cyclohexanone (1.96 g, 20.0 mmol) and THF (100 mL). Potassiumbis(trimethylsilyl)amide (0.5 M solution in THF, 52 mL, 26 mmol) was added dropwise at –78 °C over a period of 5 min. After 30 min, the resulting reaction mixture was treated with diethyl chlorophosphate (4.34 mL, 30.0 mmol) and stirred for 2 h at –78 C. Subsequently, the reaction mixture was allowed to warm to ambient temperature before it was quenched with a sat. aq. NH_4Cl solution. The aqueous layer was extracted with ethyl acetate (5 × 100 mL). The combined organic phase was washed with brine, dried over $MgSO_4$ and concentrated under vacuum to afford cyclohex-1-en-1-yl diethyl phosphate (4.12 g, 17.6 mmol, 88% yield) which was used without further purification.

A 250 mL flask was charged with crude cyclohex-1-en-1-yl diethyl phosphate (2.34 g,10.0 mmol) and NaI (4.50 g, 30.0 mmol) in anhydrous dichloromethane (20 mL). TMSCl (3.82 mL, 30.0 mmol) was added dropwise and after stirring for 10 min at room temperature, the reaction mixture was filtrated. After quenching with a solution of sat. aq. $NaHCO_3$ and a solution of sat. aq. Na_2SO_3 the organic layer was separated. The aqueous phase was extracted with dichloromethane (3 × 50 mL) and the combined organic phases were dried over $MgSO_4$. After removing the solvent, the obtained crude product was

purified by flash column chromatography on silica gel with *n*-pentane to afford **145o** (205 mg, 11.5%) as a colorless oil.[169]

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.34 (tt, J = 4.0, 1.8 Hz, 1H), 2.58–2.42 (m, 2H), 2.15–2.00 (m, 2H), 1.74–1.60 (m, 4H).

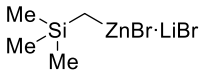
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 137.7, 97.0, 39.5, 29.1, 25.5, 21.0.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 990 (m), 1026 (m), 1056 (m), 1248 (m), 1262 (m), 1444 (m), 1462 (m), 2332 (m), 2342 (m), 2358 (m), 2368 (m), 2852 (s) , 2926 (vs).

MS (EI, 70 eV): m/z (%): 208 (55), 81 (100), 79 (41).

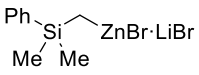
HRMS (EI) for C_6H_9I: calc. [M^+]: 207.9749; found: 207.9740.

4.5 Preparation of Alkylzinc Reagents for Transmetalation of Type 143



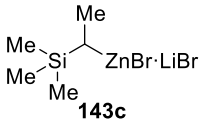
143a

The zinc reagent **143a** (0.71-0.95 M in diethyl ether) was prepared according to literature.[60] The concentration was determined by titration of a small aliquot with iodine.



143b

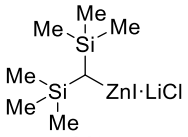
The zinc reagent **143b** (0.52 M in diethyl ether) was prepared according to **TP3** starting from the freshly prepared alkyllithium reagent.[170] The concentration was determined by titration of a small aliquot with iodine.



143c

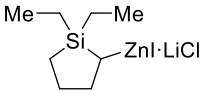
The zinc reagent **143c** (0.68 M in diethyl ether) was prepared according to **TP3** starting from the freshly prepared alkyllithium reagent.[170] The concentration was determined by titration of a small aliquot with iodine.

[169] M. Gerelle, A. J. Dalencon, M. C. Willis, *Tetrahedron Lett.* **2012**, *53*, 1954–1957.
[170] C. Lutz, P. Jones, P. Knochel, *Synthesis* **1999**, 312–316.



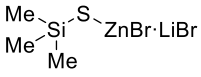
143d

The zinc reagent **143d** (0.38 M in diethyl ether) was prepared according to **TP4** starting from the corresponding alkyl iodide. The concentration was determined by titration of a small aliquot with iodine.



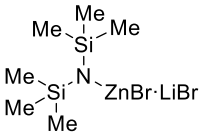
143e

The zinc reagent **143e** (0.31 M in diethyl ether) was prepared according to **TP4** starting from the corresponding alkyl iodide.[171] The concentration was determined by titration of a small aliquot with iodine.



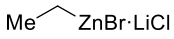
143f

The zinc reagent **143f** (0.56 M in diethyl ether) was prepared according to **TP3** starting from the freshly prepared alkyllithium reagent.[172] The concentration was determined by titration of a small aliquot with iodine.



143g

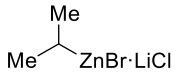
The zinc reagent **143g** (0.70 M in diethyl ether) was prepared according to **TP3** starting from the freshly prepared alkyllithium reagent.[173] The concentration was determined by titration of a small aliquot with iodine.



143h

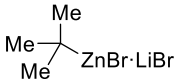
[171] Joseph et al. U.S. Patent US 2017/0288157 A1.
[172] D. Taher, A. I. Wallbank, E. A. Turner, H. L. Cuthbert, J. F. Corrigan, *Eur. J. Inorg. Chem.* **2006**, 4616–4620.
[173] D. R. Armstrong, E. Herd, D. V. Graham, E. Hevia, A. R. Kennedy, W. Clegg, L. Russo, *Dalton Trans.* **2008**, 1323-1330.

The zinc reagent **143h** (0.46 M in diethyl ether) was prepared according to **TP4** starting from the corresponding alkyl bromide. The concentration was determined by titration of a small aliquot with iodine.



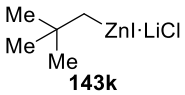
143i

The zinc reagent **143i** (0.68 M in diethyl ether) was prepared according to **TP4** starting from the corresponding alkyl bromide. The concentration was determined by titration of a small aliquot with iodine.



143j

The zinc reagent **143j** (0.82 M in diethyl ether) was prepared according to **TP3** starting from *t*-BuLi. The concentration was determined by titration of a small aliquot with iodine.



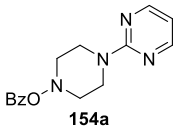
143k

The zinc reagent **143k** (0.92 M in diethyl ether) was prepared according to **TP4** starting from the corresponding alkyl iodide.[170] The concentration was determined by titration of a small aliquot with iodine.

4.6 Prepared *O*-Hydroxylamine Benzoates of Type 154

All electrophiles were prepared according to literature.[109e-f]

4-(Pyrimidin-2-yl)piperazin-1-yl benzoate (154a):



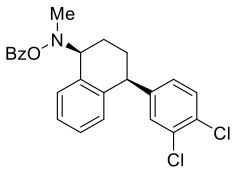
154a

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.34 (d, J = 4.8 Hz, 2H), 8.05–7.99 (m, 2H), 7.61–7.54 (m, 1H), 7.45 (dd, J = 8.4, 7.1 Hz, 2H), 6.55 (t, J = 4.8 Hz, 1H), 4.65 (d, J = 13.3 Hz, 2H), 3.54 (q, J = 11.8, 11.3 Hz, 4H), 3.02 (t, J = 10.6 Hz, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 164.8, 161.5, 158.0, 133.4, 129.6, 128.6, 110.5, 56.0, 42.3.

The analytical data was in accordance with literature values.[109f]

_O_-Benzoyl-_N_-((1_S_,4_S_)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydronaphthalen-1-yl)-_N_-methylhydroxylamine (154b):



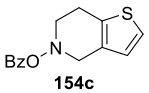
154b

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.93–7.83 (m, 2H), 7.76 (dd, J = 8.9, 7.5 Hz, 1H), 7.58–7.52 (m, 1H), 7.41 (t, J = 7.8 Hz, 2H), 7.26–7.23 (m, 2H), 7.22–7.16 (m, 1H), 7.15–7.10 (m, 1H), 6.87 (m, 2H), 4.24 (dd, J = 7.6, 4.9 Hz, 1H), 4.17–4.10 (m, 1H), 2.99 (s, 3H), 2.32–2.23 (m, 1H), 2.23–2.09 (m, 2H), 2.07–1.97 (m, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 164.8, 147.6, 138.6, 136.0, 133.1, 132.3, 130.8, 130.3, 130.1, 130.0, 129.6, 129.5, 129.5, 128.6, 128.6, 127.9, 126.9, 65.6, 44.2, 42.8, 29.4, 20.0.

The analytical data was in accordance with literature values.[109f]

6,7-Dihydrothieno[3,2-c]pyridin-5(4_H_)-yl benzoate (154c):



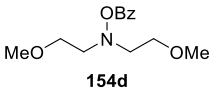
154c

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.99 (d, J = 7.7 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.48–7.36 (m, 2H), 7.15 (d, J = 5.2 Hz, 1H), 6.76 (d, J = 5.2 Hz, 1H), 4.62–4.15 (m, 2H), 3.58 (t, J = 6.0 Hz, 2H), 3.11 (t, J = 6.1 Hz, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 165.1, 133.3, 132.5, 131.2, 129.7, 129.3, 128.6, 125.4, 123.7, 55.8, 53.2, 23.0.

The analytical data was in accordance with literature values.[109f]

_O_-Benzoyl-_N_,_N_-bis(2-methoxyethyl)hydroxylamine (154d):



154d

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.05–7.97 (m, 2H), 7.59–7.52 (m, 1H), 7.43 (t, J = 7.8 Hz, 2H), 3.60 (t, J = 5.8 Hz, 4H), 3.28 (s, 6H), 3.25 (t, J = 5.8 Hz, 4H).

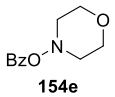
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 165.6, 133.2, 129.6, 129.3, 128.5, 77.5, 77.2, 76.8, 69.8, 59.3, 59.0.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2887 (w), 1740 (s), 1450 (m), 1314 (w), 1242 (s), 1199 (m), 1176 (w), 1160 (w), 1116 (s), 1087 (m), 1079 (m), 1056 (s), 1023 (s), 1002 (w), 962 (w), 837 (w), 802 (w), 706 (vs), 687 (m), 668 (w).

MS (70 eV, EI): m/z (%): 208 (25), 121 (18), 105 (100), 77 (27), 59 (7).

HRMS (EI) for $C_{13}H_{19}NO_4$: calc. $[M]^{+\bullet}$: 253.1314, found: 253.1314.

Morpholino benzoate (154e):



154e

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.04–7.98 (m, 2H), 7.60–7.54 (m, 1H), 7.44 (dd, *J* = 8.4, 7.1 Hz, 2H), 4.02–3.93 (m, 2H), 3.91–3.82 (m, 2H), 3.45 (d, *J* = 10.3 Hz, 2H), 3.04 (td, *J* = 10.5, 3.5 Hz, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 164.7, 133.3, 129.6, 129.2, 128.6, 77.5, 77.2, 76.8, 66.0, 57.1.

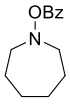
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2846 (w), 1728 (s), 1454 (w), 1315 (w), 1268 (m), 1263 (m), 1246 (s), 1177 (w), 1165 (w), 1099 (m), 1082 (m), 1066 (m), 1049 (m), 1023 (m), 1007 (m), 998 (w), 921 (w), 872 (w), 857 (m), 852 (m), 794 (w), 709 (vs), 686 (w), 677 (m).

MS (70 eV, EI): m/z (%): 122 (5), 105 (100), 77 (22).

HRMS (EI) for $C_{11}H_{13}NO_3$: calc. $[M]^{+\bullet}$: 207.0895, found: 207.0896.

The analytical data was in accordance with literature values.[109e]

Azepan-1-yl benzoate (154f):



154f

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.04–7.96 (m, 2H), 7.59–7.48 (m, 1H), 7.43 (dd, *J* = 8.4, 7.0 Hz, 2H), 3.42–3.23 (m, 4H), 1.86–1.78 (m, 4H), 1.73–1.64 (m, 4H).

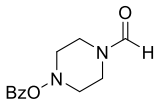
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 164.9, 133.0, 129.8, 129.5, 128.5, 77.5, 77.2, 76.8, 59.6, 26.5, 24.2.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2942 (w), 2936 (w), 2924 (w), 2907 (w), 2846 (w), 1728 (s), 1450 (m), 1311 (w), 1248 (s), 1212 (w), 1197 (w), 1176 (m), 1085 (m), 1065 (s), 1022 (m), 1001 (w), 943 (m), 935 (w), 810 (w), 801 (w), 715 (vs), 688 (m), 668 (w).

MS (70 eV, EI): m/z (%): 122 (23), 105 (100), 77 (27).

HRMS (EI) for $C_{13}H_{17}NO_2$: calc. $[M]^{+\bullet}$: 219.1259, found: 219.1255.

4-Formylpiperazin-1-yl benzoate (154g):



154g

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.06 (s, 1H), 8.01–7.95 (m, 2H), 7.60–7.54 (m, 1H), 7.43 (dd, *J* = 8.5, 7.1 Hz, 2H), 4.29 (d, *J* = 12.3 Hz, 1H), 3.74–3.20 (m, 5H), 3.04–2.76 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 164.5, 160.7, 133.5, 129.5, 128.8, 128.6, 77.5, 77.2, 76.8, 56.3, 55.3, 43.6, 38.0.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2922 (w), 2859 (w), 2851 (w), 2358 (w), 1724 (s), 1706 (w), 1700 (w), 1695 (w), 1669 (vs), 1662 (vs), 1635 (s), 1616 (m), 1596 (m), 1580 (w), 1569 (w), 1558 (w), 1539 (w), 1506 (w), 1490 (w), 1464 (w), 1440 (s), 1437 (s), 1424 (m), 1398 (m), 1373 (w), 1357 (w), 1316 (w), 1295 (w), 1275 (m), 1246 (vs), 1238 (s), 1208 (m), 1179 (m), 1166 (w), 1128 (w), 1113 (m), 1089 (m), 1080 (m), 1063 (s), 1022 (s), 1000 (m), 965 (w), 869 (w), 809 (w), 789 (w), 781 (w), 713 (s), 689 (m), 677 (m), 667 (m).

MS (70 eV, EI): m/z (%):122 (14), 105 (100), 77 (25), 56 (6).

HRMS (EI) for $C_{12}H_{14}N_2O_3$: calc. $[M]^{+\bullet}$: 234.1004, found: 234.1000.

4.7 Prepared New Chiral Epoxides of Type 157

(*R*)-2-Benzyloxirane (*R*-157a):

(*R*)-**157a**

The epoxide (*R*)-**157a** was prepared according to **TP10** using phenylmagnesium chloride (0.5 M, 48 mL, 24 mmol, 1.2 equiv), CuI (152.4 mg, 4 mol%) and (*R*)-epichlorohydrin (*R*-**156**, 1.6 mL, 1.85 g, 20 mmol, 1.0 equiv). After quenching of the alcohol, the mixture was extracted with Et_2O (3 × 100 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated. The resulting yellow oil was dissolved in a 1:1 mixture of Et_2O (5 mL) and water (5 mL), treated with KOH (2.47 g, 44 mmol, 2.2 equiv) and heated to 60 °C. After 1 h, a second charge of KOH (561 mg, 10 mmol, 0.5 equiv) was added. When TLC indicated consumption of the starting material, the mixture was extracted with Et_2O (3×20 mL). The combined organic layers were dried with $MgSO_4$, filtered and carefully concentrated.

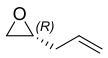
^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.35–7.29 (m, 2H), 7.26–7.21 (m, 2H), 3.15 (tdd, *J* = 5.5, 3.9, 2.7 Hz, 1H), 2.92 (dd, *J* = 14.5, 5.7 Hz, 1H), 2.86–2.77 (m, 2H), 2.55 (dd, *J* = 5.0, 2.6 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 137.3, 129.1, 128.7, 126.8, 52.6, 47.0, 38.9.

$[\alpha]_D^{20}$: + 17.0 (c = 1.86., EtOH); Lit: $[\alpha]_D$: +17.5 (c = 1.94, EtOH);

The data is in accordance with literature values.[174]

(*R*)-2-Allyloxirane (*R*-157b):



(*R*)-**157b**

The epoxide (*R*)-**157b** was prepared according to **TP10** using vinylmagnesium chloride (0.5 M, 48 mL, 24 mmol, 1.2 equiv), CuI (152.4 mg, 4 mol%) and (*R*)-epichlorohydrin (*R*-**156**, 1.6 mL, 1.85 g, 20 mmol, 1.0 equiv). The combined organic layers were dried with $MgSO_4$, filtered and carefully concentrated. The resulting oil was treated with KOH (2.47 g, 44 mmol, 2.2 equiv) and heated to 60 °C. When TLC indicated consumption of the starting material, the mixture was extracted with Et_2O (3×20 mL). The combined organic layers were dried with $MgSO_4$, filtered and distilled off (300 mbar, 75 °C).

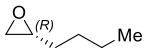
^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 5.89–5.76 (m, 1H), 5.20–5.06 (m, 2H), 3.03–2.95 (m, 1H), 2.76 (dd, *J* = 5.0, 3.9 Hz, 1H), 2.50 (dd, *J* = 5.0, 2.7 Hz, 1H), 2.38–2.24 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 133.1, 117.7, 51.3, 46.7, 36.6.

$[\alpha]_D^{20}$: −5.0 (c = 1.3., $CHCl_3$); Lit: $[\alpha]_D$: (*S*)-enantiomer +5.2 (c = 1.4, $CHCl_3$).

The data is in accordance with literature values.[119]

(*R*)-2-Butyloxirane (*R*-157c):



(*R*)-**157c**

The epoxide (*R*)-**157c** was prepared according to **TP10** using propylmagnesium chloride (0.5 M, 48 mL, 24 mmol, 1.2 equiv), CuI (152.4 mg, 4 mol%) and (*R*)-epichlorohydrin (*R*-**156**, 1.6 mL, 1.85 g, 20 mmol, 1.0 equiv). The combined organic layers were dried with $MgSO_4$, filtered and carefully concentrated. The resulting oil was treated with KOH (2.47 g, 44 mmol, 2.2 equiv) and heated to 60 °C. When TLC indicated consumption of the starting material, the mixture was extracted with Et_2O

[174] M. Amatore, T. D. Beeson, S. P. Brown, D. W. C. Macmillan, *Angew. Chem. Int. Ed.* **2009**, *48*, 5121–5124.

(3×20 mL). The combined organic layers were dried with $MgSO_4$, filtered and distilled off (300 mbar, 115 °C).

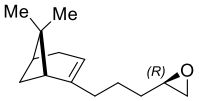
^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 2.90 (tdd, *J* = 5.6, 3.9, 2.7 Hz, 1H), 2.75 (dd, *J* = 5.0, 4.0 Hz, 1H), 2.46 (dd, *J* = 5.1, 2.8 Hz, 1H), 1.53 (tdd, *J* = 6.9, 5.5, 1.7 Hz, 2H), 1.49–1.31 (m, 3H), 0.91 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 52.55, 47.29, 32.33, 28.24, 22.67, 14.14.

$[\alpha]_D^{20}$: +10.5 (c = 1.05, $CHCl_3$); Lit: $[\alpha]_D^{20}$: +9.1 (c = 1.00, $CHCl_3$).

The data is in accordance with literature values.[175]

(*R*)-2-(3-((1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)propyl)oxirane (*R,R,S*-157d):



(*R,R,S*)-**157d**

According to a modified literature procedure,[176] a dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum was charged with magnesium turnings (340 mg, 14.0 mmol, 1.4 equiv). Dry THF (5 mL) was added as well as a corn of I_2 for activation. A solution of (1*R*)-nopol bromide[177] (2.75 g, 12.0 mmol, 1.2 equiv) in 5 mL of dry THF was added dropwise at 0 °C. After addition, the mixture was stirred at room temperature for 3 h. The concentration of the Grignard reagent was determined by titration with I_2 in THF.

The epoxide (*R*)-**157d** was afterwards prepared according to **TP10** using (1*R*)-nopolmagnesium bromide (ca. 0.5 M, 20 mL, 10 mmol, 1.2 equiv), CuI (61 mg, 4 mol%) and (*R*)-epichlorohydrin (*R*-**156**, 627 µL, 740 mg, 8 mmol, 1.0 equiv). After quenching of the alcohol, the mixture was extracted with Et_2O (3 × 100 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated. The resulting yellow oil was dissolved in a 1:1 mixture of Et_2O (5 mL) and water (5 mL), treated with KOH (953 mg, 17 mmol, 2.2 equiv) and heated to 60 °C. When TLC indicated consumption of the starting material, the mixture was extracted with Et_2O (3×20 mL). The combined organic layers were dried with $MgSO_4$, filtered and carefully concentrated.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 5.23–5.14 (m, 1H), 2.95–2.86 (m, 1H), 2.75 (dd, *J* = 5.1, 4.0 Hz, 1H), 2.46 (dd, *J* = 5.0, 2.7 Hz, 1H), 2.35 (dt, *J* = 8.5, 5.6 Hz, 1H), 2.29–2.12 (m, 2H), 2.10–2.05 (m, 1H), 2.03–1.91 (m, 3H), 1.61–1.39 (m, 4H), 1.26 (s, 3H), 1.13 (d, *J* = 8.5 Hz, 1H), 0.82 (s, 3H).

[175] A. Berkessel, E. Ertürk, *Adv. Synth. Catal.* **2006**, *348*, 2619–2625.
[176] G. S. Silverman, P. E. Rakita, *Handbook of Grignard Reagents* **1996**, CRC Press, Florida.
[177] B. Akgun, D. G. Hall, *Angew. Chem. Int. Ed.* **2016**, *55*, 3909-3913.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.1, 116.3, 52.5, 47.4, 45.8, 41.0, 38.1, 36.7, 32.4, 31.8, 31.4, 26.5, 23.7, 21.4.

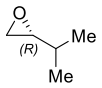
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3041 (w), 3026 (w), 2984 (m), 2914 (vs), 2879 (s), 2833 (m), 1481 (w), 1467 (m), 1456 (m), 1433 (m), 1410 (w), 1381 (m), 1364 (m), 1346 (w), 1331 (w), 1262 (w), 1219 (w), 1204 (w), 1182 (w), 1128 (w), 1099 (w), 1080 (w), 957 (w), 944 (w), 935 (w), 920 (m), 886 (m), 866 (m), 832 (s), 794 (m), 777 (m), 758 (w), 736 (w).

MS (70 eV, EI): m/z (%): 145 (46), 131 (24), 117 (56), 105 (38), 91 (100).

HRMS (EI) for $C_{14}H_{22}O$: calc. $[M]^{+\bullet}$: 206.1671, found: 206.1664.

$[\alpha]_D^{20}$: −24.8 (c = 1.48, $CHCl_3$).

(*R*)-2-Isopropyloxirane (*R*-157e):



(*R*)-**157e**

The chiral epoxide (*R*)-**157e** was prepared according to a literature procedure.[122]

^{1}H-NMR ($CDCl_3$, 400 MHz): 2.74–2.66 (m, 2H), 2.50 (dd, *J* = 4.8, 3.0 Hz, 1H), 1.47 (dq, *J* = 13.4, 6.7 Hz, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H).

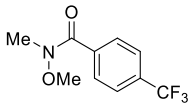
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 57.8, 46.3, 30.9, 19.2, 18.3.

$[\alpha]_D^{20}$: −6.1 (c = 1.00, $CHCl_3$), Lit: $[\alpha]_D^{20}$: −6.2 (c = 1.05, $CHCl_3$).

The data is in accordance with literature values.[122]

4.8 Prepared Electrophiles of Type 151

_N_-methoxy-_N_-methyl-4-(trifluoromethyl)benzamide (151r):



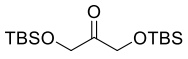
151r

The Weinreb amide **151r** was prepared according to a literature procedure.[178]

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.79 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H), 3.53 (s, 3H), 3.38 (s, 3H).

The data is in accordance with literature values.

2,2,3,3,9,9,10,10-Octamethyl-4,8-dioxa-3,9-disilaundecan-6-one (151s):



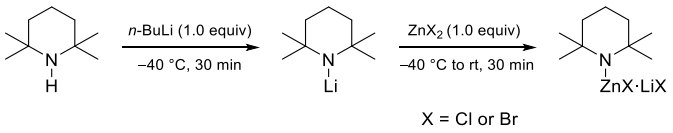
151s

The ketone 3g was prepared according to a literature procedure.[179]

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 4.41 (s, 4H), 0.92 (s, 18H), 0.09 (s, 12H).

The data is in accordance with literature values.

4.9 Preparation of TMPZnCl·LiCl or TMPZnBr·LiBr

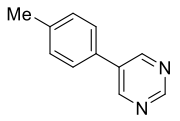


A dry and argon flushed Schenk-flask, equipped with a magnetic stirring bar, was charged with TMPH (1.3 mL, 10.0 mmol, 1.0 equiv) and dry THF (10 mL). The reaction mixture was cooled to −40 °C and *n*-BuLi (1.6 M, 6.3 mL, 10 mmol, 1.0 equiv) was added dropwise. The reaction mixture was stirred at −40 °C for 30 min until a milky white solution was formed. A solution of ZnX_2 (X = Cl or Br, 1 M in THF, 10 mL, 10 mmol, 1.0 equiv) was added at −40 °C and the reaction mixture was warmed to room temperature. The slightly yellow solution was stirred for 30 min. The concentration was determined by titration of an aliquot with benzoic acid.

[178] H. J. A. Dale, C. Nottingham, C. Poree, G. C. Lloyd-Jones, *J. Am. Chem. Soc.* **2021**, *143*, 2097–2107.
[179] K. Ravindar, M. S. Reddy, P. Deslongchamps, *Org. Lett.* 13, 3178–3181.

4.10 Prepared 5-Substituted Pyrimidines of Type 160

5-(*p*-Tolyl)pyrimidine (160b):



160b

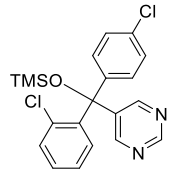
5-(*p*-Tolyl)pyrimidine (**160b**) was prepared according to literature known procedures.[149] 5-Bromopyrimidine (3.18 g, 20 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (605 mg, 1 mmol, 5 mol%), K_2CO_3 (22.11 g, 160 mmol, 8.0 equiv) and *p*-tolylboronic acid (5.44 g, 40 mmol, 2.0 equiv) were dissolved in THF (140 mL) and H_2O (140 mL). The reaction mixture was stirred overnight at 80 °C. After cooling to room temperature brine (150 mL) was added. The mixture was extracted with ethyl acetate (4 x 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was evaporated. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 3:1 containing 1% triethylamine to afford **160b** (2.61 g, 15.3 mmol, 77% yield) as a white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.09 (s, 1H), 8.83 (s, 2H), 7.40–7.35 (m, 2H), 7.22 (d, J = 7.9 Hz, 2H), 2.33 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.1, 154.5, 138.9, 134.0, 131.2, 130.0, 126.6, 21.1.

The analytical data was in accordance with literature values.[149]

5-((2-Chlorophenyl)(4-chlorophenyl)((trimethylsilyl)oxy)methyl)pyrimidine (160e):



160e

To a flask charged with THF (20 mL) and (3-chlorophenyl)(4-chlorophenyl)(pyrimidin-5-yl)methanol[150] (1.66 g, 5 mmol, 1.0 equiv) TMSCl (1.3 mL, 10 mmol, 2.0 equiv) was added dropwise at 0°C. The reaction mixture was allowed to warm to room temperature overnight, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified *via* flash column chromatography on silica gel with with EtOAc/*i*-hexanes = 1:9 to afford 5-((3-

chlorophenyl)(4-chlorophenyl)((trimethylsilyl)oxy)methyl)pyrimidine (**160e**, 1.98 g, 4.9 mmol, 98% yield) as yellow needles.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.15 (s, 1H), 8.94 (s, 2H), 7.84–7.77 (m, 1H), 7.42–7.33 (m, 5H), 7.33–7.28 (m, 2H), -0.09 (s, 9H).

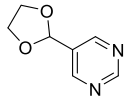
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 155.9, 154.5, 140.3, 140.2, 140.1, 134.6, 133.4, 132.4, 130.6, 130.1, 129.6, 128.9, 127.4, 81.5, 1.9.

MS (70 eV, EI): m/z = 315 (32), 313 (52), 291 (34), 243 (21), 223 (22), 214 (21), 189 (63), 187 (26), 177 (100), 73 (58).

HRMS (EI) for $C_{20}H_{20}Cl_2N_2OSi$: calc. [M^+]: 402.0722, found: 402.0716.

M.p. (°C): 114-116.

5-(1,3-Dioxolan-2-yl)pyrimidine (160f):



160f

5-(1,3-Dioxolan-2-yl)pyrimidine (**160f**) was prepared according to a modified literature procedure.[151] A round bottom flask was equipped with a Dean Stark trap and reflux condenser and charged with pyrimidine-5-carbaldehyde (1.08 g, 10 mmol, 1.0 equiv). Toluene (25 mL) and *p*-toluene sulfonic acid monohydrate (3.8 g, 20 mmol, 2.0 equiv) were added and the reaction mixture was stirred at 105 °C overnight. After cooling to room temperature, the reaction mixture was quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with EtOAc (3 x 30 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc to afford 5-(1,3-dioxolan-2-yl)pyrimidine (**160f**, 1.03 g, 6.8 mmol, 68% yield) as a brown solid.

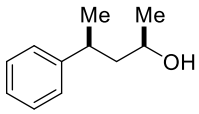
^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.24 (s, 1H), 8.83 (s, 2H), 5.89 (s, 1H), 4.15–4.06 (m, 4H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 159.4, 155.6, 131.7, 100.4, 65.7

5 Preparation of Optically Enriched Secondary Alkyl Alcohols

The optically enriched secondary alkyl alcohols *anti*-**158c**, (*R*)- and (*S*)-**158d and** (*S*)-**158e** were prepared according to literature procedures.[61-63]

syn-4-Phenylpentan-2-ol (*syn*-158a):



syn-**158a**

2,4-*syn*-*tert*-Butyldimethyl((4-phenylpentan-2-yl)oxy)silane[63] (3.98 g, 14 mmol, 1.0 equiv) was dissolved in THF (45 mL) and cooled to 0 °C. Tetrabutylammonium fluoride trihydrate (8.83 g, 28 mmol, 2.0 equiv) was added in one portion and the reaction mixture was warmed to ambient temperature overnight. The reaction mixture was quenched with sat. aq. NH_4Cl and extracted with diethyl ether (3 × 100 mL). The combined organic phases were dried over $MgSO_4$ and evaporated. The obtained crude product was purified by flash column chromatography with *i*-hexane/diethyl ether (2:1) to afford *syn*-**158a** (1.82 g, 11.21 mmol, 80%, dr = 99:1) as light yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.33–7.27 (m, 2H), 7.23–7.16 (m, 3H), 3.83–3.71 (m, 1H), 2.93–2.80 (m, 1H), 1.91–1.77 (m, 1H), 1.71–1.60 (m, 1H), 1.31–1.25 (m, 4H), 1.19 (d, J = 6.1 Hz, 3H).

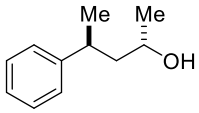
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.4, 128.7, 127.0, 126.3, 66.6, 48.0, 37.1, 23.9, 22.5.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3344 (w), 3083 (w), 3059 (w), 3025 (w), 2960 (m), 2924 (m), 2870 (m), 1493 (m), 1452 (m), 1375 (m), 1302 (w), 1255 (w), 1130 (m), 1082 (w), 1060 (m), 1033 (w), 1002 (w), 948 (w), 907 (w), 837 (w), 761 (m), 699 (vs).

MS (70 eV, EI): m/z (%): 146 (16), 131 (100), 129 (20), 115 (17), 105 (38), 91 (39).

HRMS (EI) for $C_{11}H_{16}O$: calc. $[M-H]^{+\bullet}$: 163.1123, found: 163.1071.

anti-4-Phenylpentan-2-ol (*anti*-158a):



anti-**158a**

Analogous to *syn*-**158a**, *anti*-**158a** (2.24 g, 13.64 mmol, 97%, dr = 1:99) was obtained as light yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.35–7.28 (m, 2H), 7.25–7.15 (m, 3H), 3.60–3.51 (m, 1H), 3.04–2.90 (m, 1H), 1.73–1.67 (m, 2H), 1.33 (s, 1H), 1.27 (d, J = 7.0 Hz, 3H).

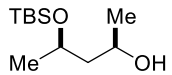
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 146.9, 128.6, 127.3, 126.2, 66.1, 47.8, 36.7, 24.3, 23.2.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3343 (w), 3083 (w), 3063 (w), 3026 (w), 2960 (s), 2925 (m), 2872 (m), 2358 (m), 1602 (w), 1494 (m), 1452 (m), 1374 (m), 1139 (m), 1113 (w), 1083 (w), 1054 (m), 1025 (m), 951 (w), 899 (w), 830 (w), 762 (s), 699 (vs).

MS (70 eV, EI): m/z (%): 146 (23), 131 (58), 105 (100), 91 (47), 77 (20), 74 (22), 59 (39), 45 (44), 43 (21).

HRMS (EI) for $C_{11}H_{16}O$: calc. $[M]^{+\bullet}$: 164.1201, found: 164.1176.

***syn*-4-((*Tert*-butyldimethylsilyl)oxy)pentan-2-ol (*syn*-158b):**



syn-**158b**

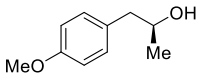
A dry and argon-flushed *Schlenk*-flask was charged with a suspension of NaH (0.88 g, 60 wt% in mineral oil, 22.0 mmol) in THF (220 mL) and cooled to 0 °C. A solution of *syn*-pentan-2,4-diol (2.08 g, 20.0 mmol, dr = 99:1) in THF (20 mL) was added and the resulting solution was stirred for 30 min at 0 °C before let warm to room temperature. Then a solution of TBSCl (3.01 g, 20.0 mmol) in THF (10 mL) was added dropwise and the mixture was stirred for 20 h at room temperature. The reaction mixture was quenched with saturated NH_4Cl aqueous solution at 0 °C and was extracted with EtOAc (3 × 100 mL). The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel with *i*-hexane/ethyl acetate (5:1) to afford *syn*-**158b** (4.20 g, 95%, dr = 99:1) as yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 4.24–4.12 (m, 2H), 3.44 (d, J = 2.1 Hz, 1H), 1.71–1.61 (m, 1H), 1.54–1.44 (m, 1H), 1.23 (d, J = 6.3 Hz, 3H), 1.17 (d, J = 6.2 Hz, 3H), 0.89 (s, 9H), 0.09 (d, J = 0.9 Hz, 3H), 0.08 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 67.9, 64.5, 45.8, 25.9, 23.9, 22.8, 18.1, –4.4, –4.9.

The analytical data was in accordance with literature values.[63]

(*S*)-1-(4-Methoxyphenyl)propan-2-ol (*S*-158f):



(*S*)-**158f**

The alcohol (*S*)-**158f** was prepared according to **TP6** from (*S*)-propylene oxide (4.18 mL, 3.48 g, 59.7 mmol, 1.0 equiv) dissolved in THF (60 mL) and the corresponding arylmagnesium reagent in THF (75.0 mL, 71.6 mmol, 0.95 M, 1.2 equiv). The crude product was purified *via* flash column

chromatography on silica gel with *n*-pentane/diethyl ether (2:1) to afford (*S*)-**158f** (7.09 g, 42.4 mmol, 71%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.17–7.09 (m, 2H), 6.90–6.82 (m, 2H), 4.04–3.91 (m, 1H), 3.80 (s, 3H), 2.74 (dd, *J* = 13.6, 4.7 Hz, 1H), 2.62 (dd, *J* = 13.6, 8.0 Hz, 1H), 1.49 (d, *J* = 3.7 Hz, 1H), 1.24 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 158.4, 130.6, 130.5, 114.1, 69.1, 55.4, 45.0, 22.8.

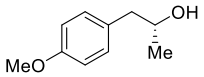
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3371 (w), 2965 (w), 2930 (w), 2907 (w), 2836 (w), 1612 (m), 1510 (vs), 1463 (m), 1456 (m), 1446 (w), 1441 (w), 1372 (w), 1300 (m), 1243 (vs), 1203 (w), 1176 (s), 1109 (m), 1076 (m), 1033 (s), 941 (m), 930 (m), 846 (m), 831 (m), 806 (s), 754 (m).

MS (70 eV, EI): m/z (%): 166 (10), 122 (64), 121 (100), 107 (13), 91 (12).

HRMS (EI) for $C_{10}H_{14}O_2$: calc. $[M]^{+\bullet}$: 166.0994, found: 166.0987.

$[\alpha]_D^{20}$: +28.4 (c = 1.23, $CHCl_3$).

(*R*)-1-(4-Methoxyphenyl)propan-2-ol (*R*-158f):



(*R*)-**158f**

The alcohol (*R*)-**158f** was prepared according to **TP6** from (*R*)-propylene oxide (1.04 mL, 863 mg, 14.9 mmol, 1.0 equiv) dissolved in in THF (15 mL) and the corresponding arylmagnesium reagent in THF (18.8 mL, 17.9 mmol, 0.95 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (2:1) to afford (*R*)-**158f** (1.73 g, 10.4 mmol, 70%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.17–7.09 (m, 2H), 6.90–6.82 (m, 2H), 4.03–3.92 (m, 1H), 3.80 (s, 3H), 2.74 (dd, *J* = 13.6, 4.7 Hz, 1H), 2.62 (dd, *J* = 13.6, 8.0 Hz, 1H), 1.51 (d, *J* = 3.2 Hz, 1H), 1.24 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = δ 158.4, 130.6, 130.5, 114.1, 69.1, 55.4, 45.0, 22.8.

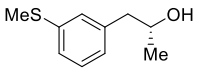
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3363 (w), 2964 (w), 2928 (w), 2924 (w), 2906 (w), 2834 (w), 1612 (m), 1510 (vs), 1462 (m), 1456 (m), 1442 (w), 1373 (w), 1300 (m), 1243 (vs), 1176 (s), 1109 (m), 1076 (m), 1033 (s), 941 (m), 930 (m), 846 (m), 832 (w), 805 (s), 754 (m).

MS (70 eV, EI): m/z (%): 166 (5), 122 (68), 121 (100), 107 (17), 91 (20).

HRMS (EI) for $C_{10}H_{14}O_2$: calc. $[M]^{+\bullet}$: 166.0994, found: 166.0987.

$[\alpha]_D^{20}$: −29.0 (c = 1.35, $CHCl_3$).

(*R*)-1-(3-(Methylthio)phenyl)propan-2-ol (*R*-158g):



(*R*)-**158g**

The alcohol (*R*)-**158g** was prepared according to **TP6** from (*R*)-propylene oxide (0.34 mL, 283 mg, 4.87 mmol, 1.0 equiv) dissolved in THF (5 mL) and the corresponding arylmagnesium reagent in THF (7.04 mL, 5.84 mmol, 0.83 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (2:1) to afford (*R*)-**158g** (577 mg, 3.16 mmol, 65%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.24 (t, *J* = 7.6 Hz, 1H), 7.17–7.08 (m, 2H), 6.98 (dt, *J* = 7.5, 1.4 Hz, 1H), 4.07–3.97 (m, 1H), 2.76 (dd, *J* = 13.5, 4.8 Hz, 1H), 2.66 (dd, *J* = 13.4, 8.0 Hz, 1H), 2.48 (s, 3H), 1.54 (d, *J* = 3.6 Hz, 1H), 1.25 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 139.4, 138.8, 129.1, 127.5, 126.2, 124.7, 68.9, 45.8, 23.0, 15.8.

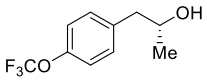
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3397 (m), 3334 (m), 2970 (m), 2930 (m), 2919 (m), 1592 (m), 1570 (m), 1487 (m), 1475 (m), 1441 (s), 1425 (m), 1372 (m), 1356 (m), 1331 (m), 1278 (w), 1210 (m), 1111 (s), 1084 (s), 1071 (s), 1049 (m), 1028 (m), 936 (s), 879 (w), 775 (s), 769 (s), 755 (s), 699 (s), 693 (vs), 684 (s).

MS (70 eV, EI): m/z (%): 182 (55), 138 (95), 123 (24), 121 (10), 91 (100).

HRMS (EI) for $C_{10}H_{14}OS$: calc. $[M]^{+\bullet}$: 182.0765, found: 182.0759.

$[\alpha]_D^{20}$: −28.6 (c = 0.85, $CHCl_3$).

(*R*)-1-(4-(Trifluoromethoxy)phenyl)propan-2-ol (*R*-158h):



(*R*)-**158h**

The alcohol (*R*)-**158h** was prepared according to **TP6** from (*R*)-propylene oxide (0.686 mL, 569 mg, 9.80 mmol, 1.0 equiv) dissolved in THF (10 mL) and the corresponding arylmagnesium reagent in THF (11.5 mL, 11.8 mmol, 1.02 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (*R*)-**158h** (1.51 g, 6.86 mmol, 70%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.26–7.21 (m, 2H), 7.19–7.13 (m, 2H), 4.09–3.96 (m, 1H), 2.79 (dd, *J* = 13.6, 4.8 Hz, 1H), 2.71 (dd, *J* = 13.6, 7.8 Hz, 1H), 1.42 (s, 1H), 1.25 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.0, 137.5, 130.8, 121.2, 68.9, 45.1, 23.1.

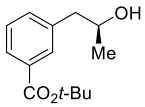
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3352 (w), 2972 (vw), 2929 (vw), 1509 (m), 1458 (vw), 1376 (vw), 1253 (vs), 1219 (s), 1195 (s), 1154 (vs), 1106 (s), 1080 (m), 1048 (w), 1020 (m), 946 (w), 935 (m), 921 (w), 858 (w), 841 (w), 827 (w), 806 (m), 773 (w), 672 (w).

MS (70 eV, EI): m/z (%): 176 (100), 109 (11), 91 (14).

HRMS (EI) for $C_{17}H_{16}FO_2$: calc. $[M-H]^{+\bullet}$: 219.0633, found: 219.0626.

$[\alpha]_D^{20}$: −20.3 (c = 0.95, $CHCl_3$).

***tert*-Butyl (*S*)-3-(2-hydroxypropyl)benzoate (*S*-158i):**



(*S*)-**158i**

A solution of *tert*-butyl 3-iodobenzoate (1.52 g, 5 mmol, 1.0 equiv) in THF (10 mL) was cooled to −50 °C before dropwise addition of *i*PrMgCl·LiCl (1.2 M, 5 mL, 6 mmol, 1.2 equiv). The reaction mixture was stirred at −50 °C for 1 and subsequently charged with CuI (95 mg, 0.5 mmol, 0.1 equiv). Then, (*S*)-propylene oxide (0.35 mL, 290 mg, 5.0 mmol, 1.0 equiv) in THF (5 mL) was added. The reaction was let warm to ambient temperature overnight and quenched with sat. aq. NH_4Cl solution. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with *i*-hexane/ethyl acetate (2:1) to afford (*S*)-**158i** (922 mg, 3.9 mmol, 78%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.91–7.80 (m, 2H), 7.42–7.33 (m, 2H), 4.11–4.01 (m, 1H), 2.83 (dd, *J* = 13.5, 4.9 Hz, 1H), 2.75 (dd, *J* = 13.5, 7.9 Hz, 1H), 1.59 (s, 9H), 1.47 (d, *J* = 4.0 Hz, 1H), 1.26 (dd, *J* = 6.1, 0.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 165.9, 138.8, 133.7, 132.4, 130.4, 128.5, 127.8, 81.2, 69.0, 45.6, 28.3, 23.1.

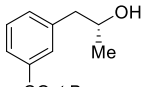
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3410 (w), 2974 (w), 2931 (w), 1710 (s), 1695 (m), 1586 (w), 1477 (w), 1456 (w), 1442 (w), 1392 (w), 1367 (m), 1293 (s), 1256 (m), 1206 (m), 1158 (vs), 1110 (s), 1085 (s), 1048 (m), 1001 (w), 943 (m), 929 (w), 849 (m), 823 (w), 811 (w), 755 (m), 745 (s), 707 (w), 696 (m), 674 (w).

MS (70 eV, EI): m/z (%): 163 (27), 136 (100), 91 (18).

HRMS (EI) for $C_{14}H_{20}O_3$: calc. $[M-C_2H_8O]^{+\bullet}$: 192.1150, found: 192.1148.

$[\alpha]_D^{20}$: +19.9 (c = 1.00, $CHCl_3$).

***tert*-Butyl (*R*)-3-(2-hydroxypropyl)benzoate (*R*-158i):**



(*R*)-**158i**

A solution of *tert*-butyl 3-iodobenzoate (3.04 g, 10 mmol, 1.0 equiv) in THF (10 mL) was cooled to −50 °C before dropwise addition of *i*PrMgCl·LiCl (1.2 M, 10 mL, 12 mmol, 1.2 equiv). The reaction mixture was stirred at −50 °C for 1 and subsequently charged with CuI (190 mg, 1.0 mmol, 0.1 equiv). Then, (*R*)-propylene oxide (0.70 mL, 580 mg, 10.0 mmol, 1.0 equiv) in THF (10 mL) was added. The reaction was let warm to ambient temperature overnight and quenched with sat. aq. NH_4Cl solution. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with *i*-hexane/ethyl acetate (2:1) to afford (*R*)-**158i** (1.75 g, 7.4 mmol, 74%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.90–7.81 (m, 2H), 7.41–7.32 (m, 2H), 4.10–4.01 (m, 1H), 2.83 (dd, *J* = 13.5, 4.9 Hz, 1H), 2.75 (dd, *J* = 13.5, 7.8 Hz, 1H), 1.59 (s, 9H), 1.48 (d, *J* = 4.0 Hz, 1H), 1.26 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 165.9, 138.8, 133.7, 132.4, 130.4, 128.5, 127.8, 81.2, 69.0, 45.6, 28.3, 23.1.

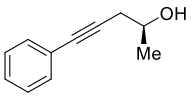
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3417 (w), 2974 (w), 2930 (w), 1710 (s), 1695 (m), 1586 (w), 1477 (w), 1456 (w), 1441 (w), 1393 (w), 1367 (m), 1293 (s), 1256 (m), 1206 (m), 1158 (vs), 1110 (s), 1085 (s), 1049 (m), 1001 (w), 943 (m), 849 (m), 823 (w), 810 (w), 755 (m), 745 (s), 708 (w), 696 (m), 673 (w).

MS (70 eV, EI): m/z (%): 163 (29), 136 (100), 91 (21), 57 (70).

HRMS (EI) for $C_{14}H_{20}O_3$: calc. $[M-C_2H_8O]^{+\bullet}$: 192.1150, found: 192.1147.

$[\alpha]_D^{20}$: −17.0 (c = 1.04, $CHCl_3$).

(*S*)-5-Phenylpent-4-yn-2-ol (*S*-158j):



(*S*)-**158j**

A solution of ethynylbenzene (1.02 g, 10 mmol, 1.0 equiv) in THF (10 mL) was cooled to −78 °C before dropwise addition of *i*PrMgCl·LiCl (1.2 M, 12.5 mL, 15 mmol, 1.5 equiv). The reaction mixture

was let warm to room temperature overnight and subsequently charged with CuI (190 mg, 1 mmol, 0.1 equiv). Then, (*S*)-propylene oxide (0.84 mL, 697 mg, 12.0 mmol, 1.2 equiv) in THF (12 mL) was added. The reaction was let warm to ambient temperature overnight and quenched with sat. aq. NH_4Cl solution. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (3:1) to afford (*S*)-**158j** (1.01 g, 6.3 mmol, 63%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.46–7.37 (m, 2H), 7.36–7.26 (m, 4H), 4.11–4.00 (m, 1H), 2.64 (dd, *J* = 16.6, 5.1 Hz, 1H), 2.56 (dd, *J* = 16.6, 6.6 Hz, 1H), 1.96 (d, *J* = 4.8 Hz, 1H), 1.33 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 131.8, 128.4, 128.1, 123.5, 86.2, 83.2, 66.7, 30.2, 22.6.

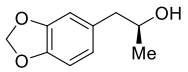
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3399 (m), 3338 (w), 2976 (w), 2931 (w), 1596 (w), 1487 (m), 1446 (m), 1441 (m), 1427 (w), 1371 (w), 1356 (m), 1332 (m), 1283 (w), 1210 (m), 1176 (w), 1110 (m), 1092 (m), 1071 (s), 1027 (m), 1000 (w), 934 (s), 919 (m), 880 (w), 768 (m), 760 (s), 755 (vs), 693 (vs).

MS (70 eV, EI): m/z (%): 160(31), 115 (100), 105 (62), 77 (17).

HRMS (EI) for $C_{11}H_{12}O$: calc. $[M]^{+\bullet}$: 160.0888, found: 160.0881.

$[\alpha]_D^{20}$: +18.4 (c = 0.48, $CHCl_3$).

(*S*)-1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-ol (*S*-158k):



(*S*)-**158k**

The alcohol (*S*)-**158k** was prepared according to **TP6** from (*S*)-propylene oxide (0.66 mL, 549 mg, 9.5 mmol, 1.0 equiv) dissolved in THF (10 mL) and the corresponding arylmagnesium reagent in THF (12.7 mL, 11.3 mmol, 0.89 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (2:1) to afford (*S*)-**158k** (1.26 g, 6.99 mmol, 74%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.76 (d, *J* = 7.9 Hz, 1H), 6.71 (d, *J* = 1.7 Hz, 1H), 6.66 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.94 (s, 2H), 3.99–3.93 (m, 1H), 2.71 (dd, *J* = 13.6, 4.6 Hz, 1H), 2.59 (dd, *J* = 13.6, 8.1 Hz, 1H), 1.53 (d, *J* = 3.6 Hz, 1H), 1.23 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.9, 146.3, 132.3, 122.4, 109.8, 108.5, 101.0, 69.1, 45.6, 22.9.

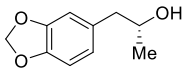
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3373 (w), 2967 (w), 2890 (w), 2228 (w), 1607 (w), 1501 (s), 1488 (s), 1440 (s), 1372 (w), 1347 (w), 1243 (vs), 1187 (m), 1118 (m), 1098 (m), 1077 (m), 1035 (vs), 936 (s), 927 (s), 920 (s), 865 (w), 838 (w), 802 (s), 777 (m), 771 (m), 757 (w), 714 (w).

MS (70 eV, EI): m/z (%): 180 (25), 136 (49), 135 (100), 77 (13).

HRMS (EI) for $C_{10}H_{12}O_3$: calc. [M]$^{+\bullet}$: 180.0786, found: 180.0779.

$[\alpha]_D^{20}$: +27.3 (c = 1.14, $CHCl_3$).

(*R*)-1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-ol (*R*-158k):



(*R*)-**158k**

The alcohol (*R*)-**158k** was prepared according to **TP6** from (*R*)-propylene oxide (0.66 mL, 549 mg, 9.5 mmol, 1.0 equiv) dissolved in THF (10 mL) and the corresponding arylmagnesium reagent in THF (12.7 mL, 11.3 mmol, 0.89 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (2:1) to afford (*R*)-**158k** (1.32 g, 7.33 mmol, 76%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.75 (d, *J* = 7.8 Hz, 1H), 6.70 (d, *J* = 1.7 Hz, 1H), 6.67–6.63 (m, 1H), 5.92 (s, 2H), 3.99–3.91 (m, 1H), 2.70 (dd, *J* = 13.6, 4.8 Hz, 1H), 2.59 (dd, *J* = 13.6, 8.0 Hz, 1H), 1.22 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.9, 146.3, 132.3, 122.4, 109.8, 108.4, 101.0, 69.0, 45.5, 22.8.

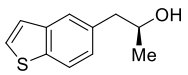
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3378 (w), 2967 (w), 2887 (w), 2228 (w), 1607 (w), 1501 (s), 1488 (s), 1440 (s), 1372 (w), 1347 (w), 1243 (vs), 1187 (m), 1118 (m), 1098 (m), 1077 (m), 1035 (vs), 992 (vw), 936 (s), 927 (s), 865 (w), 838 (w), 802 (s), 777 (m), 771 (m), 757 (w), 724 (vw), 714 (w).

MS (70 eV, EI): m/z (%): 180 (25), 135 (100), 106 (7), 77 (13).

HRMS (EI) for $C_{10}H_{12}O_3$: calc. [M]$^{+\bullet}$: 180.0786, found: 180.0780.

$[\alpha]_D^{20}$: −26.4 (c = 0.93, $CHCl_3$).

(*S*)-1-(Benzo[*b*]thiophen-5-yl)propan-2-ol (*S*-158l):



(*S*)-**158l**

The alcohol (*S*)-**158l** was prepared according to **TP6** from (*S*)-propylene oxide (0.70 mL, 581 mg, 10.0 mmol, 1.0 equiv) dissolved in THF (10 mL) and the corresponding arylmagnesium reagent in THF (18.8 mL, 12.0 mmol, 0.64 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (3:1) to afford (*S*)-**158l** (1.25 g, 6.49 mmol, 65%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.83 (d, *J* = 8.2 Hz, 1H), 7.71–7.64 (m, 1H), 7.44 (d, *J* = 5.5 Hz, 1H), 7.30 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.21 (dd, *J* = 8.2, 1.7 Hz, 1H), 4.08 (m, 1H), 2.93 (dd, *J* = 13.5, 4.7 Hz, 1H), 2.80 (dd, *J* = 13.5, 8.1 Hz, 1H), 1.52 (d, *J* = 3.8 Hz, 1H), 1.28 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.2, 138.2, 134.7, 127.0, 126.1, 124.3, 123.8, 122.7, 69.2, 45.8, 23.0.

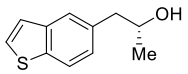
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3335 (w), 2965 (w), 2924 (w), 1454 (m), 1435 (s), 1420 (s), 1372 (s), 1345 (w), 1326 (w), 1306 (w), 1274 (w), 1259 (w), 1223 (w), 1202 (w), 1159 (w), 1145 (w), 1120 (vs), 1078 (vs), 1048 (vs), 946 (s), 935 (s), 925 (s), 897 (m), 893 (m), 831 (s), 800 (vs), 768 (m) 754 (vs) 702 (vs), 689 (vs), 668 (s).

MS (70 eV, EI): m/z (%): 192 (15), 147 (100), 121 (6), 45 (2).

HRMS (EI) for $C_{11}H_{12}OS$: calc. $[M]^{+\bullet}$: 192.0609, found: 192.0601.

$[\alpha]_D^{20}$: +18.1 (c = 1.09, $CHCl_3$).

(*R*)-1-(Benzo[*b*]thiophen-5-yl)propan-2-ol (*R*-158l):



(*R*)-**158l**

The alcohol (*R*)-**158l** was prepared according to **TP6** from (*R*)-propylene oxide (0.70 mL, 581 mg, 10.0 mmol, 1.0 equiv) dissolved in THF (10 mL) and the corresponding arylmagnesium reagent in THF (18.8 mL, 12.0 mmol, 0.64 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (3:1) to afford (*R*)-**158l** (1.42 g, 7.4 mmol, 74%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.82 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 1.6 Hz, 1H), 7.44 (d, *J* = 5.4 Hz, 1H), 7.30 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.20 (dd, *J* = 8.2, 1.7 Hz, 1H), 4.12–4.00 (m, 1H), 2.90 (dd, *J* = 13.5, 4.9 Hz, 1H), 2.80 (dd, *J* = 13.5, 7.9 Hz, 1H), 2.45 (s, 1H), 1.27 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.1, 138.0, 134.6, 126.9, 126.0, 124.3, 123.7, 122.6, 69.1, 45.7, 22.8.

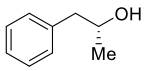
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3337 (w), 2965 (m), 2931 (m), 2929 (m), 2917 (w), 2915 (w), 1709 (w), 1696 (w), 1454 (w), 1436 (m), 1420 (m), 1370 (m), 1308 (m), 1306 (m), 1260 (m), 1158 (m), 1146 (w), 1118 (s), 1075 (s), 1046 (s), 946 (m), 936 (m), 924 (m), 904 (w), 900 (m), 891 (w), 845 (m), 832 (m), 803 (s), 800 (s), 768 (m), 761 (m), 754 (s), 702 (vs), 690 (vs), 668 (m)

MS (70 eV, EI): m/z (%): 192 (29), 148 (100), 147 (95), 45 (13).

HRMS (EI) for $C_{11}H_{12}OS$: calc. $[M]^{+\bullet}$: 192.0609, found: 192.0608.

$[\alpha]_D^{20}$: −17.7 (c = 2.01, $CHCl_3$).

(*R*)-1-Phenylpropan-2-ol (*R*-158m):



(*R*)-**158m**

The alcohol (*R*)-**158m** was prepared according to **TP6** from (*R*)-propylene oxide (700 µL, 580 mg, 10.0 mmol, 1.0 equiv) in THF (20 mL), CuI (76 mg, 4 mol%) and phenylmagnesium chloride in THF (24.0 mL, 12.0 mmol, 0.5 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:9 to afford (*R*)-**158m** (1.02 g, 7.5 mmol, 75%) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.36–7.29 (m, 2H), 7.23 (dd, *J* = 7.3, 5.7 Hz, 2H), 4.03 (dqd, *J* = 8.0, 6.2, 4.8 Hz, 1H), 2.80 (dd, *J* = 13.4, 4.8 Hz, 1H), 2.70 (dd, *J* = 13.5, 8.0 Hz, 1H), 1.55 (s, 1H), 1.25 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 138.5, 129.4, 128.6, 126.5, 68.9, 45.8, 22.8.

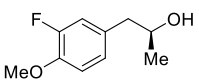
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3349 (w), 3063 (vw), 3028 (w), 2969 (w), 2929 (w), 1600 (vw), 1496 (w), 1453 (m), 1374 (w), 1310 (w), 1209 (w), 1197 (w), 1180 (vw), 1156 (vw), 1116 (m), 1078 (m), 1040 (w), 1031 (w), 939 (m), 911 (w), 838 (w), 740 (s), 698 (vs).

MS (70 eV, EI): m/z (%):117 (21), 91 (100).

HRMS (EI) for $C_9H_{11}O$: calc. $[M-H]^{+\bullet}$: 135.0810; found: 135.0802.

$[\alpha]_D^{20}$: −36.3 (c = 1.91, $CHCl_3$)

(*S*)-1-(3-Fluoro-4-methoxyphenyl)propan-2-ol (*S*-158n):



(*S*)-**158n**

The alcohol (*S*)-**158n** was prepared according to **TP6** from (*S*)-propylene oxide (1.17 mL, 970 mg, 16.7 mmol, 1.0 equiv) in THF (34 mL), CuI (127 mg, 4 mol%) and the corresponding arylmagnesium reagent in THF (40 mL, 20.0 mmol, 0.5 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:4 to afford (*S*)-**158n** (2.06 g, 11.2 mmol, 67%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.00–6.93 (m, 1H), 6.91 (dd, *J* = 4.3, 2.0 Hz, 2H), 4.04–3.92 (m, 1H), 3.88 (s, 3H), 2.72 (dd, *J* = 13.7, 4.8 Hz, 1H), 2.62 (dd, *J* = 13.7, 8.0 Hz, 1H), 1.48 (s, 1H), 1.23 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.4 (d, *J* = 245.7 Hz), 146.4 (d, *J* = 10.6 Hz), 131.7 (d, *J* = 6.0 Hz), 125.1 (d, *J* = 3.5 Hz), 117.1 (d, *J* = 17.8 Hz), 113.6 (d, *J* = 2.3 Hz), 68.9, 56.5, 44.8 (d, *J* = 1.4 Hz), 22.9.

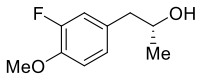
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3357 (w), 2967 (w), 2932 (w), 2840 (w), 1624 (w), 1584 (w), 1516 (vs), 1463 (m), 1456 (m), 1443 (m), 1430 (m), 1373 (w), 1312 (m), 1272 (vs), 1223 (s), 1183 (w), 1125 (vs), 1079 (m), 1052 (w), 1027 (s), 956 (w), 929 (w), 874 (w), 805 (m), 761 (m), 752 (w).

MS (70 eV, EI): m/z (%): 141 (8), 140 (100), 139 (91), 125 (67), 109 (17), 96 (15), 77 (17), 45 (9).

HRMS (EI) for $C_{10}H_{13}FO_2$: calc. $[M]^{+\bullet}$: 184.0900; found: 184.0892.

$[\alpha]_D^{20}$: +18.4 (c = 1.06, $CHCl_3$).

(*R*)-1-(3-Fluoro-4-methoxyphenyl)propan-2-ol (*R*-158n):



(*R*)-**158n**

The alcohol (*R*)-**158n** was prepared according to **TP6** from (*R*)-propylene oxide (1.17 mL, 970 mg, 16.7 mmol, 1.0 equiv) in THF (34 mL), CuI (127 mg, 4 mol%) and the corresponding arylmagnesium reagent in THF (40 mL, 20.0 mmol, 0.5 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:4 to afford (*R*)-**158n** (1.99 g, 10.8 mmol, 65%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.00–6.86 (m, 3H), 3.98 (q, *J* = 5.9 Hz, 1H), 3.87 (s, 3H), 2.72 (dd, *J* = 13.7, 4.7 Hz, 1H), 2.62 (dd, *J* = 13.7, 8.0 Hz, 1H), 1.48 (s, 1H), 1.23 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.4 (d, *J* = 245.7 Hz), 146.4 (d, *J* = 10.7 Hz), 131.7 (d, *J* = 6.1 Hz), 125.1 (d, *J* = 3.5 Hz), 117.1 (d, *J* = 17.9 Hz), 113.6 (d, *J* = 2.2 Hz), 68.9, 56.5, 44.8 (d, *J* = 1.4 Hz), 22.9.

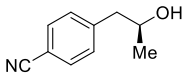
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3367 (w), 2966 (w), 2933 (w), 2840 (w), 1624 (w), 1584 (w), 1517 (vs), 1463 (m), 1456 (m), 1443 (m), 1430 (m), 1373 (w), 1313 (m), 1273 (vs), 1223 (s), 1183 (w), 1125 (vs), 1078 (m), 1053 (w), 1027 (s), 956 (w), 929 (w), 874 (w), 805 (m), 761 (m), 751 (w).

MS (70 eV, EI): m/z (%):141 (8), 140 (100), 139 (92), 125 (66), 109 (17), 96 (15), 77 (18), 45 (9).

HRMS (EI) for $C_{10}H_{13}FO_2$: calc. $[M]^{+\bullet}$: 184.0900; found: 184.0894.

$[\alpha]_D^{20}$: −21.0 (c = 0.98, $CHCl_3$).

(*S*)-4-(2-Hydroxypropyl)benzonitrile (*S*-158o):



(*S*)-**158o**

A solution of 4-iodobenzonitrile (4.58 g, 20 mmol, 1.0 equiv) in THF (10 mL) was cooled to −50 °C before dropwise addition of *i*-PrMgCl·LiCl (1.2 M, 20 mL 24 mmol, 1.2 equiv).[180] The reaction mixture was stirred at −50 °C for 10 min and subsequently charged with CuI (152 mg, 0.8 mmol, 4 mol% equiv). Then, (*S*)-propylene oxide (1.4 mL, 1.16 g, 20.0 mmol, 1.0 equiv) in THF (40 mL). The reaction was let warm to ambient temperature overnight and quenched with sat. aq. NH_4Cl solution. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:9 to afford (*S*)-**158o** (1.45 g, 9.0 mmol, 45%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.64–7.57 (m, 2H), 7.37–7.30 (m, 2H), 4.06 (m, 1H), 2.88–2.73 (m, 2H), 1.42 (s, 1H), 1.26 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 144.5, 132.3, 130.4, 119.1, 110.4, 68.6, 45.7, 23.4.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3364 (m), 2957 (s), 2925 (s), 2870 (m), 1610 (w), 1514 (w), 1455 (s), 1428 (m), 1413 (m), 1375 (s), 1334 (m), 1316 (m), 1291 (m), 1260 (m), 1202 (m), 1189 (m), 1168 (m), 1154 (m), 1124 (s), 1120 (s), 1055 (vs), 1014 (s), 939 (s), 931 (m), 838 (m), 825 (m), 771 (w), 743 (s), 702 (m), 699 (m), 692 (m).

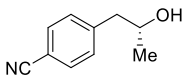
MS (70 eV, EI): m/z (%): 117 (100), 90 (22), 45 (10)

HRMS (EI) for $C_{10}H_{11}ON$: calc. $[M-Me]^{+\bullet}$: 146.0606, found: 146.0600.

$[\alpha]_D^{20}$: −11.8 (c = 1.32, $CHCl_3$).

[180] B. Heinz, D. Djukanovic, M. A. Ganiek, B. Martin, B. Schenkel, P. Knochel, *Org. Lett.* **2020**, *22*, 493–496.

(*R*)-4-(2-Hydroxypropyl)benzonitrile (*R*-158o):



(*R*)-**158o**

A solution of 4-iodobenzonitrile (4.58 g, 20 mmol, 1.0 equiv) in THF (10 mL) was cooled to −50 °C before dropwise addition of *i*-PrMgCl·LiCl (1.2 M, 20 mL 24 mmol, 1.2 equiv).[180] The reaction mixture was stirred at −50 °C for 10 min and subsequently charged with CuI (152 mg, 0.8 mmol, 4 mol% equiv). Then, (*R*)-propylene oxide (1.4 mL, 1.16 g, 20.0 mmol, 1.0 equiv) in THF (40 mL). The reaction was let warm to ambient temperature overnight and quenched with sat. aq. NH_4Cl solution. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:9 to afford (*R*)-**158o** (2.17 g, 13.4 mmol, 67%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.63–7.56 (m, 2H), 7.36–7.30 (m, 2H), 4.05 (p, J = 6.2 Hz, 1H), 2.87–2.72 (m, 2H), 1.25 (d, J = 6.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 144.5, 132.3, 130.4, 119.1, 110.4, 68.6, 45.7, 23.4.

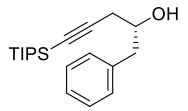
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3318 (w), 2960 (m), 2930 (m), 2873 (w), 2225 (m), 1608 (s), 1586 (m), 1512 (s), 1447 (m), 1375 (m), 1368 (m), 1286 (s), 1251 (m), 1228 (m), 1205 (m), 1190 (m), 1168 (s), 1117 (m), 1105 (m), 1065 (m), 1014 (m), 838 (vs), 699 (m).

MS (70 eV, EI): m/z (%): 117 (100), 90 (22), 45 (10).

HRMS (EI) for $C_{10}H_{11}ON$: calc. $[M-H]^{+\bullet}$: 160.0762, found: 160.00756.

$[\alpha]_D^{20}$: +11.6 (c = 1.18, $CHCl_3$).

(*R*)-1-Phenyl-5-(tri*iso*propylsilyl)pent-4-yn-2-ol (*R*-158p):



(*R*)-**158p**

The alcohol (*R*)-**158p** was prepared according to a modified literature procedure.[122] A solution of (triisopropylsilyl)acetylene (6.3 mL, 5.11 g, 28 mmol, 1.4 equiv) in THF (28 mL) was cooled to −78 °C. Then, *n*-BuLi (1.6 M, 25 mL, 40 mmol, 2.0 equiv) was added and the mixture was allowed to warm to −30 °C and stirred at this temperature for 15 minutes. The reaction mixture was cooled down to −78 °C again and a solution of (*R*)-**157a** in THF (20 mmol, ca. 0.5 M, 40 mL) was added dropwise. $BF_3{\cdot}Et_2O$ (2.98 g, 21 mmol, 1.05 equiv) was added and the mixture was allowed to warm to room

temperature overnight. A solution of sat. aq. NH_4Cl was added, the phases were separated and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:4 to afford (*R*)-**158p** (5.13 g, 16.2 mmol, 81%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.37–7.28 (m, 2H), 7.27–7.20 (m, 3H), 3.98 (dq, *J* = 7.3, 5.7 Hz, 1H), 2.96 (dd, *J* = 13.5, 5.6 Hz, 1H), 2.85 (dd, *J* = 13.5, 7.3 Hz, 1H), 2.55–2.40 (m, 2H), 1.99–1.85 (m, 1H), 1.09 (d, *J* = 3.5 Hz, 18H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 138.1, 129.6, 128.7, 126.7, 104.6, 84.1, 71.2, 42.6, 28.1, 18.8, 11.4.

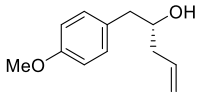
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3374 (w), 3029 (w), 2942 (s), 2891 (m), 2864 (s), 2173 (m), 1602 (w), 1497 (w), 1463 (m), 1456 (m), 1383 (w), 1366 (w), 1292 (w), 1243 (w), 1164 (w), 1073 (m), 1049 (m), 1018 (s), 996 (m), 918 (w), 882 (vs), 742 (s), 699 (s), 675 (s), 663 (s).

MS (70 eV, EI): m/z (%): 255 (38), 131 (36), 103 (40), 91 (100).

HRMS (EI) for $C_{20}H_{32}OSi$: calc. $[M]^{+\bullet}$: 316.2222, found: 316.2215.

$[\alpha]_D^{20}$: −17.8 (c = 1.2, $CHCl_3$).

(*R*)-1-(4-Methoxyphenyl)pent-4-en-2-ol (*R*-158q):



(*R*)-**158q**

The alcohol (*R*)-**158q** was prepared according to **TP6** from (*R*)-**157b** (672 mg, 8.0 mmol, 1.0 equiv) dissolved in THF (16 mL), CuI (61 mg, 4 mol%) and the corresponding aryl magnesium reagent in THF (19.2 mL, 9.6 mmol, 0.5 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:2 to afford (*R*)-**158q** (1.21 g, 6.3 mmol, 79%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.17–7.11 (m, 2H), 6.90–6.84 (m, 2H), 5.95–5.80 (m, 1H), 5.21–5.10 (m, 2H), 3.80 (s, 4H), 2.77 (dd, *J* = 13.7, 4.9 Hz, 1H), 2.66 (dd, *J* = 13.7, 7.9 Hz, 1H), 2.39–2.28 (m, 1H), 2.21 (dtt, *J* = 14.1, 7.7, 1.2 Hz, 1H), 1.71 (d, *J* = 3.1 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 158.4, 134.9, 130.5, 130.4, 118.2, 114.1, 71.9, 55.4, 42.5, 41.2.

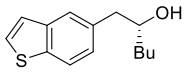
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3412 (w), 3075 (vw), 3002 (vw), 2933 (w), 2911 (w), 2836 (w), 1640 (w), 1612 (m), 1584 (w), 1511 (vs), 1464 (w), 1456 (w), 1441 (w), 1420 (w), 1354 (vw), 1318 (w), 1300 (m), 1243 (vs), 1177 (m), 1108 (w), 1033 (s), 997 (m), 914 (m), 880 (w), 830 (m), 806 (s), 753 (w).

MS (70 eV, EI): m/z (%): 159 (22), 144 (17), 121 (100), 91 (29), 77 (17).

HRMS (EI) for $C_{12}H_{16}O_2$: calc. $[M]^{+\bullet}$: 192.1150, found: 1141.

$[\alpha]_D^{20}$: −41.1 (c = 0.86, $CHCl_3$).

(*R*)-1-(Benzo[*b*]thiophen-5-yl)hexan-2-ol (*R*-158r):



(*R*)-**158r**

The alcohol (*R*)-**158r** was prepared according to **TP6** from (*R*)-**157c** (801 mg, 8.0 mmol, 1.0 equiv) dissolved in THF (16 mL), CuI (61 mg, 4 mol%) and the corresponding aryl magnesium reagent in THF (19.2 mL, 9.6 mmol, 0.5 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:2 to afford (*R*)-**158r** (1.47 g, 6.3 mmol, 79%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.83 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 1.7 Hz, 1H), 7.44 (d, *J* = 5.4 Hz, 1H), 7.30 (d, *J* = 5.4 Hz, 1H), 7.22 (dd, *J* = 8.2, 1.7 Hz, 1H), 3.91–3.83 (m, 1H), 2.97 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.76 (dd, *J* = 13.6, 8.5 Hz, 1H), 1.56–1.46 (m, 4H), 1.44–1.28 (m, 3H), 0.92 (t, *J* = 7.0 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.2, 138.1, 134.8, 126.9, 126.1, 124.3, 123.8, 122.7, 73.0, 44.1, 36.7, 28.1, 22.9, 14.3.

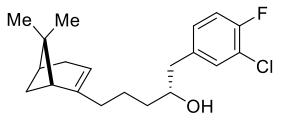
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3421 (w), 2962 (m), 2952 (m), 2922 (m), 2906 (m), 2871 (m), 2858 (m), 1465 (m), 1435 (m), 1420 (m), 1402 (w), 1349 (m), 1333 (w), 1321 (w), 1262 (w), 1223 (w), 1144 (w), 1126 (w), 1114 (w), 1067 (s), 1049 (m), 1035 (m), 1012 (w), 980 (w), 902 (w), 895 (w), 882 (w), 858 (m), 832 (m), 807 (s), 768 (m), 762 (w), 753 (s), 704 (vs), 691 (s), 667 (w).

MS (70 eV, EI): m/z (%): 216 (20), 173 (50), 160 (16), 147 (100), 129 (18).

HRMS (EI) for $C_{14}H_{18}OS$: calc. $[M]^{+\bullet}$: 234.1078, found: 234.1068.

$[\alpha]_D^{20}$: −8.2 (c = 1.15, $CHCl_3$).

(*R*)-1-(3-Chloro-4-fluorophenyl)-5-((1*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)pentan-2-ol (*R,R,S*-158s):



(*R*,*S*,*S*)-**158s**

The alcohol (*R*,*R*,*S*)-**158s** was prepared according to **TP6** from (*R*,*R*,*S*)-**157d** (1.45 g, 7.0 mmol, 1.0 equiv) dissolved in THF (16 mL), CuI (61 mg, 4 mol%) and the corresponding aryl magnesium reagent in THF (18.0 mL, 9.0 mmol, 0.5 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:3 to afford (*R*,*R*,*S*)-**158s** (1.89 g, 5.6 mmol, 80%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.26 (dd, *J* = 5.4, 1.8 Hz, 1H), 7.07 (dd, *J* = 6.8, 1.3 Hz, 2H), 5.25–5.12 (m, 1H), 3.85–3.71 (m, 1H), 2.75 (dd, *J* = 13.8, 4.4 Hz, 1H), 2.62 (dd, *J* = 13.8, 8.2 Hz, 1H), 2.34 (dt, *J* = 8.5, 5.6 Hz, 1H), 2.28–2.13 (m, 2H), 2.10–2.03 (m, 1H), 2.02–1.92 (m, 3H), 1.62–1.35 (m, 4H), 1.26 (s, 3H), 1.10 (d, *J* = 8.4 Hz, 1H), 0.80 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.0 (d, *J* = 247.2 Hz), 148.1, 135.9 (d, *J* = 4.0 Hz), 131.5, 129.2 (d, *J* = 6.9 Hz), 120.9 (d, *J* = 17.6 Hz), 116.6 (d, *J* = 20.8 Hz), 116.3, 72.5, 45.8, 43.1, 41.0, 38.1, 36.8, 36.7, 31.8, 31.4, 26.5, 23.3, 21.3.

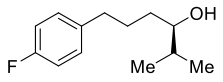
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3383 (w), 2976 (m), 2916 (s), 2872 (m), 2834 (w), 1501 (vs), 1457 (w), 1407 (w), 1382 (m), 1365 (w), 1350 (w), 1331 (w), 1264 (m), 1248 (s), 1220 (w), 1204 (w), 1182 (w), 1152 (w), 1121 (m), 1100 (m), 1075 (m), 1061 (m), 1026 (w), 886 (w), 816 (m), 796 (w), 770 (m), 708 (w), 690 (m).

MS (70 eV, EI): m/z (%): 197 (21), 175 (41), 143 (72), 131 (54), 119 (38), 105 (32), 91 (100).

HRMS (EI) for $C_{20}H_{26}ClFO$: calc. $[M]^{+\bullet}$: 336.1656, found: 336.1652.

$[\alpha]_D^{20}$: −20.8 (c = 1.2, $CHCl_3$).

(*R*)-6-(4-Fluorophenyl)-2-methylhexan-3-ol (*R*-158t):



(*R*)-**158t**

According to a modified literature procedure,[176] a dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum was charged with magnesium turnings (340 mg, 14.0 mmol, 1.4 equiv). Dry THF (5 mL) was added as well as a corn of I_2 for activation. A solution of 1-(2-bromoethyl)-4-fluorobenzene (1.68 mL, 2.43 g, 12.0 mmol, 1.2 equiv) in 5 mL of dry THF was added

dropwise at 0 °C. After addition, the mixture was stirred at room temperature for 2 h. The concentration of the Grignard reagent was determined by titration with I_2 in THF.[155]

Then, CuI (76 mg, 4 mol%) and (*R*)-6e (ca. 860 mg, ca. 0.5 M, 10.0 mmol, 1.0 equiv) was added dropwise to the diluted (ca. 0.5 M) Grignard reagent at 0 °C and allowed to warm to room temperature overnight. Thereafter, the mixture was quenched with sat. aq. NH_4Cl solution. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*R*)-**158t** (1.56 g, 7.4 mmol, 74%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.17–7.09 (m, 2H), 7.00–6.92 (m, 2H), 3.43–3.34 (m, 1H), 2.68–2.53 (m, 2H), 1.87–1.73 (m, 1H), 1.69–1.56 (m, 2H), 1.56–1.35 (m, 2H), 1.30 (d, *J* = 5.2 Hz, 1H), 0.90 (dd, *J* = 6.8, 3.5 Hz, 6H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 161.3 (d, *J* = 243.0 Hz), 138.2 (d, *J* = 3.2 Hz), 129.8 (d, *J* = 7.7 Hz), 115.1 (d, *J* = 21.0 Hz), 76.7, 35.2, 33.7, 28.2, 19.0, 17.2.

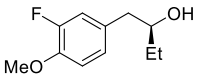
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3361 (w), 2958 (m), 2934 (m), 2891 (w), 2872 (w), 2866 (w), 1601 (w), 1509 (vs), 1462 (w), 1385 (w), 1368 (w), 1220 (s), 1157 (m), 1106 (w), 1096 (w), 1057 (w), 1016 (w), 976 (w), 830 (m), 822 (s), 760 (w), 702 (w).

MS (70 eV, EI): m/z (%): 149 (33), 135 (13), 122 (100).

HRMS (EI) for $C_{13}H_{19}FO$: calc. $[M]^{+\bullet}$: 210.1420, found: 210.1410.

$[\alpha]_D^{20}$: −16.7 (c = 1.63, $CHCl_3$).

(*S*)-1-(3-Fluoro-4-methoxyphenyl)butan-2-ol (*S*-158u):



(*S*)-**158u**

The alcohol (*S*)-**158u** was prepared according to **TP6** from (*S*)-butylene oxide (700 µL, 577 mg, 8.0 mmol, 1.0 equiv) dissolved in THF (16 mL), CuI (61 mg, 4 mol%) and the corresponding aryl magnesium reagent in THF (19.2 mL, 9.6 mmol, 0.5 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**158u** (1.35 g, 6.8 mmol, 71%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.01–6.84 (m, 3H), 3.87 (s, 3H), 3.70 (tt, *J* = 7.5, 4.6 Hz, 1H), 2.75 (dd, *J* = 13.8, 4.3 Hz, 1H), 2.57 (dd, *J* = 13.8, 8.3 Hz, 1H), 1.61–1.42 (m, 3H), 0.99 (t, *J* = 7.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.4 (d, *J* = 245.6 Hz), 146.3 (d, *J* = 10.7 Hz), 131.8 (d, *J* = 6.1 Hz), 125.1 (d, *J* = 3.5 Hz), 117.1 (d, *J* = 17.9 Hz), 113.6, 74.0, 56.4, 42.6, 29.7, 10.2.

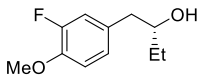
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3377 (w), 3008 (vw), 3004 (vw), 2934 (w), 2877 (w), 2840 (w), 1624 (w), 1584 (w), 1516 (vs), 1463 (m), 1443 (m), 1429 (m), 1379 (vw), 1311 (m), 1271 (vs), 1222 (s), 1182 (w), 1149 (vw), 1125 (vs), 1056 (w), 1025 (s), 977 (m), 956 (m), 875 (w), 846 (w), 805 (m), 778 (vw), 760 (s), 741 (w)

MS (70 eV, EI): m/z (%): 165 (20), 140 (100), 125 (62), 109 (28), 77 (12).

HRMS (EI) for $C_{11}H_{15}FO_2$: calc. $[M]^{+\bullet}$: 198.1056, found: 198.1047.

$[\alpha]_D^{20}$: +21.5 (c = 0.78, $CHCl_3$).

(*R*)-1-(3-Fluoro-4-methoxyphenyl)butan-2-ol (*R*-158u):



(*R*)-**158u**

The alcohol (*R*)-**158u** was prepared according to **TP6** from (*R*)-butylene oxide (700 µL, 577 mg, 8.0 mmol, 1.0 equiv) dissolved in THF (16 mL), CuI (61 mg, 4 mol%) and the corresponding aryl magnesium reagent in THF (19.2 mL, 9.6 mmol, 0.5 M, 1.2 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*R*)-**158u** (1.01 g, 5.1 mmol, 85%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.99–6.86 (m, 3H), 3.86 (s, 3H), 3.69 (m, 1H), 2.74 (dd, *J* = 13.8, 4.3 Hz, 1H), 2.56 (dd, *J* = 13.7, 8.3 Hz, 1H), 1.62–1.42 (m, 3H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 245.4 Hz), 146.2 (d, *J* = 10.7 Hz), 131.8 (d, *J* = 6.0 Hz), 125.1 (d, *J* = 3.4 Hz), 117.1 (d, *J* = 17.9 Hz), 113.5 (d, *J* = 2.2 Hz), 74.0, 56.4, 42.6, 42.6, 29.6, 10.1.

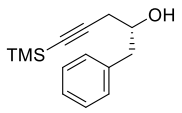
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3381 (w), 2964 (w), 2936 (w), 2878 (w), 2841 (w), 1625 (w), 1585 (w), 1516 (vs), 1463 (m), 1454 (m), 1443 (m), 1430 (m), 1311 (m), 1272 (vs), 1223 (s), 1183 (w), 1125 (s), 1056 (w), 1026 (s), 977 (m), 956 (m), 876 (w), 805 (m), 760 (s), 743 (w).

MS (70 eV, EI): m/z (%): 140 (100), 125 (65), 109 (25), 97 (13), 77 (24).

HRMS (EI) for $C_{10}H_{15}FO_2$: calc. $[M]^+$: 198.1056, found: 198.1050.

$[\alpha]_D^{20}$: −21.7 (c = 0.78, $CHCl_3$).

(*R*)-1-Phenyl-5-(trimethylsilyl)pent-4-yn-2-ol (*R*-158v):



(*R*)-**158v**

The alcohol (*R*)-**158v** was prepared according to a modified literature procedure.[122] A solution of (trimethylsilyl)acetylene (4.0 mL, 2.75 g, 28 mmol, 1.4 equiv) in THF (28 mL) was cooled to −78 °C. Then, *n*-BuLi (1.6 M, 25 mL, 40 mmol, 2.0 equiv) was added and the mixture was allowed to warm to −30 °C and stirred at this temperature for 15 minutes. The reaction mixture was cooled down to −78 °C again and a solution of (*R*)-**157d** in THF (20 mmol, ca. 0.5 M, 40 mL) was added dropwise. $BF_3 \cdot Et_2O$ (2.98 g, 21 mmol, 1.05 equiv) was added and the mixture was allowed to warm to room temperature overnight. A solution of sat. aq. NH_4Cl was added, the phases were separated and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate/*i*-hex = 1:4 to afford (*R*)-**158v** (3.57 g, 15.4 mmol, 77%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.37–7.31 (m, 2H), 7.28–7.23 (m, 3H), 3.99 (dq, *J* = 7.1, 5.7 Hz, 1H), 2.93 (dd, *J* = 13.6, 5.6 Hz, 1H), 2.84 (dd, *J* = 13.6, 7.3 Hz, 1H), 2.51–2.38 (m, 2H), 0.20 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 138.0, 129.5, 128.7, 126.7, 103.1, 88.1, 71.0, 42.6, 28.1, 0.2.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3402 (vw), 3029 (vw), 2958 (w), 2900 (vw), 2175 (w), 1603 (vw), 1497 (w), 1454 (w), 1418 (w), 1355 (vw), 1249 (m), 1077 (w), 1049 (w), 1022 (m), 837 (vs), 758 (m), 742 (m), 698 (s).

MS (70 eV, EI): m/z (%): 193 (42), 121 (19), 103 (27), 97 (20), 91 (100), 73 (99).

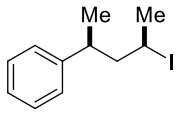
HRMS (EI) for $C_{14}H_{19}OSi$: calc. $[M-H]^{+\bullet}$: 231.1198, found: 231.1198.

$[\alpha]_D^{20}$: −16.0 (c = 1.49, $CHCl_3$).

Preparation of Optically Enriched Secondary Alkyl Iodides

The chiral secondary alkyl iodides *syn*- and *anti*-**142a**, *rac*-**142b**, *syn*-**142**, (*R*)- and (*S*)-**142d** as well as (*R*)- and (*S*)-**142e** were prepared according to literature known procedures.[61-63]

syn-4-Iodopentan-2-yl)benzene (*syn*-142a):



syn-**142a**

The secondary alkyl iodide *syn*-**142a** was prepared according to **TP7** from the alcohol *anti*-**158a** (820 mg, 5.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (1000:1) to afford *syn*-**142a** (890 g, 3.2 mmol, 65%, dr = 98:2) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.34–7.29 (m, 2H), 7.23–7.19 (m, 3H), 4.13–4.05 (m, 1H), 2.97–2.88 (m, 1H), 2.33–2.26 (m, 1H), 1.92 (d, *J* = 6.8 Hz, 3H), 1.88–1.79 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 3H).

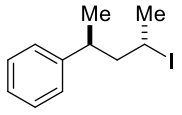
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 146.2, 128.8, 127.1, 126.4, 51.6, 40.0, 28.8, 27.8, 21.3.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3060 (w), 3025 (w), 2960 (m), 2921 (m), 2867 (w), 1603 (w), 1492 (m), 1452 (m), 1377 (m), 1234 (w), 1204 (w), 1150 (w), 1121 (m), 1061 (w), 762 (m), 699 (vs).

MS (70 eV, EI): m/z (%): 131 (11), 127 (13), 105 (100), 91 (29), 79 (11).

HRMS (EI) for $C_{11}H_{15}I$: calc. $[M]^{+\bullet}$: 274.0218, found: 274.0214.

anti-4-Iodopentan-2-yl)benzene (anti-142a):



anti-**142a**

The secondary alkyl iodide *anti*-**142a** was prepared according to **TP7** from the alcohol *syn*-**158a** (820 mg, 5.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (1000:1) to afford *anti*-**142a** (768 g, 2.9 mmol, 58%, dr = 1:99) as a pale yellow oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.33–7.28 (m, 2H), 7.25–7.19 (m, 3H), 3.74–3.65 (m, 1H), 3.01–2.95 (m, 1H), 2.14–2.07 (m, 1H), 1.87 (d, *J* = 6.8 Hz, 3H), 1.73–1.65 (m, 1H), 1.30 (d, *J* = 7.0 Hz, 3H).

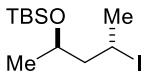
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 145.6, 128.7, 127.3, 126.6, 51.3, 40.5, 29.9, 29.7, 22.6.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3081 (vw), 3060 (vw), 3025 (w), 2957 (w), 2912 (w), 2867 (w), 2358 (vw), 1739 (vw), 1602 (w), 1493 (m), 1451 (m), 1441 (w), 1423 (w), 1376 (w), 1359 (w), 1267 (vw), 1231 (m), 1201 (w), 1149 (m), 1122 (w), 1089 (w), 1064 (w), 1031 (w), 1011 (w), 934 (vw), 908 (w), 869 (w), 762 (s), 744 (w), 699 (vs).

MS (70 eV, EI): m/z (%): 131 (16), 127 (17), 105 (100), 91 (34), 79 (11).

HRMS (EI) for $C_{11}H_{15}I$: calc. $[M]^{+\bullet}$: 274.0218, found: 274.0215.

***Tert*-butyl((*anti*-4-iodopentan-2-yl)oxy)dimethylsilane (anti-142b):**



anti-**142b**

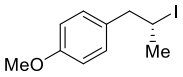
The secondary alkyl iodide *anti*-**142b** was prepared according to **TP7** from the alcohol *syn*-**158b** (1.09 g, 5.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (100:1) to afford *anti*-**142b** (1.24 g, 3.78 mmol, 76%, dr = 1:99) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 4.17 (m, 1H), 3.92 (m, 1H), 2.19 (m, 1H), 1.93 (d, J = 6.8 Hz, 3H), 1.70 (dt, J = 14.1 and 6.5 Hz, 1H), 1.12 (d, J = 6.0 Hz, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] =68.9, 52.9, 28.9, 26.0, 25.2, 23.1, 18.2, –4.1, –4.6.

The analytical data was in accordance with literature values.[63]

(*R*)-1-(2-Iodopropyl)-4-methoxybenzene (*R*-142f):



(*R*)-**142f**

The secondary alkyl iodide (*R*)-**142f** was prepared according to TP3 from the alcohol (*S*)-**158f** (1.66 g, 10.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (200:1) to afford (*R*)-**142f** (1.64 g, 5.94 mmol, 59%, 94% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.12–7.08 (m, 2H), 6.87–6.83 (m, 2H), 4.35–4.26 (m, 1H), 3.80 (s, 3H), 3.23 (dd, J = 14.2, 7.1 Hz, 1H), 3.00 (dd, J = 14.2, 7.6 Hz, 1H), 1.89 (d, J = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] 158.6, 132.0, 130.1, 113.9, 55.4, 48.7, 29.6, 28.1.

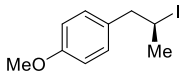
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2961 (w), 2933 (w), 2916 (w), 2909 (w), 2862 (w), 2833 (w), 2166 (w), 1610 (m), 1583 (w), 1509 (vs), 1463 (w), 1451 (w), 1440 (m), 1375 (w), 1301 (m), 1245 (vs), 1225 (s), 1198 (w), 1176 (s), 1145 (m), 1113 (m), 1090 (w), 1055 (w), 1033 (s), 987 (w), 886 (w), 832 (m), 808 (m), 753 (m), 711 (w).

MS (70 eV, EI): m/z (%): 149 (98), 121 (100), 115 (5), 91 (18), 77 (8).

HRMS (EI) for $C_{10}H_{13}IO$: calc. $[M]^{+\bullet}$: 276.0011, found: 276.0005.

$[\alpha]_D^{20}$: −33.0 (c = 0.95, $CHCl_3$).

(*S*)-1-(2-Iodopropyl)-4-methoxybenzene (*S*-142f):



(*S*)-**142f**

The secondary alkyl iodide (*S*)-**142f** was prepared according to **TP7** from the alcohol (*R*)-**158f** (1.66 g, 10.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (200:1) to afford (*S*)-**142f** (1.44 g, 5.21 mmol, 52%, 94% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.13–7.07 (m, 2H), 6.88–6.81 (m, 2H), 4.35-4.26 (m, 1H), 3.80 (s, 3H), 3.23 (dd, *J* = 14.2, 7.2 Hz, 1H), 3.00 (dd, *J* = 14.2, 7.6 Hz, 1H), 1.89 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 158.6, 132.0, 130.1, 113.9, 55.4, 48.8, 29.6, 28.1.

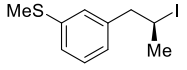
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2954 (w), 2916 (w), 2833 (w), 2166 (w), 1610 (m), 1583 (w), 1509 (vs), 1463 (w), 1451 (w), 1440 (m), 1375 (w), 1301 (m), 1245 (vs), 1225 (s), 1198 (w), 1176 (s), 1145 (m), 1113 (m), 1055 (w), 1033 (s), 987 (w), 886 (w), 832 (m), 808 (m), 753 (m).

MS (70 eV, EI): m/z (%): 149 (100), 147 (8), 121 (99), 115 (8), 91 (20), 77 (11).

HRMS (EI) for $C_{10}H_{13}IO$: calc. $[M]^{+\bullet}$: 276.0011, found: 276.0005.

$[\alpha]_D^{20}$: +33.6 (c = 0.99, $CHCl_3$).

(*S*)-(3-(2-Iodopropyl)phenyl)(methyl)sulfane (*S*-142g):



(*S*)-**142g**

The secondary alkyl iodide (*S*)-**142g** was prepared according to **TP7** from the alcohol (*R*)-**158g** (260 mg, 1.43 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on

silica gel with *n*-pentane/diethyl ether (100:1) to afford (*S*)-**142g** (212 mg, 0.73 mmol, 51%, 99% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.23 (t, *J* = 7.7 Hz, 1H), 7.17–7.14 (m, 1H), 7.07 (t, *J* = 1.9 Hz, 1H), 6.95 (dt, *J* = 7.4, 1.4 Hz, 1H), 4.37–4.28 (m, 1H), 3.26 (dd, *J* = 14.1, 7.2 Hz, 1H), 3.03 (dd, *J* = 14.1, 7.5 Hz, 1H), 2.49 (s, 3H), 1.90 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.4, 138.7, 129.0, 127.2, 125.9, 125.0, 49.4, 28.2, 28.1, 15.9.

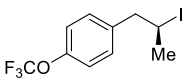
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2979 (m), 2963 (m), 2917 (m), 2886 (m), 2861 (m), 2226 (s), 2166 (m), 2155 (m), 1607 (m), 1590 (m), 1571 (m), 1504 (m), 1474 (m), 1439 (s), 1429 (s), 1419 (m), 1412 (m), 1375 (s), 1225 (s), 1204 (m), 1146 (s), 1135 (s), 1116 (m), 1090 (m), 1057 (s), 989 (m), 967 (m), 895 (m), 884 (m), 872 (m), 843 (s), 814 (s), 779 (vs), 699 (vs), 682 (s).

MS (70 eV, EI): m/z (%): 291 (10), 165 (76), 137 (100), 117 (42), 115 (29), 91 (17).

HRMS (EI) for $C_{10}H_{13}IS$: calc. $[M]^{+\bullet}$: 291.9783, found: 291.9777.

$[\alpha]_D^{20}$: −17.3 (c = 0.42, $CHCl_3$).

(*S*)-1-(2-Iodopropyl)-4-(trifluoromethoxy)benzene (*S*-142h):



(*S*)-**142h**

The secondary alkyl iodide (*S*)-**142h** was prepared according to **TP7** from the alcohol (*R*)-1**58h** (220 mg, 1.00 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (500:1) to afford (*S*)-**142h** (247 mg, 0.75 mmol, 75%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.22–7.19 (m, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 4.34. –4.26 (m, 1H), 3.25 (dd, *J* = 14.2, 7.5 Hz, 1H), 3.07 (dd, *J* = 14.2, 7.1 Hz, 1H), 1.91 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.2, 138.4, 130.4, 128.8, 128.1, 126.8, 121.9, 121.1, 119.3, 77.2, 48.7, 28.3, 27.9.

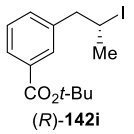
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2964 (vw), 2921 (vw), 2166 (w), 1595 (vw), 1508 (m), 1490 (w), 1451 (w), 1445 (w), 1436 (w), 1419 (vw), 1378 (w), 1252 (vs), 1217 (vs), 1195 (s), 1154 (vs), 1111 (m), 1057 (m), 1020 (m), 989 (w), 943 (w), 920 (w), 892 (w), 869 (w), 842 (m), 809 (m), 787 (w), 771 (w), 743 (w), 696 (w), 671 (m).

MS (70 eV, EI): m/z (%): 203 (88), 175 (100), 114 (8), 108 (9).

HRMS (EI) for $C_{10}H_{10}F_3IO$: calc. $[M]^{+\bullet}$: 329.9728, found: 329.9715.

$[\alpha]_D^{20}$: +28.8 (c = 0.94, $CHCl_3$).

***tert*-Butyl (*R*)-3-(2-iodopropyl)benzoate (*R*-142i):**



(*R*)-**142i**

The secondary alkyl iodide (*R*)-**142i** was prepared according to **TP7** from the alcohol (*S*)-**158i** (1.18 g, 5.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (200:1) to afford (*R*)-**142i** (1.07 g, 3.1 mmol, 62%, 96% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.90–7.87 (m, 1H), 7.80 (q, *J* = 1.4 Hz, 1H), 7.39– 7.34 (m, 2H), 4.35 (h, *J* = 7.0 Hz, 1H), 3.31 (dd, *J* = 14.1, 7.5 Hz, 1H), 3.11 (dd, *J* = 14.1, 7.2 Hz, 1H), 1.91 (d, *J* = 6.8 Hz, 3H), 1.60 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 165.8, 139.9, 133.2, 132.4, 129.9, 128.5, 128.1, 81.3, 49.2, 28.3, 28.3, 28.0.

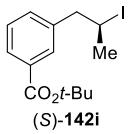
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2975 (w), 2928 (w), 2865 (vw), 1709 (s), 1607 (vw), 1587 (w), 1477 (w), 1441 (w), 1392 (w), 1376 (w), 1366 (m), 1293 (s), 1256 (m), 1228 (w), 1204 (m), 1158 (vs), 1111 (s), 1102 (s), 1083 (m), 1057 (w), 1001 (w), 990 (w), 933 (w), 918 (w), 849 (m), 821 (w), 810 (w), 756 (s), 744 (s), 696 (m), 672 (w).

MS (70 eV, EI): m/z (%): 273 (23), 219 (100), 163 (24), 135 (77), 91 (11).

HRMS (EI) for $C_{14}H_{19}O_2I$: calc. $[M]^{+\bullet}$: 346.0430, found: 346.0421.

$[\alpha]_D^{20}$: −31.5 (c = 0.95, $CHCl_3$).

***tert*-Butyl (*S*)-3-(2-iodopropyl)benzoate (*S*-142i):**



(*S*)-**142i**

The secondary alkyl iodide (*S*)-**142i** was prepared according to **TP7** from the alcohol (*R*)-**158i** (1.18 g, 5.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (200:1) to afford (*S*)-**142i** (1.02 g, 2.95 mmol, 59%, 97% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.91–7.86 (m, 1H), 7.80 (q, *J* = 1.4 Hz, 1H), 7.39– 7.34 (m, 2H), 4.34 (h, *J* = 7.0 Hz, 1H), 3.31 (dd, *J* = 14.1, 7.5 Hz, 1H), 3.11 (dd, *J* = 14.1, 7.3 Hz, 1H), 1.91 (d, *J* = 6.8 Hz, 3H), 1.60 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 165.8, 139.9, 133.2, 132.4, 129.9, 128.1, 81.3, 49.2, 28.3, 28.3, 28.1.

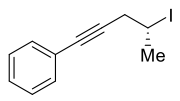
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2976 (w), 2929 (w), 2863 (vw), 1709 (s), 1607 (vw), 1587 (w), 1476 (w), 1442 (w), 1392 (w), 1376 (w), 1366 (m), 1293 (s), 1256 (m), 1228 (w), 1204 (m), 1158 (vs), 1111 (s), 1101 (s), 1083 (m), 1057 (w), 1001 (w), 990 (w), 933 (w), 917 (w), 883 (vw), 849 (m), 821 (w), 810 (w), 756 (s), 744 (s), 696 (m), 672 (w).

MS (70 eV, EI): m/z (%): 273 (22), 219 (87), 163 (27), 135 (100), 91 (21), 57 (23).

HRMS (EI) for $C_{14}H_{19}O_2I$: calc. $[M]^{+\bullet}$: 346.0430, found: 346.0432.

$[\alpha]_D^{20}$: +31.9 (c = 0.93, $CHCl_3$).

(*R*)-(4-Iodopent-1-yn-1-yl)benzene (*R*-142j):



(*R*)-**142j**

The secondary alkyl iodide (*R*)-**142j** was prepared according to **TP7** from the alcohol (*S*)-**158j** (160 mg, 1.00 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (100:1) to afford (*R*)-**142j** (130 mg, 0.48 mmol, 48%, 94% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.46–7.41 (m, 2H), 7.32–7.28 (m, 3H), 4.35–4.26 (m, 1H), 3.07 (dd, *J* = 17.2, 5.9 Hz, 1H), 2.97 (dd, *J* = 17.2, 7.3 Hz, 1H), 2.02 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 131.7, 128.4, 128.2, 123.4, 87.7, 83.1, 34.0, 28.1, 23.1.

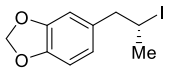
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 4334 (w), 2982 (w), 2963 (w), 2915 (w), 2912 (w), 2859 (w), 2226 (s), 2166 (m), 1607 (m), 1504 (m), 1445 (m), 1412 (m), 1376 (m), 1296 (w), 1283 (w), 1247 (w), 1226 (m), 1204 (w), 1199 (w), 1178 (w), 1150 (m), 1136 (m), 1117 (m), 1100 (w), 1089 (w), 1063 (m), 1058 (m), 1039 (w), 1020 (w), 990 (m), 895 (m), 871 (w), 843 (s), 813 (vs), 780 (w), 769 (w), 743 (w), 739 (w), 735 (w), 722 (w), 696 (w).

MS (70 eV, EI): m/z (%): 143 (49), 141 (19), 128 (100), 115 (28).

HRMS (EI) for $C_{11}H_{11}I$: calc. $[M]^{+\bullet}$: 269.9905, found: 269.9899.

$[\alpha]_D^{20}$: −20.1 (c = 0.67, $CHCl_3$).

(*R*)-5-(2-Iodopropyl)benzo[*d*][1,3]dioxole (*R*-142k):



(*R*)-**142k**

The secondary alkyl iodide (*R*)-**142k** was prepared according to **TP7** from the alcohol (*S*)-**158k** (901 mg, 5.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (250:1) to afford (*R*)-**142k** (839 mg, 2.89 mmol, 58%, 95% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.75 (d, *J* = 7.9 Hz, 1H), 6.67 (d, *J* = 1.5 Hz, 1H), 6.63 (dd, *J* = 7.9, 1.6 Hz, 1H), 5.95 (s, 2H), 4.32–4.23 (m, 1H), 3.20 (dd, *J* = 14.2, 7.2 Hz, 1H), 2.96 (dd, *J* = 14.2, 7.5 Hz, 1H), 1.90 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.8, 146.5, 133.7, 122.2, 109.4, 108.4, 101.1, 49.3, 29.1, 28.1.

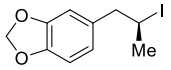
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2979 (w), 2970 (w), 2962 (w), 2920 (w), 2891 (w), 2882 (w), 2860 (w), 2834 (vw), 2775 (vw), 2163 (w), 1607 (w), 1500 (s), 1486 (vs), 1440 (s), 1374 (w), 1359 (w), 1273 (w), 1244 (vs), 1222 (m), 1187 (m), 1145 (m), 1121 (m), 1096 (m), 1058 (m), 1035 (vs), 988 (w), 963 (vw), 939 (m), 927 (s), 893 (m), 872 (w), 852 (w), 806 (s), 780 (w), 769 (s), 753 (w), 743 (w), 724 (w), 714 (w), 696 (w), 653 (w).

MS (70 eV, EI): m/z (%): 163 (100), 135 (49), 133 (19), 105 (24).

HRMS (EI) for $C_{10}H_{11}IO_2$: calc. $[M]^{+\bullet}$: 289.9804, found: 289.9800.

$[\alpha]_D^{20}$: −34.4 (c = 0.94, $CHCl_3$).

(*S*)-5-(2-Iodopropyl)benzo[*d*][1,3]dioxole (*S*-142k):



(*S*)-**142k**

The secondary alkyl iodide (*S*)-**142k** was prepared according to **TP7** from the alcohol (*R*)-**158k** (1.08 g, 6.00 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane/diethyl ether (250:1) to afford (*S*)-**142k** (1.46 g, 5.05 mmol, 84%, 93% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.75 (d, *J* = 7.9 Hz, 1H), 6.67–6.62 (m, 2H), 5.95 (s, 2H), 4.32–4.23 (m, 1H), 3.20 (dd, *J* = 14.1, 7.2 Hz, 1H), 2.96 (dd, *J* = 14.2, 7.5 Hz, 1H), 1.89 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.7, 146.5, 133.6, 122.2, 109.4, 108.3, 101.1, 49.2, 29.1, 28.0.

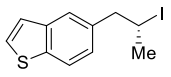
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2963 (w), 2891 (w), 2882 (w), 2834 (vw), 2775 (vw), 2166 (w), 1607 (w), 1500 (s), 1486 (vs), 1440 (s), 1374 (w), 1359 (w), 1273 (w), 1244 (vs), 1222 (m), 1188 (m), 1145 (m), 1121 (m), 1096 (m), 1058 (m), 1035 (vs), 988 (w), 939 (m), 927 (s), 893 (m), 871 (w), 852 (w), 805 (s), 783 (w), 769 (m), 744 (w), 725 (w), 721 (w), 714 (w), 696 (w), 654 (w).

MS (70 eV, EI): m/z (%): 163 (100), 135 (60), 11 (24), 105 (37), 79 (14).

HRMS (EI) for $C_{10}H_{11}IO_2$: calc. $[M]^{+\bullet}$: 289.9804, found: 289.9797.

$[\alpha]_D^{20}$: +38.5 (c = 0.99, $CHCl_3$).

(*R*)-5-(2-Iodopropyl)benzo[*b*]thiophene (*R*-142l):



(*R*)-**142l**

The secondary alkyl iodide (*R*)-**142l** was prepared according to **TP7** from the alcohol (*S*)-**158l** (961 mg, 5.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford (*R*)-**142l** (1.12 g, 3.7 mmol, 74%, 93% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.82 (d, *J* = 8.3 Hz, 1H), 7.64 (d, *J* = 1.7 Hz, 1H), 7.45 (d, *J* = 5.4 Hz, 1H), 7.31 (d, *J* = 5.4 Hz, 1H), 7.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 4.45–4.36 (m, 1H), 3.42 (dd, *J* = 14.1, 7.2 Hz, 1H), 3.18 (dd, *J* = 14.1, 7.6 Hz, 1H), 1.92 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 138.4, 136.0, 127.0, 125.6, 124.0, 123.8, 122.6, 49.6, 28.9, 28.2.

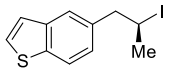
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2962 (w), 2914 (w), 2871 (w), 1436 (s), 1420 (s), 1374 (m), 1325 (w), 1260 (w), 1230 (m), 1219 (m), 1159 (m), 1147 (s), 1139 (s), 1115 (m), 1088 (m), 1061 (s) 1049 (vs), 987 (m), 939 (w), 892 (m), 858 (w), 830 (s), 805 (s), 767 (m), 753 (vs), 703 (vs) 668 (vs).

MS (70 eV, EI): m/z (%): 301 (2), 175 (59), 147 (100), 134 (8).

HRMS (EI) for $C_{11}H_{11}IS$: calc. $[M]^{+\bullet}$: 301.9626, found: 301.9621.

$[\alpha]_D^{20}$: +35.3 (c = 0.98, $CHCl_3$).

(*S*)-5-(2-Iodopropyl)benzo[*b*]thiophene (*S*-142l):



(*S*)-**142l**

The secondary alkyl iodide (*S*)-**142l** was prepared according to **TP7** from the alcohol (*R*)-**158l** (961 mg, 5.0 mmol, 1.0 equiv). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford (*S*)-**142l** (1.16 g, 3.85 mmol, 77%, 97% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.84–7.82 (m, 1H), 7.68–7.61 (m, 1H), 7.45 (d, *J* = 5.5 Hz, 1H), 7.32 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.18 (dd, *J* = 8.2, 1.7 Hz, 1H), 4.41 (h, *J* = 7.0 Hz, 1H), 3.43 (dd, *J* = 14.1, 7.2 Hz, 1H), 3.19 (dd, *J* = 14.1, 7.6 Hz, 1H), 1.93 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 134.0, 138.4, 135.9, 127.0, 125.5, 123.9, 123.8, 122.6, 77.5, 77.2, 76.8, 49.5, 28.9, 28.2.

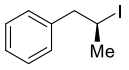
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2963 (w), 2917 (w), 2857 (w), 1434 (m), 1420 (m), 1374 (m), 1325 (w), 1260 (w), 1230 (w), 1218 (w), 1159 (w), 1147 (m), 1140 (m), 1115 (m), 1101 (w), 1088 (m), 1061 (m), 1049 (s), 1026 (w), 987 (w), 892 (m), 830 (m), 806 (m), 767 (m), 753 (s), 743 (m), 701 (vs), 688 (vs), 668 (m).

MS (70 eV, EI): m/z (%): 175 (63), 147 (100).

HRMS (EI) for $C_{11}H_{11}IS$: calc. $[M]^{+\bullet}$: 301.9626, found:301.9617.

$[\alpha]_D^{20}$: −35.5 (c = 1.02, $CHCl_3$).

(*S*)-(2-Iodopropyl)benzene (*S*-142m):



(*S*)-**142m**

The iodide (*S*)-142m was prepared according to **TP7** from the alcohol (*R*)-**158m** (681 mg, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:1000 to afford (*S*)-**158m** (1.02 g, 4.15 mmol, 83%) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.35–7.27 (m, 3H), 7.21–7.16 (m, 2H), 4.35 (h, *J* = 7.0 Hz, 1H), 3.30 (dd, *J* = 14.1, 7.2 Hz, 1H), 3.07 (dd, *J* = 14.1, 7.6 Hz, 1H), 1.90 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 139.8, 129.1, 128.6, 127.0, 49.6, 28.6, 28.2.

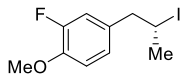
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3062 (vw), 3027 (w), 2964 (w), 2918 (w), 2861 (vw), 1601 (vw), 1585 (vw), 1495 (w), 1452 (m), 1376 (w), 1297 (vw), 1281 (vw), 1227 (w), 1200 (vw), 1145 (m), 1134 (m), 1112 (w), 1080 (w), 1065 (w), 1048 (w), 1030 (w), 1002 (vw), 988 (w), 916 (w), 896 (w), 880 (vw), 860 (vw), 816 (vw), 800 (vw), 742 (s), 696 (vs).

MS (70 eV, EI): m/z (%): 119 (47), 91 (100).

HRMS (EI) for $C_9H_{11}I$: calc. $[M]^{+\bullet}$: 245.9905, found: 245.9902.

$[\alpha]_D^{20}$: +42.5 (c = 1.37, $CHCl_3$).

(*R*)-2-Fluoro-4-(2-iodopropyl)-1-methoxybenzene (*R*-142n):



(*R*)-**142n**

The iodide (*R*)-**142n** was prepared according to **TP7** from the alcohol (*S*)-**158n** (921 mg, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:250 to afford (*R*)-**142n** (1.16 g, 3.95 mmol, 79%, 95% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.96–6.85 (m, 3H), 4.27 (h, *J* = 7.0 Hz, 1H), 3.88 (s, 3H), 3.18 (dd, *J* = 14.3, 7.5 Hz, 1H), 2.98 (dd, *J* = 14.3, 7.2 Hz, 1H), 1.89 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 245.8 Hz), 146.6 (d, *J* = 10.6 Hz), 132.8 (d, *J* = 6.0 Hz), 124.8 (d, *J* = 3.6 Hz), 116.7 (d, *J* = 18.2 Hz), 113.3 (d, *J* = 2.2 Hz), 56.4, 48.5 (d, *J* = 1.1 Hz), 28.5, 28.1.

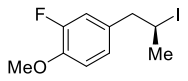
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3000 (w), 2962 (w), 2935 (w), 2912 (w), 2862 (w), 2836 (w), 2166 (w), 1622 (w), 1584 (w), 1514 (vs), 1462 (m), 1441 (m), 1432 (m), 1376 (w), 1315 (m), 1271 (vs), 1223 (s), 1183 (w), 1124 (vs), 1100 (w), 1061 (m), 1026 (s), 990 (w), 951 (m), 898 (w), 879 (w), 856 (w), 807 (m), 760 (s), 743 (m), 727 (w), 696 (w).

MS (70 eV, EI): m/z (%):168 (9), 167 (87), 140 (9), 139 (100), 135 (7), 109 (9), 77 (6).

HRMS (EI) for $C_{10}H_{12}FIO$: calc. $[M]^{+\bullet}$: 293.9917, found: 293.9911.

$[\alpha]_D^{20}$: −31.9 (c = 1.00, $CHCl_3$).

(*S*)-2-Fluoro-4-(2-iodopropyl)-1-methoxybenzene (*S*-142n):



(*S*)-**142n**

The iodide (*S*)-**142n** was prepared according to **TP7** from the alcohol (*R*)-**158n** (921 mg, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:250 to afford (*S*)-**142n** (1.07 g, 3.65 mmol, 73%, 98% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.95–6.86 (m, 3H), 4.27 (h, *J* = 7.0 Hz, 1H), 3.88 (s, 3H), 3.18 (dd, *J* = 14.3, 7.5 Hz, 1H), 2.98 (dd, *J* = 14.3, 7.2 Hz, 1H), 1.90 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 245.7 Hz), 146.6 (d, *J* = 10.6 Hz), 132.8 (d, *J* = 5.9 Hz), 124.8 (d, *J* = 3.6 Hz), 116.7 (d, *J* = 18.1 Hz), 113.3 (d, *J* = 2.2 Hz), 56.4, 48.5 (d, *J* = 1.2 Hz), 28.5, 28.1.

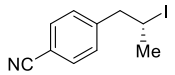
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2962 (w), 2930 (w), 2905 (w), 2891 (w), 2835 (w), 2166 (m), 1623 (w), 1584 (w), 1514 (vs), 1462 (m), 1441 (m), 1433 (m), 1375 (w), 1314 (m), 1271 (vs), 1223 (s), 1183 (w), 1124 (vs), 1100 (w), 1061 (m), 1026 (s), 990 (w), 951 (m), 898 (w), 879 (w), 856 (w), 806 (m), 760 (s), 745 (m), 700 (w), 695 (w).

MS (70 eV, EI): m/z (%):168 (9), 167 (89), 140 (8), 139 (100), 135 (7), 109 (8), 77 (6).

HRMS (EI) for $C_{10}H_{12}FIO$: calc. $[M]^{+\bullet}$: 293.9917, found: 293.9912.

$[\alpha]_D^{20}$: +37.9 (c = 0.96, $CHCl_3$).

(*R*)-4-(2-Iodopropyl)benzonitrile (*R*-142o):



(*R*)-**142o**

The iodide (*R*)-**142o** was prepared according to **TP7** from the alcohol (*S*)-**158o** (806 mg, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:100 to afford (*R*)-**142o** (718 mg, 2.65 mmol, 53%, 90% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.66–7.58 (m, 2H), 7.34–7.27 (m, 2H), 4.36–4.23 (m, 1H), 3.25 (dd, *J* = 14.3, 8.1 Hz, 1H), 3.14 (dd, *J* = 14.3, 6.5 Hz, 1H), 1.94 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 145.0, 132.4, 129.9, 119.0, 111.0, 49.1, 28.5, 26.6.

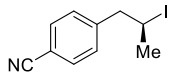
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2964 (w), 2916 (w), 2859 (w), 2226 (s), 1607 (m), 1504 (m), 1444 (m), 1412 (m), 1376 (m), 1297 (w), 1283 (w), 1226 (m), 1205 (w), 1198 (w), 1178 (m), 1150 (m), 1136 (m), 1117 (m), 1100 (w), 1088 (w), 1064 (m), 1058 (m), 1020 (w), 990 (m), 895 (m), 871 (w), 843 (s), 814 (vs), 745 (w), 740 (w), 694 (w).

MS (70 eV, EI): m/z (%): 144 (10), 116 (100), 89 (12).

HRMS (EI) for $C_{10}H_{10}NI$: calc. $[M+H]^{+\bullet}$: 271.9936, found: 271.9930.

$[\alpha]_D^{20}$: −41.1 (c = 0.94, $CHCl_3$).

(*S*)-4-(2-Iodopropyl)benzonitrile (*S*-142o):



(*S*)-**142o**

The iodide (*S*)-**142o** was prepared according to **TP7** from the alcohol (*R*)-**158o** (806 mg, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:100 to afford (*S*)-**142o** (759 mg, 2.8 mmol, 56%, 98% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.66–7.58 (m, 2H), 7.34–7.27 (m, 2H), 4.30 (m, 1H), 3.25 (dd, *J* = 14.3, 8.2 Hz, 1H), 3.14 (dd, *J* = 14.3, 6.5 Hz, 1H), 1.94 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 145.0, 132.4, 129.9, 119.0, 111.0, 49.1, 28.5, 26.6.

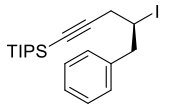
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2976 (w), 2962 (w), 2916 (w), 2858 (w), 2226 (s), 1607 (m), 1504 (m), 1444 (m), 1412 (m), 1376 (m), 1296 (w), 1283 (w), 1226 (m), 1204 (w), 1198 (w), 1178 (m), 1150 (m), 1136 (m), 1117 (m), 1099 (w), 1088 (w), 1064 (m), 1058 (m), 1020 (w), 990 (m), 895 (m), 871 (w), 843 (s), 814 (vs), 740 (w), 695 (w).

MS (70 eV, EI): m/z (%): 144 (17), 116 (100), 89 (8).

HRMS (EI) for $C_{10}H_{10}NI$: calc. $[M+H]^{+\bullet}$: 271.9936, found: 271.9931.

$[\alpha]_D^{20}$: +45.9 (c = 0.97, $CHCl_3$).

(*S*)-(4-Iodo-5-phenylpent-1-yn-1-yl)triisopropylsilane (*S*-142p):



(*S*)-**142p**

The iodide (*S*)-**142p** was prepared according to **TP7** from the alcohol (*R*)-**158p** (1.586 g, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:1000 to afford (*S*)-**142p** (1.45 g, 3.4 mmol, 68%) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.35–7.27 (m, 3H), 7.24 (dd, *J* = 8.0, 1.7 Hz, 2H), 4.30 (tt, *J* = 7.3, 5.7 Hz, 1H), 3.39 (dd, *J* = 14.1, 7.3 Hz, 1H), 3.27 (dd, *J* = 14.1, 7.3 Hz, 1H), 2.85 (dd, *J* = 5.7, 1.8 Hz, 2H), 1.12 (d, *J* = 3.6 Hz, 19H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 139.3, 129.3, 128.7, 127.1, 105.5, 84.6, 45.7, 31.2, 31.0, 18.8, 11.4.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3028 (w), 2941 (s), 2926 (m), 2890 (m), 2864 (s), 2176 (m), 2169 (m), 1602 (w), 1496 (m), 1462 (s), 1455 (m), 1442 (w), 1418 (w), 1383 (w), 1366 (w), 1346 (w), 1303 (w), 1254 (w),

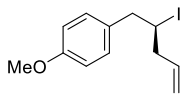
1222 (w), 1168 (w), 1124 (w), 1074 (m), 1062 (w), 1029 (m), 1019 (m), 995 (m), 956 (w), 918 (m), 882 (vs), 849 (w), 744 (s), 698 (vs), 677 (vs), 665 (vs).

MS (70 eV, EI): m/z (%): 383 (35), 255 (100), 109 (30), 91 (100), 75 (20).

HRMS (EI) for $C_{20}H_{31}ISi$: calc. $[M]^{+\bullet}$: 426.1240, found: 426.1232.

$[\alpha]_D^{20}$: +2.9 (c = 1.82, $CHCl_3$).

(*S*)-1-(2-Iodopent-4-en-1-yl)-4-methoxybenzene (*S*-142q):



(*S*)-**142q**

The iodide (*S*)-**142q** was prepared according to **TP7** from the alcohol (*R*)-**158q** (961 mg, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:100 to afford (*S*)-**142q** (861 mg, 2.85 mmol, 57%, 92% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.15 – 7.08 (m, 2H), 6.88 – 6.83 (m, 2H), 5.86 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.23 – 5.10 (m, 2H), 4.24 (qd, *J* = 7.5, 5.2 Hz, 1H), 3.80 (s, 3H), 3.19 (dd, *J* = 14.4, 7.7 Hz, 1H), 3.11 (dd, *J* = 14.4, 7.0 Hz, 1H), 2.67 – 2.51 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 158.6, 136.5, 131.9, 130.2, 118.1, 113.9, 55.4, 45.9, 43.5, 36.9.

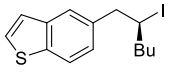
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3076 (vw), 3000 (w), 2952 (w), 2834 (w), 1640 (w), 1610 (m), 1584 (w), 1510 (vs), 1464 (m), 1439 (w), 1433 (w), 1301 (m), 1244 (vs), 1176 (s), 1130 (w), 1107 (w), 1034 (s), 1003 (w), 989 (m), 916 (m), 831 (m), 809 (m), 753 (m), 712 (vw), 697 (w).

MS (70 eV, EI): m/z (%): 260 (16), 134 (100), 121 (47), 91 (21).

HRMS (EI) for $C_{12}H_{15}IO$: calc. $[M]^{+\bullet}$: 302.0168, found: 302.0160.

$[\alpha]_D^{20}$: +6.4 (c =1.3, $CHCl_3$).

(*S*)-5-(2-Iodohexyl)benzo[*b*]thiophene (*S*-142r):



(*S*)-**142r**

The iodide (*S*)-**142r** was prepared according to **TP7** from the alcohol (*R*)-**158r** (1.17 g, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:1000 to afford (*S*)-**142r** (877 mg, 2.55 mmol, 52%, 92% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.82 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 1.7 Hz, 1H), 7.44 (d, *J* = 5.4 Hz, 1H), 7.31 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 4.39–4.29 (m, 1H), 3.41 (dd, *J* = 14.3, 7.7 Hz, 1H), 3.29 (dd, *J* = 14.3, 7.0 Hz, 1H), 1.90–1.78 (m, 1H), 1.77–1.68 (m, 1H), 1.66–1.55 (m, 1H), 1.46–1.21 (m, 3H), 0.90 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 138.3, 136.2, 127.0, 125.6, 124.0, 123.8, 122.5, 47.6, 39.5, 39.4, 32.0, 22.0, 14.1.

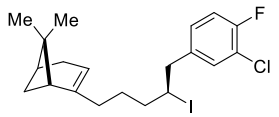
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2954 (m), 2925 (m), 2869 (w), 2856 (m), 2838 (w), 2831 (w), 1463 (w), 1455 (w), 1436 (m), 1421 (m), 1378 (w), 1326 (w), 1299 (w), 1261 (w), 1240 (w), 1226 (w), 1160 (w), 1139 (m), 1089 (m), 1050 (m), 1001 (w), 936 (w), 922 (w), 894 (m), 831 (m), 806 (m), 767 (w), 753 (s), 730 (w), 702 (vs), 689 (vs), 670 (m).

MS (70 eV, EI): m/z (%): 216 (11), 173 (33), 147 (100), 129 (15).

HRMS (EI) for $C_{14}H_{17}IS$: calc. $[M]^{+\bullet}$: 344.0096, found: 344.0086

$[\alpha]_D^{20}$: +2.3 (c = 1.3, $CHCl_3$).

(1*R*,5*S*)-2-((*S*)-5-(3-Chloro-4-fluorophenyl)-4-iodopentyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (*R*,*S*,*S*-142s):



(*R*,*S*,*S*)-**142s**

The iodide (*R*,*S*,*S*)-**142s** was prepared according to **TP7** from the alcohol (*R*,*R*,*S*)-**158s** (1.68 g, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with hexane to afford (*R*,*S*,*S*)-**142s** (1.09 g, 2.45 mmol, 49%, dr = 95:5, 98% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.22 (dd, *J* = 7.0, 2.0 Hz, 1H), 7.11–7.01 (m, 2H), 5.18–5.12 (m, 1H), 4.23–4.12 (m, 1H), 3.19 (dd, *J* = 14.4, 8.1 Hz, 1H), 3.10 (dd, *J* = 14.5, 6.6 Hz, 1H), 2.37–2.30 (m, 1H), 2.28–2.11 (m, 2H), 2.10–2.04 (m, 1H), 2.01–1.89 (m, 3H), 1.88–1.56 (m, 3H), 1.52–1.40 (m, 1H), 1.26 (s, 3H), 1.07 (d, *J* = 8.5 Hz, 1H), 0.80 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.2 (d, *J* = 247.9 Hz), 147.7, 137.0 (d, *J* = 4.0 Hz), 131.1, 128.8 (d, *J* = 7.1 Hz), 120.9 (d, *J* = 17.7 Hz), 116.7, 116.6 (d, *J* = 3.6 Hz), 46.4, 45.8, 40.9, 39.4, 38.1, 37.7, 35.9, 31.8, 31.4, 27.3, 26.5, 21.36.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2983 (w), 2914 (m), 2832 (w), 1597 (vw), 1499 (vs), 1467 (w), 1453 (w), 1434 (w), 1407 (w), 1381 (w), 1364 (w), 1330 (vw), 1302 (w), 1265 (m), 1248 (s), 1218 (w), 1203 (w), 1181

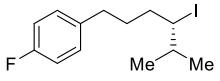
(w), 1128 (w), 1099 (vw), 1082 (w), 1061 (m), 957 (vw), 944 (vw), 914 (w), 902 (w), 886 (w), 818 (m), 800 (w), 772 (m), 750 (w), 708 (w), 688 (m).

MS (70 eV, EI): m/z (%): 319 (27), 197 (48), 145 (46), 127 (62), 105 (31), 91 (100).

HRMS (EI) for $C_{20}H_{25}ClFI$: calc. $[M]^{+\bullet}$: 446.0673, found: 446.0668.

$[\alpha]_D^{20}$: −25.3 (c = 1.73, $CHCl_3$).

(*S*)-1-Fluoro-4-(4-iodo-5-methylhexyl)benzene (*S*-142t):



(*S*)-**142t**

The iodide (*S*)-**142t** was prepared according to **TP7** from the alcohol (*R*)-**158t** (1.05 g, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with hexane to afford (*S*)-**142t** (816 mg, 2.55 mmol, 51%, 86% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.16–7.09 (m, 2H), 7.00–6.93 (m, 2H), 4.16 (dt, *J* = 9.6, 3.7 Hz, 1H), 2.69–2.54 (m, 2H), 2.03–1.83 (m, 2H), 1.76–1.56 (m, 2H), 1.28–1.18 (m, 1H), 0.97 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 161.4 (d, *J* = 243.3 Hz), 137.6 (d, *J* = 3.2 Hz), 129.8 (d, *J* = 7.8 Hz), 115.2 (d, *J* = 21.0 Hz), 51.9, 38.0, 35.0, 34.3, 32.0, 23.2, 20.1.

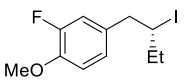
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2962 (w), 2931 (w), 2870 (w), 1601 (w), 1509 (vs), 1459 (m), 1416 (vw), 1386 (w), 1368 (w), 1316 (w), 1220 (s), 1194 (w), 1156 (m), 1123 (w), 1093 (w), 1055 (vw), 1016 (w), 922 (vw), 864 (w), 843 (m), 821 (s), 780 (w), 760 (m), 737 (w), 701 (w).

MS (70 eV, EI): m/z (%): 193 (60), 123 (23), 109 (100), 43 (16).

HRMS (EI) for $C_{13}H_{18}FI$: calc. $[M]^{+\bullet}$: 320.0437, found: 320.0448.

$[\alpha]_D^{20}$: +26.7 (c = 1.32, $CHCl_3$).

(*R*)-2-Fluoro-4-(2-iodobutyl)-1-methoxybenzene (*R*-142u):



(*R*)-**142u**

The iodide (*R*)-**142u** was prepared according to **TP7** from the alcohol (*S*)-**158u** (991 mg, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:250 to afford (*R*)-**142u** (1.03 g, 3.35 mmol, 67%, 94% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.96–6.85 (m, 3H), 4.23–4.14 (m, 1H), 3.88 (s, 3H), 3.19 (dd, *J* = 14.4, 7.9 Hz, 1H), 3.08 (dd, *J* = 14.4, 6.8 Hz, 1H), 1.76 (p, *J* = 7.0 Hz, 2H), 1.05 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 245.7 Hz), 146.5 (d, *J* = 10.7 Hz), 133.0 (d, *J* = 6.1 Hz), 124.8 (d, *J* = 3.5 Hz), 116.7 (d, *J* = 18.1 Hz), 113.3 (d, *J* = 2.2 Hz), 56.4, 46.2 (d, *J* = 1.3 Hz), 40.9, 32.7, 14.4.

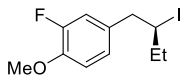
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3003 (vw), 2963 (w), 2932 (w), 2908 (w), 2874 (vw), 2837 (w), 1622 (w), 1585 (w), 1515 (vs), 1460 (m), 1454 (m), 1441 (m), 1433 (m), 1380 (w), 1310 (w), 1271 (vs), 1223 (s), 1183 (w), 1124 (s), 1094 (w), 1077 (w), 1027 (s), 954 (m), 907 (m), 872 (w), 806 (m), 783 (w), 760 (s), 741 (m), 712 (vw), 695 (m).

MS (70 eV, EI): m/z (%): 181 (12), 139 (100), 109 (5), 77 (3).

HRMS (EI) for $C_{11}H_{14}FIO$: calc. $[M]^{+\bullet}$: 308.0073, found: 308.0066.

$[\alpha]_D^{20}$: −18.0 (c = 1.16, $CHCl_3$).

(*S*)-2-Fluoro-4-(2-iodobutyl)-1-methoxybenzene (*S*-142u):



(*S*)-**142u**

The iodide (*S*)-**142u** was prepared according to **TP7** from the alcohol (*R*)-**158u** (991 mg, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:250 to afford (*S*)-**142u** (1.02 g, 3.35 mmol, 66%, 98% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.97–6.82 (m, 3H), 4.18 (dtd, *J* = 7.9, 6.7, 5.9 Hz, 1H), 3.88 (s, 3H), 3.19 (dd, *J* = 14.4, 7.9 Hz, 1H), 3.08 (dd, *J* = 14.5, 6.8 Hz, 1H), 1.82–1.72 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 245.8 Hz), 146.5 (d, *J* = 10.6 Hz), 133.0 (d, *J* = 6.0 Hz), 124.8 (d, *J* = 3.5 Hz), 116.7 (d, *J* = 18.0 Hz), 113.3 (d, *J* = 2.2 Hz), 56.4, 46.2 (d, *J* = 1.3 Hz), 40.9, 32.7, 14.4.

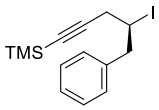
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3005 (vw), 2965 (w), 2934 (w), 2875 (w), 2838 (w), 1623 (w), 1586 (w), 1516 (vs), 1461 (m), 1454 (m), 1442 (m), 1433 (m), 1381 (w), 1311 (m), 1272 (vs), 1224 (s), 1184 (w), 1124 (s), 1094 (w), 1077 (w), 1027 (s), 954 (m), 908 (m), 872 (w), 806 (m), 784 (m), 760 (s), 741 (m), 712 (vw).

MS (70 eV, EI): m/z (%): 181 (8), 139 (100), 109 (6), 105 (5), 77 (5).

HRMS (EI) for $C_{11}H_{14}FIO$: calc. $[M]^{+\bullet}$: 308.0073, found: 308.0071.

$[\alpha]_D^{20}$: +17.7 (c = 1.18, $CHCl_3$).

(*S*)-(4-Iodo-5-phenylpent-1-yn-1-yl)trimethylsilane (*S*-142v):



(*S*)-**142v**

The iodide (*S*)-**142v** was prepared according to **TP7** from the alcohol (*R*)-**158v** (1.16 g, 5.0 mmol, 1.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:1000 to to afford (*S*)-**142v** (1.35 g, 3.95 mmol, 79%) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.36–7.27 (m, 3H), 7.25–7.20 (m, 2H), 4.32–4.24 (m, 1H), 3.35 (dd, *J* = 14.2, 7.0 Hz, 1H), 3.23 (dd, *J* = 14.2, 7.5 Hz, 1H), 2.89–2.75 (m, 2H), 0.21 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 139.2, 129.3, 128.7, 127.1, 104.3, 88.5, 45.7, 31.3, 30.7, 0.1.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3064 (vw), 3028 (vw), 2959 (w), 2898 (vw), 2838 (vw), 2177 (w), 1603 (vw), 1496 (w), 1454 (w), 1434 (vw), 1417 (w), 1304 (vw), 1249 (m), 1222 (w), 1169 (vw), 1156 (vw), 1124 (w), 1076 (vw), 1029 (w), 1021 (w), 996 (w), 957 (vw), 917 (vw), 890 (vw), 837 (vs), 758 (m), 744 (m), 697 (s), 654 (w).

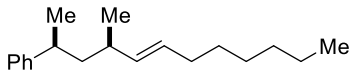
MS (70 eV, EI): m/z (%): 215 (21), 109 (25), 91 (55), 73 (100).

HRMS (EI) for $C_{14}H_{19}ISi$: calc. $[M]^{+\bullet}$: 342.0301, found: 342.0288.

$[\alpha]_D^{20}$: +5.5 (c = 1.01, $CHCl_3$).

6 Characterization of New Compounds

(*syn*-4-Methyldodec-5-en-2-yl)benzene (*syn*-146a):



syn-**146a**

The (*E*)-alkene *syn*-**146a** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and the alkenyl iodide **145a** (0.3 mmol, 71.4 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**146a** (0.043 mmol, 11.1 mg, 43%, dr = 98:2) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.32–7.26 (m, 2H), 7.21–7.14 (m, 3H), 5.35 (dt, *J* = 15.2, 6.6 Hz, 1H), 5.22 (ddt, *J* = 15.2, 7.8, 1.3 Hz, 1H), 2.74 (h, *J* = 7.0 Hz, 1H), 2.10–1.93 (m, 3H), 1.63–1.51 (m, 1H), 1.48–1.39 (m, 1H), 1.37–1.23 (m, 8H), 1.20 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.91–0.85 (m, 3H).

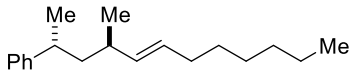
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.4 136.2, 128.9, 128.4, 127.1, 125.8, 46.1, 37.4, 34.6, 32.7, 31.9, 29.8, 29.0, 22.8, 22.1, 21.2, 14.3.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3027 (w), 2960 (m), 2925 (m), 2869 (w), 2856 (w), 2362 (vs), 2342 (s), 2220 (w), 2186 (w), 1494 (w), 1456 (w), 970 (w), 698 (m), 668 (w).

MS (EI, 70 eV): m/z (%): 145 (30), 118 (100), 117 (18), 106 (19), 105 (93), 91 (38), 79 (11).

HRMS (EI) for $C_{19}H_{30}$: calc. [M^+]: 258.2348; found: 258.2344.

(*anti*-4-Methyldodec-5-en-2-yl)benzene (*anti*-146a):



anti-**146a**

The (*E*)-alkene *anti*-**146a** was prepared according to **TP2** from the iodide *anti*-**142a** (dr = 2:98, 0.1 mmol, 27.4 mg) and the alkenyl iodide **145a** (0.3 mmol, 71.4 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *anti*-**146a** (0.039 mmol, 10.1 mg, 39%, dr = 5:95) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.31–7.25 (m, 2H), 7.20–7.12 (m, 3H), 5.37–4.98 (m, 2H), 2.82–2.70 (m, 1H), 2.01–1.94 (m, 2H), 1.92–1.84 (m, 1H), 1.61–1.53 (m, 1H), 1.49–1.41 (m, 1H), 1.40–1.23 (m, 8H), 1.20 (d, *J* = 7.0 Hz, 3H), 0.92–0.86 (m, 6H).

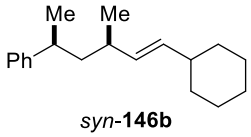
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.8, 136.1, 129.5, 128.4, 127.4, 125.9, 46.1, 37.8, 34.8, 32.8, 31.9, 29.9, 29.0, 23.4, 22.8, 21.9, 14.3.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2956 (m), 2924 (vs), 2854 (m), 2360 (w), 2342 (w), 1740 (w), 1494 (w), 1454 (w), 1376 (w), 1242 (w), 1020 (w), 970 (w), 762 (w), 700 (w)

MS (EI, 70 eV): m/z (%): 145 (28), 118 (100), 117 (16), 106 (19), 105 (90), 91 (37), 79 (11).

HRMS (EI) for $C_{19}H_{30}$: calc. [M$^+$]: 258.2348; found: 258.2344.

(*syn*-6-Cyclohexyl-4-methylhex-5-en-2-yl)benzene (*syn*-146b):



syn-**146b**

The (*E*)-alkene *syn*-**146b** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and the alkenyl iodide **145b** (0.3 mmol, 70.8 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**146b** (0.045 mmol, 11.5 mg, 45%, dr = 94:6) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.31–7.26 (m, 2H), 7.20–7.13 (m, 3H), 5.35–5.25 (m, 1H), 5.17 (ddd, *J* = 15.5, 7.7, 1.1 Hz, 1H), 2.74 (h, *J* = 7.0 Hz, 1H), 2.08–1.96 (m, 1H), 1.94–1.80 (m, 1H), 1.74–1.64 (m, 4H), 1.43 (ddd, *J* = 13.5, 8.1, 6.6 Hz, 1H), 1.32–1.22 (m, 2H), 1.20 (d, *J* = 6.9 Hz, 4H), 1.17–0.98 (m, 3H), 0.94 (d, *J* = 6.7 Hz, 3H).

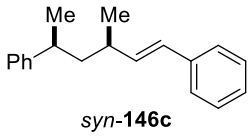
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.4, 135.0, 133.6, 128.4, 127.1, 125.8, 46.1, 40.8, 37.3, 34.6, 33.5, 33.4, 26.4, 26.3, 26.3, 22.0, 21.2.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3026 (w), 2958 (m), 2922 (vs), 2850 (m), 2360 (w), 2342 (w), 1494 (w), 1450 (m), 1376 (w), 970 (m), 760 (w), 698 (s).

MS (EI, 70 eV): m/z (%): 145 (21), 118 (70), 117 (14), 105 (100), 91 (39), 79 (25), 77 (14).

HRMS (EI) for $C_{19}H_{28}$: calc. [M$^+$]: 256.2191; found: 256.2184.

(*syn*-3-Methylhex-1-ene-1,5-diyl)dibenzene (*syn*-146c):



syn-**146c**

The (*E*)-styrene *syn*-**146c** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and the alkenyl iodide **145c** (0.3 mmol, 69.0 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**146c** (0.052 mmol, 13.0 mg, 52%, dr = 98:2) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.36–7.27 (m, 6H), 7.22–7.16 (m, 4H), 6.33 (d, *J* = 15.9 Hz, 1H), 6.07 (dd, *J* = 15.9, 8.1 Hz, 1H), 2.80 (h, *J* = 7.1 Hz, 1H), 2.27 (hept, 1H), 1.79–1.69 (m, 1H), 1.64–1.55 (m, 1H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.08 (d, *J* = 6.7 Hz, 3H).

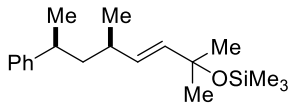
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.0, 138.0, 136.8, 128.6, 128.5, 128.2, 127.1, 127.0, 126.1, 126.0, 45.8, 37.5, 35.2, 22.4, 20.8.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3062 (w), 3026 (m), 2960 (s), 2924 (s), 2870 (m), 2362 (m), 2338 (w), 1602 (w), 1494 (m), 1452 (m), 1376 (w), 968 (m), 762 (m), 748 (s), 700 (vs).

MS (EI, 70 eV): 145 (100), 131 (71), 129 (28), 117 (40), 115 (24), 105 (63), 91 (61).

HRMS (EI) for $C_{19}H_{22}$: calc. [M^+]: 250.1717; found: 250.1722.

((*syn*-2,5-Dimethyl-7-phenyloct-3-en-2-yl)oxy)trimethylsilane (*syn*-146d):



syn-**146d**

The (*E*)-silyl ether *syn*-**146d** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and the alkenyl iodide **145d** (0.3 mmol, 85.3 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**146d** (0.039 mmol, 11.9 mg, 39%, dr = 94:6) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.30–7.27 (m, 2H), 7.19–7.16 (m, 3H), 5.50 (dd, *J* = 15.7, 1.0 Hz, 1H), 5.35 (dd, *J* = 15.6, 7.7 Hz, 1H), 2.75 (h, *J* = 7.2 Hz, 1H), 2.05 (hept, *J* = 7.1 Hz, 1H), 1.67–1.56 (m, 1H), 1.53–1.41 (m, 1H), 1.28 (s, 6H), 1.22 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.10 (s, 9H).

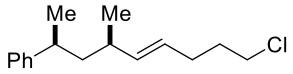
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.0, 141.7, 137.0, 132.6, 128.5, 127.1, 126.0, 73.5, 45.7, 37.4, 34.1, 31.0, 30.7, 22.5, 20.6, 2.8.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3027 (w), 2962 (s), 2927 (m), 2871 (w), 2359 (w), 2334 (w), 1494 (w), 1454 (w), 1378 (w), 1361 (w), 1258 (m), 1249 (s), 1155 (m), 1038 (s), 997 (w), 972 (w), 862 (m), 839 (vs), 808 (w), 759 (m), 700 (m).

MS (EI, 70 eV): m/z (%): 72 (20), 59 (14), 57 (27), 43 (100), 42 (53), 41 (45).

HRMS (EI) for $C_{18}H_{29}OSi$: calc. [$M-Me^+$]: 289.1988; found: 289.1980.

(*syn*-9-Chloro-4-methylnon-5-en-2-yl)benzene (*syn*-146e):



syn-**146e**

The (*E*)-alkenyl chloride *syn*-**146e** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and the alkenyl iodide **145e** (0.3 mmol, 69.1 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**146e** (0.044 mmol, 11.0 mg, 44%, dr = 98:2) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.32–7.26 (m, 2H), 7.23–7.11 (m, 3H), 5.39–5.15 (m, 2H), 3.65–3.46 (m, 2H), 2.73 (q, *J* = 7.1 Hz, 1H), 2.19–2.09 (m, 2H), 2.07–1.98 (m, 1H), 1.87–1.73 (m, 2H), 1.65–1.52 (m, 1H), 1.51–1.40 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 3H), 0.95 (d, J = 6.6 Hz, 3H).

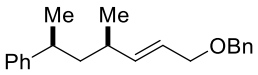
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.1, 138.0, 128.5, 127.1, 126.5, 125.9, 45.9, 44.6, 37.5, 34.6, 32.5, 29.7, 22.2, 21.0.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3062 (w), 3027 (w), 2958 (vs), 2925 (vs), 2869 (m), 2854 (m), 2361 (w), 2334 (w), 1494 (w), 1453 (m), 1377 (w), 1291 (w), 971 (m), 762 (m), 700 (s**).**

MS (EI, 70 eV): m/z (%): 145 (30), 118 (73), 117 (16), 106 (25), 105 (100), 91 (52), 79 (11).

HRMS (EI) for $C_{16}H_{23}Cl$: calc. [M^+]: 250.1488; found: 250.1483.

(*syn*-7-(Benzyloxy)-4-methylhept-5-en-2-yl)benzene (syn-146f):



syn-**146f**

The (*E*)-alkene *syn*-**146f** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and the alkenyl iodide **145f** (0.3 mmol, 82.2 mg). The crude product was extracted and purified by flash column chromatography. After prep-HPLC purification ($MeCN/H_2O$), the compound *syn*-**6f** (0.043 mmol, 12.7 mg, 43%, dr = 96:4) was obtained as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.37–7.27 (m, 6H), 7.21–7.08 (m, 3H), 5.62–5.40 (m, 2H), 4.50 (s, 2H), 3.96 (d, *J* = 4.9 Hz, 2H), 2.76 (h, *J* = 7.1 Hz, 1H), 2.10 (hept, *J* = 6.7 Hz, 1H), 1.69–1.60 (m, 1H), 1.53–1.40 (m, 1H), 1.22 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.7 Hz, 3H).

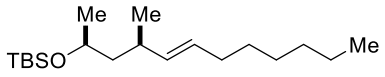
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.8, 140.6, 138.6, 128.5, 128.5, 127.7, 127.1, 126.0, 124.6, 71.9, 71.1, 45.4, 37.4, 34.3, 22.5, 20.4.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3085 (w), 3063 (w), 3028 (w), 2957 (s), 2922 (vs), 2851 (s), 2362 (w), 1738 (w), 1495 (w), 1454 (m), 1377 (w), 1362 (w), 1248 (w), 1205 (w), 1128 (w), 1099 (m), 1074 (m), 1028 (w), 1010 (w), 998 (w), 972 (m), 762 (m), 735 (m), 699 (vs).

MS (EI, 70 eV): m/z (%): 188 (16), 185 (11), 159 (21), 129 (11), 118 (22), 105 (100), 91 (95), 79 (10), 77 (11).

HRMS (EI) for $C_{21}H_{26}O$: calc. [M^+]: 294.1984; found: 294.1994.

***tert*-Butyldimethyl((*syn*-4-methyldodec-5-en-2-yl)oxy)silane (*syn*-146g):**



syn-**146g**

The (*E*)-alkene *syn*-**146g** was prepared according to **TP2** from the iodide *rac*-**142b** (dr = 50:50, 0.1 mmol, 32.8 mg) and the alkenyl iodide **145a** (0.3 mmol, 71.4 mg). Thereby, the secondary alkyllithium reagent was prepared according to literature.[63] The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**6g** (0.043 mmol, 13.4 mg, 43%, dr = 93:7) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 5.40–5.32 (m, 1H), 5.26–5.17 (m, 1H), 3.84–3.73 (m, 1H), 2.24 (hept, *J* = 14.2, 7.0 Hz, 1H), 2.02–1.91 (m, 2H), 1.46–1.37 (m, 1H), 1.35–1.20 (m, 12H), 1.10 (d, *J* = 6.0 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H).

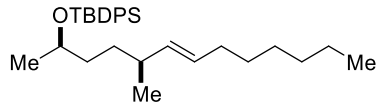
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 136.3, 129.1, 67.0, 47.7, 33.5, 32.8, 31.9, 29.8, 29.0, 26.1, 24.6, 22.8, 22.0, 18.3, 14.3, -3.9, -4.4.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2958 (s), 2926 (vs), 2856 (m), 1462 (w), 1374 (w), 1364 (w), 1254 (w), 1142 (w), 1096 (w), 1054 (w), 1006 (w), 970 (w), 836 (m), 806 (w), 774 (m).

MS (EI, 70 eV): m/z (%): 255 (91), 211 (41), 169 (39), 115 (33), 103 (62), 95 (29), 75 (100).

HRMS (EI) for $C_{19}H_{40}OSi$: calc. [M−*t*-Bu^+]: 255.2144; found: 255.2138.

***tert*-Butyl((*syn*-5-methyltridec-6-en-2-yl)oxy)diphenylsilane (*syn*-146h):**



syn-**146h**

The (*E*)-alkene *syn*-**146h** was prepared according to **TP2** from the iodide *syn*-**142c** (dr = 99:1, 0.1 mmol, 46.6 mg) and the alkenyl iodide **145a** (0.3 mmol, 71.4 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**146h** (0.046 mmol, 20.7 mg, 46%, dr = 96:4) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.70–7.65 (m, 4H), 7.43–7.33 (m, 6H), 5.33–5.23 (m, 1H), 5.21–5.13 (m, 1H), 3.81 (h, *J* = 5.9 Hz, 1H), 2.01–1.85 (m, 3H), 1.48–1.34 (m, 2H), 1.34–1.13 (m, 12H), 1.08–1.02 (m, 12H), 0.91–0.83 (m, 6H).

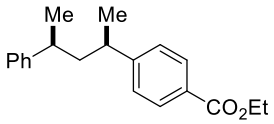
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 136.3, 136.1, 136.0, 135.2, 134.8, 129.5, 129.5, 128.8, 127.6, 127.5, 70.0, 37.3, 36.9, 32.8, 32.7, 31.9, 29.8, 29.0, 27.2, 23.4, 22.8, 21.1, 19.4, 14.3.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3072 (w), 3050 (w), 2958 (m), 2928 (s), 2856 (m), 1472 (w), 1462 (w), 1428 (m), 1390 (w), 1378 (w), 1362 (w), 1130 (m), 1110 (s), 1066 (m), 1030 (w), 998 (w), 968 (m), 822 (w), 740 (m), 702 (vs), 688 (w).

MS (EI, 70 eV): m/z (%): 394 (13), 393 (46), 200 (14), 199 (100).

HRMS (EI) for $C_{30}H_{46}OSi$: calc. [$M-H^+$]: 449.3240; found: 449.3225.

Ethyl 4-(*syn*-4-phenylpentan-2-yl)benzoate (*syn*-146i):



syn-**146i**

The ethyl benzoate derivative *syn*-**146i** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and ethyl 4-bromobenzoate **149a** (0.3 mmol, 68.7 mg). The crude product was extracted and purified by flash column chromatography. After prep-HPLC purification ($MeCN/H_2O$), the compound *syn*-**146i** (0.046 mmol, 13.6 mg, 46%, dr = 94:6) was obtained as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.98–7.94 (m, 2H), 7.32–7.26 (m, 2H), 7.23–7.18 (m, 3H), 7.16–7.07 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.70 (h, *J* = 7.2 Hz, 1H), 2.61 (h, *J* = 7.1 Hz, 1H), 1.94 (dt, *J* = 13.7, 7.5 Hz, 1H), 1.78 (dt, *J* = 13.7, 7.6 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.25 (d, *J* = 3.8 Hz, 3H), 1.23 (d, *J* = 3.8 Hz, 3H).

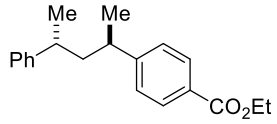
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.8, 153.2, 147.5, 129.9, 128.6, 128.4, 127.1, 127.0, 126.1, 60.9, 46.9, 37.7, 37.5, 22.3, 22.0, 14.5.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2961 (w), 2926 (w), 2871 (w), 2362 (w), 2334 (w), 1717 (s), 1610 (w), 1494 (w), 1453 (w), 1418 (w), 1377 (w), 1367 (w), 1310 (w), 1275 (vs), 1179 (w), 1108 (m), 1021 (w), 853 (w), 775 (w), 763 (w), 701 (m).

MS (EI, 70 eV): m/z (%): 251 (10), 250 (43), 207 (8), 164 (16), 105 (100), 91 (14).

HRMS (EI) for $C_{20}H_{24}O_2$: calc. [M^+]: 296.1776; found: 296.1768.

Ethyl 4-(*anti*-4-phenylpentan-2-yl)benzoate (*anti*-146i):



anti-**146i**

The ethyl benzoate derivative *anti*-**146i** was prepared according to **TP2** from the iodide *anti*-**142a** (dr = 2:98, 0.1 mmol, 27.4 mg) and ethyl 4-bromobenzoate **149a** (0.3 mmol, 68.7 mg). The crude product was extracted and purified by flash column chromatography. After prep-HPLC purification ($MeCN/H_2O$), the compound *anti*-**146i** (0.041 mmol, 12.2 mg, 41%, dr = 9:91) was obtained as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.00–7.93 (mj, 2H), 7.32–7.27 (m, 2H), 7.23–7.14 (m, 3H), 7.10–7.02 (m, 2H), 4.38 (q, *J* = 7.1 Hz, 1H), 2.59–2.49 (m, 1H), 2.49–2.37 (m, 1H), 1.96–1.80 (m, 1H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.17 (dd, *J* = 6.9, 4.2 Hz, 6H).

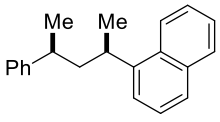
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.9, 152.9, 147.1, 129.9, 128.6, 128.5, 127.4, 127.3, 126.2, 60.9, 46.6, 38.0, 37.9, 23.5, 23.3, 14.5.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3028 (vw), 2960 (w), 2926 (w), 2870 (w), 1718 (s), 1610 (w), 1494 (w), 1454 (w), 1418 (w), 1366 (w), 1310 (w), 1274 (vs), 1180 (w), 1106 (m), 1022 (w), 856 (w), 776 (w), 764 (w), 702 (m).

MS (EI, 70 eV): m/z (%): 251 (13), 191 (65), 178 (58), 177 (20), 163 (33), 149 (20), 131 (13), 119 (11), 106 (20), 105 (100), 91 (51).

HRMS (EI) for $C_{20}H_{24}O_2$: calc. [M^+]: 296.1776; found: 296.1768.

1-(*syn*-4-Phenylpentan-2-yl)naphthalene (*syn*-146j):



syn-**146j**

The naphthalene derivative *syn*-**146j** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and 1-bromonaphthalene **149b** (0.3 mmol, 62.1 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**146j** (0.056 mmol, 15.4 mg, 56%, dr = 94:6) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.83–7.68 (m, 1H), 7.67–7.48 (m, 2H), 7.42–7.25 (m, 6H), 7.21–7.14 (m, 3H), 3.36–3.25 (m, 1H), 2.78 (qd, *J* = 6.5, 2.5 Hz, 1H), 2.02 (ddd, *J* = 14.2, 9.2, 5.4 Hz, 1H), 1.74 (ddd, 1H), 1.31 (d, *J* = 6.8 Hz, 3H), 1.17–1.10 (m, 3H).

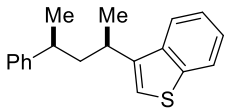
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.3, 144.1, 134.0, 131.5, 129.0, 128.6, 127.3, 126.4, 126.3, 125.7, 125.3, 123.2, 122.6, 47.2, 37.9, 23.0, 21.1.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3061 (w), 3048 (w), 3027 (w), 2959 (m), 2924 (s), 2869 (w), 2853 (m), 2360 (w), 2340 (w), 1598 (w), 1510 (w), 1494 (w), 1453 (m), 1396 (w), 1378 (w), 797 (m), 778 (vs), 763 (m), 700 (s).

MS (EI, 70 eV): m/z (%): 274 (12), 156 (86), 155 (100), 154 (17), 153 (66), 152 (32), 141 (62), 128 (23), 115 (16), 105 (23), 91 (16).

HRMS (EI) for $C_{21}H_{22}$: calc. [M^+]: 274.1722; found: 274.1715.

3-(*syn*-4-Phenylpentan-2-yl)benzo[*b*]thiophene (*syn*-146k):



syn-**146k**

The benzo[*b*]thiophene derivative *syn*-**146k** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and 3-bromobenzo[*b*]thiophene **149c** (0.3 mmol, 63.9 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**146k** (0.038 mmol, 10.7 mg, 38%, dr = 97:3) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.87–7.79 (m, 1H), 7.46–7.39 (m, 1H), 7.38–7.27 (m, 4H), 7.25–7.21 (m, 3H), 7.10–7.04 (m, 1H), 3.04–2.91 (m, 1H), 2.91–2.81 (m, 1H), 2.12 (ddd, *J* = 13.7, 9.3, 5.3 Hz, 1H), 1.79 (ddd, *J* = 13.7, 9.0, 5.8 Hz, 1H), 1.36 (d, *J* = 6.8 Hz, 3H), 1.27–1.24 (m, 7H)..

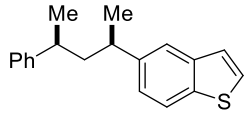
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.2, 142.9, 140.7, 138.6, 128.6, 127.3, 126.3, 124.2, 123.8, 123.0, 121.9, 119.6, 46.2, 37.8, 30.6, 23.1, 20.4.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3026 (w), 2959 (s), 2924 (s), 2870 (m), 2853 (m), 2360 (w), 2341 (w), 1493 (w), 1454 (m), 1428 (m), 1379 (w), 1028 (w), 838 (w), 761 (vs), 733 (s), 701 (s).

MS (EI, 70 eV): m/z (%): 207 (23), 162 (100), 161 (47), 147 (66), 128 (28), 115 (12).

HRMS (EI) for $C_{19}H_{20}S$: calc. [M^+]: 280.1286; found: 280.1279.

5-(*syn*-4-Phenylpentan-2-yl)benzo[*b*]thiophene (*syn*-146l):



syn-**146l**

The benzo[*b*]thiophene *syn*-**146l** was prepared according to **TP2** from the iodide *syn*-**142a** (dr = 98:2, 0.1 mmol, 27.4 mg) and 5-bromobenzo[*b*]thiophene **149d** (0.3 mmol, 63.9 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford *syn*-**146l** (0.059 mmol, 16.5 mg, 59%, dr = 98:2) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.80 (d, *J* = 8.3 Hz, 1H), 7.61 (d, *J* = 1.7 Hz, 1H), 7.42 (d, *J* = 5.4 Hz, 1H), 7.32–7.27 (m, 3H), 7.22–7.14 (m, 4H), 2.78 (h, *J* = 7.1 Hz, 1H), 2.66 (h, *J* = 7.1 Hz, 1H), 2.05–1.97 (m, 1H), 1.87–1.79 (m, 1H), 1.30 (d, *J* = 6.9 Hz, 3H), 1.25 (d, *J* = 7.0 Hz, 3H).

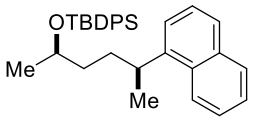
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.8, 144.0, 140.0, 137.5, 128.5, 127.1, 126.6, 126.0, 124.0, 123.9, 122.5, 121.7, 47.3, 37.5, 29.9, 22.7, 22.3.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3026 (w), 2957 (m), 2924 (s), 2853 (m), 2360 (w), 2334 (w), 1494 (w), 1453 (m), 1438 (w), 1421 (w), 1377 (w), 1090 (w), 1053 (w), 1028 (w), 891 (w), 821 (w), 809 (w), 760 (w), 700 (vs).

MS (EI, 70 eV): m/z (%): 162 (60), 161 (30), 148 (10), 147 (100), 128 (39), 117 (11).

HRMS (EI) for $C_{19}H_{20}S$: calc. [M^+]: 280.1286; found: 280.1280.

***tert*-Butyl((*syn*-5-(naphthalen-1-yl)hexan-2-yl)oxy)diphenylsilane (*syn*-146m):**



syn-**146m**

The naphthalene derivative *syn*-**146m** was prepared according to **TP2** from the iodide *syn*-**142c** (dr = 99:1, 0.1 mmol, 46.6 mg) and 1-bromonaphthalene **149b** (0.3 mmol, 62.1 mg). The crude product was purified by flash column chromatography on silica gel with ethyl acetate/*n*-pentane = 1/200 to afford *syn*-**146m** (0.051 mmol, 23.8 mg, 51%, dr = 97:3) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.13–7.79 (m, 1H), 7.73–7.56 (m, 3H), 7.51–7.26 (m, 6H), 3.92–3.74 (m, 1H), 3.62–3.35 (m, 1H), 1.88–1.60 (m, 1H), 1.50–1.32 (m, 1H), 1.33–1.26 (m, 1H), 1.08–0.96 (m, 7H).

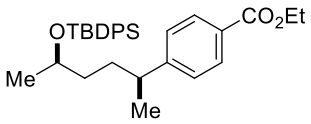
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 143.9, 136.0, 136.0, 136.0, 135.0, 134.7, 134.1, 131.8, 129.6, 129.5, 129.0, 127.6, 127.6, 127.5, 127.5, 126.3, 125.8, 125.7, 125.3, 123.4, 122.6, 69.9, 37.6, 33.1, 27.2, 23.2, 22.1, 19.4.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3070 (w), 3048 (w), 2962 (m), 2930 (s), 2857 (m), 2360 (m), 2342 (m), 1472 (w), 1461 (w), 1428 (m), 1390 (w), 1376 (w), 1362 (w), 1130 (w), 1111 (s), 1072 (m), 1052 (m), 1028 (w), 1006 (w), 998 (w), 822 (w), 797 (w), 778 (m), 740 (m), 720 (w), 702 (vs), 688 (w), 668 (w).

MS (EI, 70 eV): m/z (%): 410 (25), 409 (69), 200 (18), 199 (100), 155 (18).

HRMS (EI) for $C_{32}H_{38}OSi$: calc. [M^+]: 466.2692; found: 466.2704.

Ethyl 4-(*syn*-5-((*tert*-butyldiphenylsilyl)oxy)hexan-2-yl)benzoate (*syn*-146n):



syn-**146n**

The ethyl benzoate derivative *syn*-**146n** was prepared according to **TP2** from the iodide *syn*-**142c** (dr = 99:1, 0.1 mmol, 46.6 mg) and ethyl 4-bromobenzoate **149a** (0.3 mmol, 68.7 mg). The crude product was purified by flash column chromatography on silica gel with diethyl ether/*n*-pentane = 1/50 to afford *syn*-**146n** (0.050 mmol, 24.4 mg, 50%, dr = 96:4) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.99–7.87 (m, 1H), 7.69–7.57 (m, 2H), 7.51–7.28 (m, 3H), 7.21–7.07 (m, 1H), 4.37 (q, *J* = 7.1 Hz, 1H), 3.78 (qd, *J* = 5.9, 2.5 Hz, 0H), 2.60 (dp, *J* = 15.2, 7.3 Hz, 1H), 1.62–1.45 (m, 1H), 1.39 (t, *J* = 7.1 Hz, 2H), 1.17 (t, *J* = 6.6 Hz, 2H), 1.04–0.96 (m, 6H).

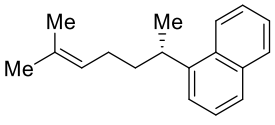
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.9, 153.2, 136.0, 136.0, 134.9, 134.6, 129.8, 129.6, 129.5, 128.3, 127.6, 127.5, 127.1, 69.6, 60.9, 40.3, 37.4, 33.6, 27.2, 23.3, 22.3, 19.4, 14.5.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2931 (w), 2858 (w), 1716 (m), 1610 (w), 1472 (w), 1462 (w), 1428 (w), 1418 (w), 1390 (vw), 1368 (w), 1310 (w), 1275 (s), 1248 (w), 1180 (w), 1105 (s), 1053 (w), 1020 (w), 1007 (w), 907 (s), 855 (w), 822 (w), 774 (w), 731 (vs), 703 (vs).

MS (EI, 70 eV): m/z (%): 432 (34), 431 (100), 200 (13), 199 (199), 187 (12), 145 (15).

HRMS (EI) for $C_{31}H_{40}O_3Si$: calc. [$M–H^+$]: 487.2668; found: 487.2668.

(*S*)-1-(6-Methylhept-5-en-2-yl)naphthalene (*S*-146o):



(*S*)-**146o**

The naphthalene derivative (*S*)-**146o** was prepared according to **TP2** from the iodide (*S*)-**142d** (0.1 mmol, 24 mg) and 1-bromonaphthalene **149b** (0.3 mmol, 62.1 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford (*S*)-**146o** (0.076 mmol, 18.1 mg, 76%, er = 91:9) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.16–8.08 (m, 1H), 7.87–7.83 (m, 1H), 7.73–7.67 (m, 1H), 7.54–7.37 (m, 4H), 5.18–5.10 (m, 1H), 3.61 (h, *J* = 6.9 Hz, 1H), 2.06–1.96 (m, 2H), 1.93–1.82 (m, 1H), 1.77–1.68 (m, 1H), 1.67 (q, *J* = 1.3 Hz, 3H), 1.47 (d, *J* = 1.3 Hz, 3H), 1.38 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 143.9, 134.1, 131.9, 131.8, 129.0, 126.3, 125.8, 125.7, 125.3, 124.6, 123.4, 122.6, 38.0, 33.2, 26.4, 25.9, 21.9, 17.8.

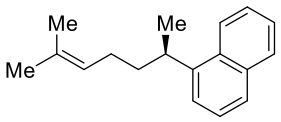
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3047 (w), 2963 (m), 2925 (m), 2856 (w), 1597 (w), 1510 (w), 1453 (w), 1396 (w), 1376 (w), 796 (m), 777 (vs).

MS (EI, 70 eV): m/z (%): 238 (23), 167 (17), 157 (12), 156 (100), 155 (72), 153 (46), 152 (17), 141 (68), 95 (8).

HRMS (EI) for $C_{18}H_{22}$: calc. [M^+]: 238.1722; found: 238.1715.

$[\alpha]_D^{20}$: –18.6 (c = 0.4, $CHCl_3$).

(*R*)-1-(6-Methylhept-5-en-2-yl)naphthalene (*R*-146o):



(*R*)-**146o**

The naphthalene derivative (*R*)-**146o** was prepared according to **TP2** from the iodide (*R*)-**142d** (0.1 mmol, 24 mg) and 1-bromonaphthalene **149b** (0.3 mmol, 62.1 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford (*R*)-**146o** (0.062 mmol, 14.8 mg, 62%, er = 9:91) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = δ 8.16–8.09 (m, 1H), 7.87–7.83 (m, 1H), 7.70 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.54–7.37 (m, 4H), 5.19–5.04 (m, 1H), 3.68–3.52 (m, 1H), 2.06–1.96 (m, 2H), 1.93–1.81 (m, 1H), 1.79–1.68 (m, 1H), 1.67 (d, *J* = 1.3 Hz, 2H), 1.47 (d, *J* = 1.3 Hz, 3H), 1.38 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 143.9, 134.1, 131.9, 131.8, 129.0, 126.3, 125.8, 125.7, 125.3, 124.6, 123.4, 122.6, 38.0, 26.4, 25.9, 21.9, 17.8.

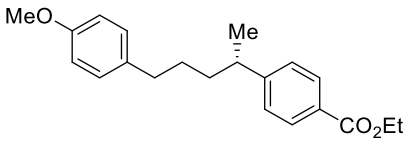
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3047 (w), 2963 (m), 2925 (m), 2855 (w), 1597 (w), 1511 (w), 1453 (w), 1396 (w), 1376 (w), 1255 (vw), 1108 (vw), 858 (vw), 796 (m), 777 (vs)

MS (EI, 70 eV): m/z (%): 238 (18), 167 (19), 157 (12), 155 (89), 153 (100), 152 (48), 141 (86), 128 (35), 115 (22).

HRMS (EI) for $C_{18}H_{22}$: calc. [M^+]: 238.1722; found: 238.1715.

[α]$_D^{20}$: +18.3 (c = 0.3, $CHCl_3$).

Ethyl (*S*)-4-(5-(4-methoxyphenyl)pentan-2-yl)benzoate (*S*-146p):



(*S*)-**146p**

The ethyl benzoate derivative (*S*)-**146p** was prepared according to **TP2** from the iodide (*S*)-**142e** (0.1 mmol, 30.4 mg) and ethyl 4-bromobenzoate **149a** (0.3 mmol, 68.7 mg). The crude product was purified by flash column chromatography on silica gel with diethyl ether/*n*-pentane = 1/50 to afford (*S*)-**146p** (0.054 mmol, 17.6 mg, 54%, er = 83:17) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): 7.99–7.90 (m, 2H), 7.25–7.17 (m, 2H), 7.05–6.97 (m, 2H), 6.85–6.75 (m, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 2.76 (h, *J* = 7.0 Hz, 1H), 2.50 (tt, *J* = 9.3, 6.9 Hz, 2H), 1.65–1.58 (m, 2H), 1.55–1.42 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): 166.9, 157.8, 153.2, 134.6, 129.8, 129.3, 128.3, 127.1, 113.8, 60.9, 55.4, 40.1, 37.8, 35.1, 29.8, 22.3, 14.5.

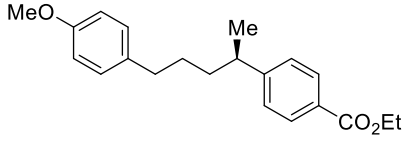
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2977 (w), 2936 (w), 2836 (w), 1729 (s), 1584 (w), 1463 (m), 1444 (m), 1391 (w), 1377 (w), 1349 (w), 1300 (m), 1244 (vs), 1176 (s), 1153 (s), 1115 (m), 1096 (m), 1063 (m), 1035 (s), 931 (w), 830 (m), 748 (w), 699 (m).

MS (EI, 70 eV): m/z (%): 326 (8), 121 (100), 86 (39), 84 (57), 74 (77), 59 (90), 45 (52), 42 (24).

HRMS (EI) for $C_{21}H_{26}O_3$: calc. [M^+]: 326.1882; found: 326.1877.

[α]$_D^{20}$: +6.4 (c = 0.5, $CHCl_3$).

Ethyl (*R*)-4-(5-(4-methoxyphenyl)pentan-2-yl)benzoate (*R*-146p):



(*R*)-**146p**

The ethyl benzoate derivative (*R*)-**146p** was prepared according to **TP2** from the iodide (*R*)-**142e** (0.1 mmol, 30.4 mg) and ethyl 4-bromobenzoate **149a** (0.3 mmol, 68.7 mg). The crude product was

purified by flash column chromatography on silica gel with diethyl ether/*n*-pentane = 1/50 to afford (*R*)-**146p** (0.046 mmol,15.0 mg, 46% yield, er = 9:91) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): 8.01–7.91 (m, 2H), 7.25–7.18 (m, 2H), 7.06–7.00 (m, 2H), 6.84–6.72 (m, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 2.81–2.69 (m, 1H), 2.51 (td, *J* = 7.8, 7.3, 2.5 Hz, 2H), 1.64–1.56 (m, 3H), 1.55–1.42 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): 166.9, 157.8, 153.2, 134.6, 129.8, 129.3, 128.4, 127.1, 113.8, 60.9, 55.4, 40.1, 37.8, 35.1, 29.8, 22.3, 14.5.

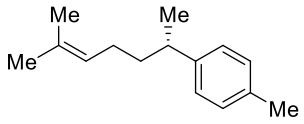
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2958 (w), 2929 (m), 2854 (w), 1716 (s), 1611 (m), 1513 (s), 1463 (w), 1443 (w), 1418 (w), 1367 (w), 1310 (w), 1299 (w), 1275 (vs), 1246 (s), 1179 (m), 1106 (m), 1037 (w), 1021 (w), 856 (w), 831 (w), 809 (w), 775 (w), 708 (w).

MS (EI, 70 eV): m/z (%): 326 (8), 121 (100), 86 (39), 84 (57), 74 (77), 59 (90), 45 (52), 42 (24).

HRMS (EI) for $C_{21}H_{26}O_3$: calc. [M^+]: 326.1882; found: 326.1874.

$[\alpha]_D^{20}$: –7.9 (c = 0.8, $CHCl_3$).

(*S*)-1-Methyl-4-(6-methylhept-5-en-2-yl)benzene (*S*-150):



(*S*)-Curcumene (*S*-**150**)

The natural product (*S*)-Curcumene (*S*-**150**) was prepared according to **TP2** from the iodide (*S*)-**142d** (0.1 mmol, 24 mg) and 4-bromotoluene **149e** as electrophile (0.3 mmol, 51 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford (*S*)-Curcumene (*S*-**150**) (0.050 mmol, 10.1 mg, 50%, er = 93:7) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.14–7.02 (m, 4H), 5.14–5.01 (m, 1H), 2.65 (h, *J* = 7.0 Hz, 1H), 2.32 (s, 3H), 1.93–1.79 (m, 2H), 1.67 (d, *J* = 1.3 Hz, 3H), 1.64–1.56 (m, 2H), 1.52 (d, *J* = 1.2 Hz, 3H), 1.21 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 144.8, 135.3, 131.5, 129.1, 127.0, 124.7, 39.1, 38.6, 26.3, 25.9, 22.6, 21.2, 17.8.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3020 (w), 2961 (s), 2923 (vs), 2854 (m), 2362 (w), 2343 (w), 1515 (m), 1455 (m), 1376 (w), 1110 (w), 1020 (w), 815 (m).

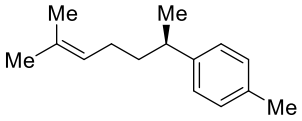
MS (EI, 70 eV): m/z (%): 145 (25), 132 (100), 131 (30), 119 (58), 117 (31), 105 (34), 91 (18).

HRMS (EI) for $C_{15}H_{22}$: calc. [M^+]: 202.1722; found: 202.1714.

$[\alpha]_D^{20}$: +35.8 (c = 0.9, $CHCl_3$).

[Lit:[181] $[\alpha]_D^{20}$ = +36.8 (c = 1.3, $CHCl_3$); Lit:[182] $[\alpha]_D^{20}$ = +37.7 (c = 0.7, $CHCl_3$).]

(*R*)-1-Methyl-4-(6-methylhept-5-en-2-yl)benzene (*R*-150):



(*R*)-Curcumene (*R*-**150**)

The natural product (*R*)-Curcumene (*R*-**150**) was prepared according to **TP2** from the iodide (*R*)-**142d** (0.1 mmol, 24 mg) and 4-bromotoluene **149e** as electrophile (0.3 mmol, 51 mg). The crude product was purified by flash column chromatography on silica gel with *n*-pentane to afford (*R*)-Curcumene (*R*-**150**) (0.046 mmol, 9.3 mg, 46%, er = 7:93) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): 7.15–7.03 (m, 4H), 5.13–5.03 (m, 1H), 2.65 (h, *J* = 7.0 Hz, 1H), 2.32 (s, 3H), 1.93–1.76 (m, 2H), 1.69–1.64 (m, 2H), 1.63–1.54 (m, 2H), 1.52 (d, *J* = 1.3 Hz, 3H), 1.21 (d, *J* = 7.0 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): 144.8, 135.3, 131.5, 129.1, 127.0, 124.7, 39.1, 38.6, 26.3, 25.9, 22.6, 21.2, 17.8.

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3020 (w), 2961 (s), 2922 (vs), 2854 (m), 2364 (w), 2343 (w), 1518 (m), 1455 (m), 1374 (w), 1110 (w), 1020 (w), 814 (m).

MS (EI, 70 eV): m/z (%): 145 (27), 132 (100), 119 (99), 117 (62), 115 (28), 105 (57), 91 (49), 77 (12).

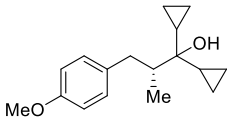
HRMS (EI) for $C_{15}H_{22}$: calc. [M^+]: 202.1722; found: 202.1722.

$[\alpha]_D^{20}$: –43.4 (c = 0.6, $CHCl_3$).

[Lit:[181] $[\alpha]_D^{20}$ = –44.6 (c = 1.2, $CHCl_3$); Lit:[183] $[\alpha]_D^{24}$ = –44.5 (c = 1.1, $CHCl_3$).]

[181] L. Wu, J.-C. Zhong, S.-K. Liu, F.-P. Liu, Z.-D. Gao, M. Wang, Q.-H, Bian, *Tetrahedron Asymmetry* **2016**, *27*, 78–83.
[182] G. Uhde, G. Ohloff, *Helv. Chim. Acta* **1972**, *55*, 2621–2625.
[183] S. Song, S.-F. Zhu, S. Yang, S. Li, Q.-L. Zhou *Angew. Chem., Int. Ed.* **2012**, *51*, 2708–2711.

(*R*)-1,1-Dicyclopropyl-3-(4-methoxyphenyl)-2-methylpropan-1-ol (*R*-152a):



(*R*)-**152a**

The tertiary alcohol (*R*)-**152a** was prepared according to **TP8** from the iodide (*R*)-**142f** (27.6 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 22.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (10:1) to afford (*R*)-**152a** (19.5 mg, 0.075 mmol, 75%, 91% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.13–7.09 (m, 2H), 6.85–6.81 (m, 2H), 3.79 (s, 3H), 3.19 (dd, *J* = 13.2, 3.0 Hz, 1H), 2.26 (dd, *J* = 13.2, 11.3 Hz, 1H), 1.93–1.87 (m, 1H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.92–0.85 (m, 2H), 0.51–0.40 (m, 6H), 0.35–0.26 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.7, 134.4, 130.2, 113.7, 72.7, 55.4, 47.9, 37.3, 16.8, 15.9, 14.2, 1.6, 1.4, −0.9, –1.0.

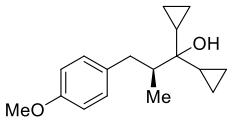
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3005 (w), 2961 (w), 2937 (w), 1748 (w), 1710 (vs), 1610 (w), 1511 (s), 1464 (w), 1441 (w), 1419 (w), 1360 (s), 1299 (w), 1246 (s), 1220 (s), 1177 (m), 1091 (w), 1033 (m), 999 (m), 977 (w), 928 (w), 913 (w), 901 (w), 833 (w), 809 (w), 758 (w).

MS (70 eV, EI): m/z (%): 213 (5), 150 (15), 134 (16), 121 (100), 111 (91), 91 (15), 69 (69).

HRMS (EI) for $C_{17}H_{24}O_2$: calc. $[M]^{+\bullet}$: 260.1776, found: 260.1770.

$[\alpha]_D^{20}$: +14.0 (c = 0.94, $CHCl_3$).

(*S*)-1,1-Dicyclopropyl-3-(4-methoxyphenyl)-2-methylpropan-1-ol (*S*-152a):



(*S*)-**152a**

The tertiary alcohol (*S*)-**152a** was prepared according to **TP8** from the iodide (*S*)-**142f** (27.6 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 22.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (10:1) to afford (*S*)-**152a** (21.1 mg, 0.081 mmol, 81%, 90% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.13–7.09 (m, 2H), 6.85–6.81 (m, 2H), 3.79 (s, 3H), 3.19 (dd, *J* = 13.3, 3.0 Hz, 1H), 2.26 (dd, *J* = 13.2, 11.3 Hz, 1H), 1.39–1.86 (m, 1H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.90–0.85 (m, 2H), 0.48–0.40 (m, 6H), 0.36–0.25 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.7, 134.4, 130.2, 113.7, 72.7, 55.4, 47.9, 37.3, 16.8, 15.9, 14.2, 1.6, 1.4, -0.9, -1.0.

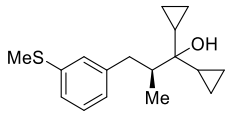
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3528 (vw), 3084 (vw), 3003 (w), 2956 (w), 2925 (w), 2876 (w), 2854 (w), 2833 (w), 1610 (w), 1583 (w), 1511 (vs), 1484 (vw), 1464 (w), 1441 (w), 1421 (w), 1373 (w), 1300 (w), 1246 (s), 1177 (m), 1102 (w), 1034 (m), 994 (m), 976 (w), 927 (w), 913 (w), 901 (w), 884 (vw), 831 (w), 807 (w), 757 (w).

MS (70 eV, EI): m/z (%): 150 (13), 134 (15), 121 (100), 111 (73), 91 (19), 77 (12), 69 (74).

HRMS (EI) for $C_{17}H_{24}O_2$: calc. $[M]^{+\bullet}$: 260.1776, found: 260.1771.

$[\alpha]_D^{20}$: −17.8 (c = 1.46, $CHCl_3$).

(*S*)-1,1-Dicyclopropyl-2-methyl-3-(3-(methylthio)phenyl)propan-1-ol (*S*-152b):



(*S*)-**152b**

The tertiary alcohol (*S*)-**152b** was prepared according to **TP8** from the iodide (*S*)-**142g** (29.2 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 22.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (*S*)-**152b** (20.2 mg, 0.073 mmol, 73%, 99% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.21 (t, *J* = 7.6 Hz, 1H), 7.11–7.07 (m, 2H), 6.98 (dt, *J* = 7.4, 1.4 Hz, 1H), 3.23 (dd, *J* = 13.1, 2.9 Hz, 1H), 2.49 (s, 3H), 2.29 (dd, *J* = 13.1, 11.4 Hz, 1H), 1.96–1.91 (m, 1H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.91–0.85 (m, 3H), 0.50–0.41 (m, 6H), 0.36–0.26 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 143.2, 138.1, 128.8, 127.6, 126.3, 123.9, 72.7, 47.7, 38.2, 16.9, 16.0, 15.8, 14.2, 1.7, 1.4, −0.9, –0.9.

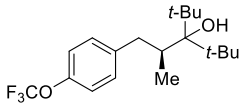
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3006 (s), 2962 (s), 2931 (s), 2924 (s), 2921 (s), 2361 (s), 2258 (s), 2234 (s), 2219 (s), 2169 (vs), 2156 (s), 2139 (s), 2094 (s), 2067 (s), 1591 (s), 1570 (s), 1476 (s), 1458 (s), 1440 (s), 1424 (s), 1374 (s), 1023 (s), 995 (s), 975 (s), 780 (s), 777 (s).

MS (70 eV, EI): m/z (%): 166 (10), 137 (18), 111 (100), 91 (15), 69 (69).

HRMS (EI) for $C_{17}H_{24}OS$: calc. $[M]^{+\bullet}$: 276.1548, found: 276.1544.

$[\alpha]_D^{20}$: −25.4 (c = 0.56, $CHCl_3$).

(*S*)-3-(*tert*-Butyl)-2,4,4-trimethyl-1-(4-(trifluoromethoxy)phenyl)pentan-3-ol (*S*-152c):



(*S*)-**152c**

The tertiary alcohol (*S*)-**152c** was prepared according to **TP8** from the iodide (*S*)-**142h** (33.0 mg, 0.1 mmol, 1.0 equiv) and 2,2,4,4-tetramethylpentan-3-one (**151b**, 28.4 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (30:1) to afford (*S*)-**152c** (22.5 mg, 0.065 mmol, 65%, 98% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.22–7.18 (m, 2H), 7.13–7.10 (m, 2H), 3.53–3.46 (m, 1H), 2.42–2.31 (m, 2H), 1.48 (s, 1H), 1.22 (s, 9H), 1.15 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.3, 143.0, 130.4, 120.9, 81.8, 43.9, 43.7, 43.5, 40.0, 30.2, 30.1, 18.8.

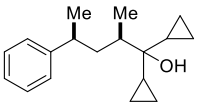
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3006 (w), 2964 (m), 2912 (m), 2877 (m), 1502 (m), 1488 (vs), 1440 (m), 1394 (m), 1381 (w), 1369 (m), 1244 (vs), 1205 (m), 1187 (m), 1085 (w), 1038 (vs), 983 (m), 929 (s), 867 (w), 802 (m), 792 (m), 768 (w).

MS (70 eV, EI): m/z (%): 289 (8), 202 (27), 174 (100), 87 (33), 57 (79).

HRMS (EI) for $C_{15}H_{20}F_3O_2$: calc. $[M\text{-}(t\text{-Bu})]^{+\bullet}$: 289.1415, found: 289.1413.

$[\alpha]_D^{20}$: −13.6 (c = 0.62, $CHCl_3$).

***syn*-1,1-Dicyclopropyl-2-methyl-4-phenylpentan-1-ol (*syn*-152d):**



syn-**152d**

The tertiary alcohol *syn*-**152d** was prepared according to **TP8** from the iodide *syn*-**142a** (27.4 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 22.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford *syn*-**4d** (19.1 mg, 0.074 mmol, 74%, dr = 96:4) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.29 (dd, *J* = 7.6, 1.1 Hz, 2H), 7.20–7.17 (m, 3H), 2.81 (m, 1H), 2.13 (m, 1H), 1.45-1.41 (m, 1H), 1.35–1.34 (m, 1H), 1.26–1.24 (m, 3H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.75–0.71 (m, 3H), 0.58 (s, 1H), 0.44–0.08 (m, 8H).

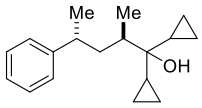
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.0, 128.5, 128.5, 127.4, 127.1, 126.0, 72.5, 42.7, 39.8, 38.0, 24.8, 16.4, 16.1, 14.5, 1.5, 1.2, 1.1, -1.0.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2975 (m), 2932 (m), 2858 (m), 2364 (m), 2336 (m), 2184 (w), 2172 (m), 2145 (w), 1731 (w), 1717 (w), 1556 (w), 1381 (m), 1350 (m), 1296 (w), 1236 (w), 1194 (w), 1179 (w), 1151 (m), 1118 (vs), 1076 (m), 1042 (w), 1024 (w), 929 (w), 853 (vw), 784 (vw), 748 (vw), 730 (vw), 702 (vw), 658 (vw).

MS (70 eV, EI): m/z (%): 111 (63), 91 (39), 69 (100).

HRMS (EI) for $C_{18}H_{26}O$: calc. $[M-C_3H_5]^{+\bullet}$: 217.1592, found: 217.1586.

***anti*-1,1-Dicyclopropyl-2-methyl-4-phenylpentan-1-ol (*anti*-152d):**



anti-**152d**

The tertiary alcohol a*nti*-**152d** was prepared according to **TP8** from the iodide *anti*-**142a** (27.4 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 22.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford *anti*-**152d** (18.1 mg, 0.7 mmol, 70%, dr = 5:95) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.32–7.28 (m, 2H), 7.24–7.21 (m, 2H), 7.21–7.17 (m, 1H), 2.80–2.78 (m, 1H), 2.00–1.94 (m, 1H), 1.79 (m, 1H), 1.50–1.43 (m, 1H), 1.23 (d, J = 6.9 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H), 0.87–0.79 (m, 3H), 0.44–0.35 (m, 6H), 0.27–0.22 (m, 2H).

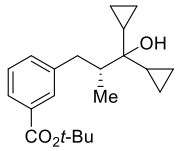
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 149.3, 128.5, 127.1, 125.9, 72.8, 43.1, 40.8, 37.7, 20.8, 16.4, 16.2, 14.9, 1.7, 1.3, -1.0.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3006 (w), 2954 (m), 2924 (s), 2870 (m), 2854 (m), 2166 (w), 1493 (w), 1455 (m), 1419 (w), 1375 (m), 1260 (w), 1179 (w), 1139 (w), 1101 (w), 1051 (w), 1020 (m), 990 (m), 974 (m), 930 (w), 906 (m), 845 (w), 824 (w), 815 (w), 778 (w), 773 (w), 760 (m), 745 (m), 736 (w), 732 (w), 727 (w), 722 (m), 718 (w), 713 (w), 699 (vs), 681 (w), 672 (m), 667 (m), 659 (w).

MS (70 eV, EI): m/z (%): 225 (28), 105 (34), 97 (100), 75 (68).

HRMS (EI) for $C_{18}H_{26}O$: calc. $[M]^{+\bullet}$: 258.1984, found: 258.1978.

***tert*-Butyl (*R*)-3-(3,3-dicyclopropyl-3-hydroxy-2-methylpropyl)benzoate (*R*-152e):**



(*R*)-**152e**

The tertiary alcohol (*R*)-**152e** was prepared according to **TP8** from the iodide (*R*)-**142i** (34.6 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 22.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (2:1) to afford (*R*)-**152e** (21.5 mg, 0.65 mmol, 65%, 93% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.83–7.79 (m, 2H), 7.37–7.30 (m, 2H), 3.29 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.38 (dd, *J* = 13.1, 11.5 Hz, 1H), 1.99–1.94 (m, 1H), 1.60 (s, 9H), 0.95–0.86 (m, 6H), 0.55–0.43 (m, 6H), 0.37–0.27 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.2, 142.6, 133.5, 132.0, 130.2, 128.1, 126.9, 81.0, 72.7, 47.7, 38.0, 28.4, 16.9, 15.9, 14.1, 1.7, 1.4, -0.8, -0.9.

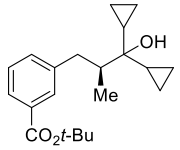
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3527 (vw), 3005 (w), 2975 (w), 2931 (w), 2878 (vw), 1711 (s), 1699 (s), 1605 (w), 1586 (w), 1477 (w), 1457 (w), 1440 (w), 1392 (w), 1368 (m), 1291 (s), 1256 (m), 1208 (w), 1159 (vs), 1110 (m), 1087 (m), 1062 (w), 1054 (w), 1023 (m), 998 (m), 977 (m), 935 (w), 929 (w), 914 (w), 865 (w), 849 (m), 824 (w), 812 (w), 758 (m), 746 (m), 704 (w), 668 (w).

MS (70 eV, EI): m/z (%): 257 (17), 207 (23), 164 (26), 135 (41), 111 (100), 91 (19), 69 (83).

HRMS (EI) for $C_{17}H_{21}O_2$: calc. $[M-O\textit{t}\text{-Bu}]^{+\bullet}$: 257.1542, found: 257.1536.

$[\alpha]_D^{20}$: +10.1 (c = 0.81, $CHCl_3$).

***tert*-Butyl (*S*)-3-(3,3-dicyclopropyl-3-hydroxy-2-methylpropyl)benzoate (*S*-152e):**



(*S*)-**152e**

The tertiary alcohol (*S*)-**152e** was prepared according to **TP8** from the iodide (*R*)-**142i** (34.6 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 22.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (2:1) to afford (*S*)-**152e** (23.8 mg, 0.72 mmol, 72%, 93% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.81 (dt, *J* = 9.0, 1.9 Hz, 2H), 7.37–7.30(m, 2H), 3.29 (dd, *J* = 13.1, 2.9 Hz, 1H), 2.38 (dd, *J* = 13.1, 11.5 Hz, 1H), 2.00–1.94 (m, 1H), 1.60 (s, 9H), 0.93–0.86 (m, 6H), 0.51–0.43 (m, 6H), 0.37–0.27 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.2, 142.6, 133.5, 132.0, 130.2, 128.1, 126.9, 81.0, 72.7, 47.7, 38.0, 28.4, 16.9, 15.9, 14.2, 1.7, 1.4, -0.8, -0.9.

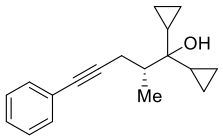
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3528 (vw), 3006 (w), 2976 (w), 2933 (w), 2879 (w), 1711 (s), 1699 (s), 1605 (w), 1587 (w), 1478 (w), 1458 (w), 1441 (w), 1392 (w), 1368 (m), 1292 (s), 1256 (m), 1208 (w), 1160 (vs), 1111 (m), 1087 (m), 1055 (w), 1023 (m), 997 (m), 978 (m), 930 (w), 914 (w), 850 (m), 825 (w), 758 (m), 746 (m), 704 (w).

MS (70 eV, EI): m/z (%): 257 (18), 207 (14), 164 (27), 135 (41), 111 (100), 91 (18), 69 (80).

HRMS (EI) for $C_{17}H_{21}O_2$: calc. $[M-O\textit{t}\text{-Bu}]^{+\bullet}$: 257.1542, found: 257.1535.

$[\alpha]_D^{20}$: −12.7 (c = 1.0, $CHCl_3$).

(*R*)-1,1-Dicyclopropyl-2-methyl-5-phenylpent-4-yn-1-ol (*R*-152f):



(*R*)-**152f**

The tertiary alcohol (*R*)-**152f** was prepared according to **TP8** from the iodide (*R*)-**142j** (27.0 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 22.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1) to afford (*R*)-**152f** (18.6 mg, 0.73 mmol, 73%, 93% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.38 (dq, *J* = 8.6, 3.2, 2.8 Hz, 2H), 7.27 (t, *J* = 2.9 Hz, 1H), 7.25 (s, 1H), 2.83 (dd, *J* = 16.7, 4.5 Hz, 1H), 2.46 (dd, *J* = 16.7, 9.2 Hz, 1H), 2.04–2.02 (m, 1H), 1.25 (d, *J* = 7.0 Hz, 3H), 1.21 (s, 1H), 0.88–0.82 (m, 2H), 0.51–0.38 (m, 5H), 0.35–0.29 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 131.6, 128.3, 127.7, 124.0, 90.4, 81.8, 72.5, 45.0, 22.4, 17.6, 15.6, 15.3, 1.5, 0.7, -0.5, -0.8.

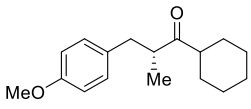
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3006 (w), 2969 (w), 2965 (w), 2935 (w), 1597 (w), 1490 (m), 1460 (w), 1442 (w), 1424 (w), 1373 (w), 1303 (w), 1177 (w), 1114 (w), 1069 (w), 1023 (m), 995 (m), 973 (m), 928 (w), 912 (m), 880 (w), 864 (w), 843 (w), 823 (w), 754 (vs), 734 (w), 690 (vs), 669 (w).

MS (70 eV, EI): m/z (%): 213 (27), 211 (100), 178 (18), 141 (25), 128 (40), 115 (50), 111 (47).

HRMS (EI) for $C_{18}H_{22}O$: calc. $[M-H]^{+\bullet}$: 253.1592, found: 253.1586

$[\alpha]_D^{20}$: −12.2 (c = 0.41, $CHCl_3$).

(*R*)-1-Cyclohexyl-3-(4-methoxyphenyl)-2-methylpropan-1-one (*R*-152g):



(*R*)-**152g**

The ketone (*R*)-**152g** was prepared according to **TP8** from the iodide (*R*)-**142f** (27.6 mg, 0.1 mmol, 1.0 equiv) and cyclohexanecarbaldehyde (**151c**, 24 µL, 22.4 mg, 0.2 mmol, 2.0 equiv). The crude alcohol was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1). Both diastereoisomers of the alcohol were then dissolved in DCM (1 mL) and oxidized with DMP[118] (212 mg, 0.15 mmol, 1.5 equiv). The reaction was stirred for 10 min at ambient temperature before quenching with sat. aq. NH_4Cl and extracted with Et_2O (3 × 50 mL). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1) to afford (*R*)-**152g** (17.7 mg, 0.068 mmol, 68%, 90% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.07–7.02 (m, 2H), 6.82–6.77 (m, 2H), 3.78 (s, 3H), 2.98–2.84 (m, 2H), 2.51–2.42 (m, 1H), 2.35–2.18 (m, 1H), 1.78–1.66 (m, 3H), 1.35–1.08 (m, 7H), 1.06–1.02 (m, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 217.5, 158.1, 132.3, 130.1, 113.8, 55.4, 50.7, 46.9, 38.6, 28.4, 28.1, 26.0, 25.8, 25.8, 17.1.z

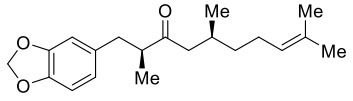
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3411 (vw), 2929 (m), 2855 (w), 1708 (vs), 1612 (w), 1584 (vw), 1512 (s), 1449 (m), 1420 (w), 1361 (s), 1300 (w), 1246 (s), 1220 (s), 1178 (m), 1144 (w), 1107 (w), 1091 (w), 1035 (m), 992 (m), 892 (vw), 833 (w), 824 (w), 809 (w), 754 (vw).

MS (70 eV, EI): m/z (%): 177 (15), 121 (100), 83 (14).

HRMS (EI) for $C_{17}H_{24}O_2$: calc. $[M]^{+\bullet}$: 260.1776, found: 260.1771.

$[\alpha]_D^{20}$: +59.2 (c = 0.76, $CHCl_3$).

(2*S*,5*S*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-2,5,9-trimethyldec-8-en-3-one (2*S*,5*S*-152h):



(2*S*,5*S*)-**152h**

The ketone (2*S*,5*S*)-**152h** was prepared according to **TP8** from the iodide (*S*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and (*S*)-(−)-citronellal (**6d**, 30.9 mg, 0.2 mmol, 2.0 equiv). The crude alcohol was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1). Both diastereoisomers

of the alcohol were then dissolved in DCM (1 mL) and oxidized with DMP[118] (212 mg, 0.15 mmol, 1.5 equiv). The reaction was stirred for 10 min at ambient temperature before quenching with sat. aq. NH_4Cl and extracted with Et_2O (3 × 50 mL). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1) to afford (2*S*,5*S*)-**152h** (24.0 mg, 0.076 mmol, 76%, dr = 95:5) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.71 (d, *J* = 7.9 Hz, 1H), 6.63 (d, *J* = 1.7 Hz, 1H), 6.59 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.91 (q, *J* = 1.4 Hz, 2H), 5.10–5.02 (m, 1H), 2.89 (dd, *J* = 13.5, 7.2 Hz, 1H), 2.75 (h, *J* = 7.0 Hz, 1H), 2.46 (dd, *J* = 13.5, 7.3 Hz, 1H), 2.24 (qd, *J* = 16.4, 6.8 Hz, 2H), 1.93 (tq, *J* = 15.0, 7.1 Hz, 3H), 1.68 (d, *J* = 1.5 Hz, 3H), 1.58 (d, *J* = 1.3 Hz, 3H), 1.27–1.06 (m, 2H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 214.0, 147.7, 146.0, 133.8, 131.6, 124.5, 122.1, 109.5, 108.3, 101.0, 49.7, 48.7, 38.8, 37.1, 28.6, 25.8, 25.6, 19.9, 17.8, 16.5.

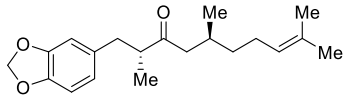
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2923 (m), 2873 (w), 2854 (w), 1709 (m), 1504 (m), 1489 (s), 1455 (m), 1442 (s), 1402 (w), 1375 (m), 1245 (vs), 1189 (m), 1121 (w), 1099 (w), 1039 (vs), 985 (w), 930 (m), 858 (w), 810 (m), 771 (w).

MS (70 eV, EI): m/z (%): 147 (8), 135 (100), 105 (9), 79 (17), 77 (14).

HRMS (EI) for $C_{20}H_{28}O_3$: calc. $[M]^{+\bullet}$: 316.2038, found: 316.2032.

$[\alpha]_D^{20}$: +27.7 (c = 0.9, $CHCl_3$).

(2*R*,5*S*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-2,5,9-trimethyldec-8-en-3-one (2*R*,5*S*-152h):



(2*R*,5*S*)-**152h**

The ketone (2*R*,5*S*)-**152h** was prepared according to **TP8** from the iodide (*R*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and (*S*)-(−)-citronellal (**151d**, 30.9 mg, 0.2 mmol, 2.0 equiv). The crude alcohol was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1). Both diastereoisomers of the alcohol were then dissolved in DCM (1 mL) and oxidized with DMP (212 mg, 0.15 mmol, 1.5 equiv). The reaction was stirred for 10 min at ambient temperature before quenching with sat. aq. NH_4Cl and extracted with Et_2O (3 × 50 mL). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1) to afford (2*R*,5*S*)-**152h** (23.4 mg, 0.074 mmol, 74%, dr = 5:95) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.71 (d, *J* = 7.9 Hz, 1H), 6.64 (d, *J* = 1.7 Hz, 1H), 6.59 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.93–5.90 (m, 2H), 5.09–5.02 (m, 1H), 2.88 (dd, *J* = 13.5, 7.2 Hz, 1H), 2.75 (h, *J* =

7.0 Hz, 1H), 2.49–2.42 (m, 1H), 2.37 (dd, *J* = 16.4, 5.6 Hz, 1H), 2.12 (dd, *J* = 16.4, 7.9 Hz, 1H), 2.03–1.84 (m, 3H), 1.69–1.64 (m, 3H), 1.60–1.57 (m, 3H), 1.24–1.07 (m, 2H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 214.2, 147.7, 146.0, 133.7, 131.6, 124.5, 122.1, 109.5, 108.3, 101.0, 49.8, 48.7, 38.9, 37.1, 28.6, 25.9, 25.6, 19.9, 17.8, 16.5.

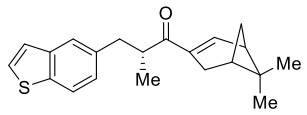
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3402 (w), 2923 (m), 2873 (m), 2854 (m), 1709 (m), 1504 (m), 1489 (s), 1456 (m), 1442 (s), 1402 (w), 1375 (m), 1245 (vs), 1190 (m), 1121 (w), 1099 (w), 1039 (s), 930 (m), 858 (w), 810 (m), 770 (w), 724 (vw).

MS (70 eV, EI): m/z (%): 147 (7), 135 (100), 105 (9), 79 (16), 77 (13).

HRMS (EI) for $C_{20}H_{28}O_3$: calc. $[M]^{+\bullet}$: 316.2038, found: 316.2034.

$[\alpha]_D^{20}$: −27.7 (c = 0.6, $CHCl_3$).

(*R*)-3-(Benzo[*b*]thiophen-5-yl)-1-((1*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-en-3-yl)-2-methylpropan-1-one (*R*,*R*,*S*-152i):



(*R*,*R*,*S*)-**152i**

The ketone (*R*,*R*,*S*)-**152i** was prepared according to **TP8** from the iodide (*R*)-**142l** (30.2 mg, 0.1 mmol, 1.0 equiv) and (1*R*)-(−)-myrtenal (**151e**, 31 µL, 30.9 mg, 0.2 mmol, 2.0 equiv). The crude alcohol was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1). Both diastereoisomers of the alcohol were then dissolved in DCM (1 mL) and oxidized with DMP[118] (212 mg, 0.15 mmol, 1.5 equiv). The reaction was stirred for 10 min at ambient temperature before quenching with sat. aq. NH_4Cl and extracted with Et_2O (3 × 50 mL). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1) to afford (*R*,*R*,*S*)-**152i** (14.9 mg, 0.046 mmol, 46%, dr = 95:5) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.75 (dt, *J* = 8.3, 0.8 Hz, 1H), 7.56 (d, *J* = 1.7 Hz, 1H), 7.39 (d, *J* = 5.4 Hz, 1H), 7.24 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.14 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.65 (tt, *J* = 3.3, 1.5 Hz, 1H), 3.54 (q, *J* = 7.0 Hz, 1H), 3.11 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.92 (td, *J* = 5.7, 1.6 Hz, 1H), 2.72 (dd, *J* = 13.6, 7.0 Hz, 1H), 2.49–2.25 (m, 3H), 2.09–2.04 (m, 1H), 1.27 (s, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 9.1 Hz, 1H), 0.44 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 202.8, 148.8, 140.0, 137.7, 136.8, 136.4, 126.6, 125.8, 123.9, 123.8, 122.3, 41.3, 40.3, 40.2, 39.7, 37.4, 32.7, 31.1, 25.9, 20.6, 18.1.

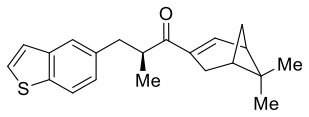
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2922 (vs), 2869 (m), 2854 (m), 1726 (w), 1657 (vs), 1612 (m), 1585 (w), 1456 (m), 1436 (m), 1421 (m), 1380 (m), 1367 (m), 1327 (w), 1309 (w), 1278 (w), 1264 (m), 1247 (m), 1230 (m), 1208 (w), 1196 (w), 1185 (w), 1175 (w), 1161 (w), 1136 (m), 1102 (w), 1090 (m), 1073 (w), 1049 (m), 1016 (w), 975 (w), 959 (w), 946 (w), 935 (w), 890 (m), 846 (w), 832 (m), 806 (m), 781 (w), 768 (w), 754 (m), 743 (m), 718 (w), 700 (s), 693 (s).

MS (70 eV, EI): m/z (%): 281 (15), 161 (24), 147 (100), 119 (20), 91 (25), 57 (31).

HRMS (EI) for $C_{21}H_{24}OS$: calc. $[M]^{+\bullet}$: 324.1548, found: 324.1553.

[α]$_D^{20}$: −45.9 (c = 0.88, $CHCl_3$).

(*S*)-3-(Benzo[*b*]thiophen-5-yl)-1-((1*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-en-3-yl)-2-methylpropan-1-one (*S*,*R*,*S*-152i):



(*S*,*R*,*S*)-**152i**

The ketone (*S*,*R*,*S*)-**152i** was prepared according to **TP8** from the iodide (*S*)-**142l** (30.2 mg, 0.1 mmol, 1.0 equiv) and (1*R*)-(−)-myrtenal (**151e**, 31 µL, 30.9 mg, 0.2 mmol, 2.0 equiv). The crude alcohol was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1). Both diastereoisomers of the alcohol were then dissolved in DCM (1 mL) and oxidized with DMP[118] (212 mg, 0.15 mmol, 1.5 equiv). The reaction was stirred for 10 min at ambient temperature before quenching with sat. aq. NH_4Cl and extracted with Et_2O (3 × 50 mL). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1) to afford (*S*,*R*,*S*)-**152i** (15.9 mg, 0.049 mmol, 49%, dr = 3:97) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.76 (dt, *J* = 8.3, 0.8 Hz, 1H), 7.58 (d, *J* = 1.7 Hz, 1H), 7.41 (d, *J* = 5.5 Hz, 1H), 7.28–7.25 (m, 1H), 7.15 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.67–6.62 (m, 1H), 3.50 (h, *J* = 7.0 Hz, 1H), 3.10 (dd, *J* = 13.5, 7.0 Hz, 1H), 2.91 (td, *J* = 5.7, 1.6 Hz, 1H), 2.72 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.39–2.32 (m, 3H), 2.11–2.03 (m, 1H), 1.30 (s, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.80 (d, *J* = 9.1 Hz, 1H), 0.71 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 202.8, 148.7, 140.0, 137.7, 136.6, 136.5, 126.6, 125.9, 124.0, 123.8, 122.3, 41.6, 40.3, 40.1, 39.8, 37.5, 32.6, 31.1, 26.0, 20.9, 18.1.

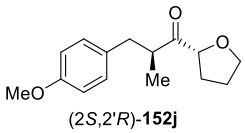
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2971 (w), 2924 (w), 1655 (m), 1612 (w), 1456 (w), 1436 (w), 1421 (w), 1381 (w), 1367 (w), 1327 (vw), 1310 (w), 1278 (w), 1264 (w), 1229 (w), 1220 (w), 1175 (w), 1160 (w), 1137 (w), 1102 (w), 1089 (w), 1048 (w), 975 (w), 959 (w), 945 (w), 936 (w), 890 (w), 832 (w), 807 (w), 751 (vs), 721 (w), 700 (m), 692 (m), 666 (w).

MS (70 eV, EI): m/z (%): 281 (30), 147 (100), 91 (16).

HRMS (EI) for $C_{21}H_{24}OS$: calc. $[M]^{+\bullet}$: 324.1548, found: 324.1539.

$[\alpha]_D^{20}$: +63.3 (c = 1.21, $CHCl_3$).

(*S*)-3-(4-Methoxyphenyl)-2-methyl-1-((*R*)-tetrahydrofuran-2-yl)propan-1-one (2*S*,2'*R*-152j):



(2*S*,2'*R*)-**152j**

The ketone (2*S*,2*'R*)-**152j** was prepared according to **TP8** from the iodide (*S*)-**142f** (27.6 mg, 0.1 mmol, 1.0 equiv) and (*R*)-tetrahydrofuran-2-carbonyl chloride (**151f**, 26.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (2:1) to afford (2*S*,2*'R*)-**152j** (22.1 mg, 0.089 mmol, 89%, dr = 11:89) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.09–7.05 (m, 2H), 6.82–6.78 (m, 2H), 4.35–4.30 (m, 1H), 3.95–3.84 (m, 2H), 3.77 (s, 3H), 3.13–3.08 (m, 1H), 3.00 (dd, *J* = 13.3, 7.3 Hz, 1H), 2.47 (dd, *J* = 13.4, 7.1 Hz, 1H), 2.02–1.97 (m, 1H), 1.84–1.72 (m, 2H), 1.65–1.59 (m, 1H), 1.16–1.12 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 214.8, 158.2, 132.1, 130.2, 113.9, 82.9, 69.5, 55.4, 44.6, 38.1, 28.4, 25.5, 16.7.

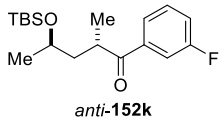
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2974 (m), 2934 (m), 2930 (m), 2916 (m), 2867 (m), 2858 (m), 2851 (m), 2178 (w), 1727 (m), 1723 (m), 1712 (m), 1612 (m), 1512 (s), 1461 (m), 1442 (m), 1380 (m), 1350 (w), 1300 (m), 1246 (vs), 1176 (m), 1152 (m), 1116 (vs), 1073 (m), 1035 (s), 933 (w), 843 (m), 833 (m), 830 (m), 816 (m), 809 (m), 803 (m).

MS (70 eV, EI): m/z (%): 147 (9), 127 89), 121 (100), 115 (7), 91 (28), 77 (19), 71 (90).

HRMS (EI) for $C_{15}H_{20}O_3$: calc. $[M]^{+\bullet}$:248.1412, found: 248.1406.

$[\alpha]_D^{20}$: +33.2 (c = 0.47, $CHCl_3$).

***anti*-4-((*tert*-Butyldimethylsilyl)oxy)-1-(3-fluorophenyl)-2-methylpentan-1-one (*anti*-152k):**



anti-**152k**

The ketone *anti*-**152k** was prepared according to **TP8** from the iodide *anti*-**142b** (32.8 mg, 0.1 mmol, 1.0 equiv) and 3-fluorobenzoyl chloride (**151g**, 31.7 mg, 0.2 mmol, 2.0 equiv). The crude product was

purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (10:1) to afford *anti*-**152k** (15.4 mg, 0.052 mmol, 52%, dr = 5:95) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.76–7.74 (m, 1H), 7.67–7.63 (m, 1H), 7.47–7.41 (m, 1H), 7.28–7.23 (m, 1H), 3.84–3.78 (m, 1H), 3.66–3.69 (m, 1H), 2.11–2.04 (m, 1H), 1.51–1.45 (m, 1H), 1.17 (d, *J* = 6.1 Hz, 3H), 0.81 (s, 9H), -0.0 (s, 3H), -0.2 (s, 3H).

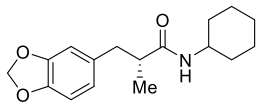
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 202.9, 130.4, 130.3, 124.3, 120.1, 119.9, 115.4, 115.2, 66.9, 43.1, 37.5, 26.0, 24.4, 19.2, 18.1, -4.1, -4.8.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2954 (m), 2927 (s), 2855 (m), 1716 (w), 1689 (m), 1588 (m), 1484 (w), 1471 (m), 1461 (m), 1441 (m), 1373 (w), 1361 (m), 1254 (vs), 1225 (m), 1166 (w), 1146 (m), 1124 (m), 1085 (m), 1044 (s), 1023 (m), 1006 (m), 989 (m), 971 (m), 938 (w), 888 (w), 835 (vs), 824 (s), 805 (s), 774 (vs), 747 (s), 700 (w), 674 (m).

MS (70 eV, EI): m/z (%): 267 (27), 175 (38), 123 (53), 75 (100).

HRMS (EI) for $C_{18}H_{29}FO_2Si$: calc. $[M\text{-}Me]^{+\bullet}$:309.1686, found: 309.1682.

(*R*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-*N*-cyclohexyl-2-methylpropanamide (*R*-152l):



(*R*)-**152l**

The amide (*R*)-**152l** was prepared according to **TP8** from the iodide (*R*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and cyclohexylisocyanate (**151h**, 26 µL, 25.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (*R*)-**152l** (23.2 mg, 0.080 mmol, 80%, 94% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.71 (d, *J* = 7.9 Hz, 1H), 6.66 (d, *J* = 1.7 Hz, 1H), 6.61 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.93–5.88 (m, 2H), 5.04 (d, *J* = 8.3 Hz, 1H), 3.76–3.64 (m, 1H), 2.84 (dd, *J* = 13.5, 8.7 Hz, 1H), 2.58 (dd, *J* = 13.5, 6.1 Hz, 1H), 2.35–2.23 (m, 1H), 1.87–1.78 (m, 1H), 1.77–1.66 (m, 2H), 1.67–1.50 (m, 2H), 1.39–1.23 (m, 2H), 1.15 (d, *J* = 6.7 Hz, 3H), 1.12–0.83 (m, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 174.5, 147.6, 146.0, 133.9, 122.0, 109.5, 108.2, 100.9, 47.9, 44.4, 40.5, 33.2, 25.6, 24.9, 24.9, 17.8.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3285 (m), 2961 (w), 2960 (w), 2958 (w), 2934 (m), 2923 (m), 2873 (w), 2851 (w), 1636 (s), 1539 (m), 1537 (m), 1504 (s), 1483 (s), 1459 (w), 1457 (w), 1445 (m), 1436 (m), 1419 (w), 1401 (w), 1399 (w), 1395 (vw), 1380 (w), 1366 (w), 1349 (w), 1312 (w), 1273 (vw), 1260 (w), 1243 (vs), 1231 (m), 1200 (m), 1185 (m), 1152 (w), 1124 (w), 1100 (m), 1088 (w), 1073 (vw), 1062 (w),

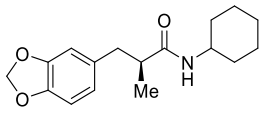
1051 (m), 1041 (m), 974 (w), 939 (m), 928 (s), 912 (w), 903 (vw), 892 (m), 883 (m), 875 (m), 849 (vw), 816 (m), 806 (m), 792 (w), 781 (w), 770 (w), 728 (m), 718 (m), 696 (w), 694 (w), 684 (m), 668 (w).

MS (70 eV, EI): m/z (%): 289 (18), 175 (17), 162 (42), 135 (100).

HRMS (EI) for $C_{17}H_{23}NO_3$: calc. $[M]^{+\bullet}$: 289.1678, found: 289.1673.

$[\alpha]_D^{20}$: +52.2 (c = 0.96, $CHCl_3$).

(*S*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-*N*-cyclohexyl-2-methylpropanamide (*S*-152l):



(*S*)-**152l**

The amide (*S*)-**152l** was prepared according to **TP8** from the iodide (*S*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and cyclohexylisocyanate (**151h**, 26 µL, 25.0 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (*S*)-**152l** (23.4 mg, 0.081 mmol, 81%, 94% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.71 (d, *J* = 7.9 Hz, 1H), 6.66 (d, *J* = 1.7 Hz, 1H), 6.61 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.93–5.89 (m, 2H), 5.02 (d, *J* = 8.3 Hz, 1H), 3.70 (tdt, *J* = 10.6, 8.1, 3.9 Hz, 1H), 2.84 (dd, *J* = 13.5, 8.8 Hz, 1H), 2.58 (dd, *J* = 13.6, 6.1 Hz, 1H), 2.28 (dp, *J* = 8.7, 6.7 Hz, 1H), 1.87–1.79 (m, 1H), 1.75–1.60 (m, 2H), 1.58 (s, 2H), 1.41–1.23 (m, 2H), 1.13–0.80 (m, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 174.5, 147.6, 146.0, 133.9, 122.0, 109.5, 108.3, 100.9, 47.9, 44.5, 40.5, 33.2, 25.6, 24.9, 24.9, 17.8.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3285 (m), 2933 (m), 2923 (m), 2851 (w), 1636 (s), 1609 (w), 1542 (m), 1539 (m), 1536 (m), 1534 (m), 1518 (w), 1512 (w), 1504 (s), 1483 (s), 1469 (w), 1465 (w), 1459 (w), 1457 (w), 1445 (m), 1437 (m), 1380 (w), 1366 (w), 1312 (w), 1260 (w), 1244 (vs), 1231 (m), 1200 (m), 1185 (m), 1152 (w), 1124 (w), 1101 (m), 1062 (w), 1052 (m), 1041 (m), 974 (w), 939 (m), 928 (m), 912 (w), 892 (m), 883 (m), 875 (m), 816 (m), 805 (m), 792 (w), 781 (w), 771 (w), 728 (w), 718 (m), 684 (m).

MS (70 eV, EI): m/z (%): 289 (16), 175 (13), 162 (40), 135 (100).

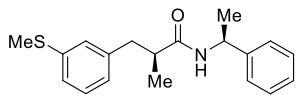
HRMS (EI) for $C_{17}H_{23}NO_3$: calc. $[M]^{+\bullet}$: 289.1678, found: 289.1672.

$[\alpha]_D^{20}$: −50.5 (c = 0.84, $CHCl_3$).

A solution of alkyl iodide (*S*-**142k**, 0.08 M, 1.00 equiv) and cyclohexyl isocyanate (**151h**, 0.20 M, 2.50 equiv) in hexane:Et_2O (2:1) and a solution of *t*-BuLi (ca. 0.20 M in hexane, 2.85 equiv) were prepared. The solution of *t*-BuLi was pumped by pump A (flow rate A: 5.7 mL/min) into a precooling

loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The solution of the alkyl iodide was pumped by pump B (flow rate B: 5.0 mL/min) into a second precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The precooled solutions were mixed in a T-shaped mixer and passed within a residence time of (t^1 = 5.5 to 5.6 s) through a coil reactor (V_R = 1.0 mL) at the corresponding temperature (T^1 = –20 to 25 °C). The stream was subsequently upon reaching steady state injected for 2 min 30 s into a flask charged with sat. aq. NH_4Cl. The aqueous phase was extracted Et_2O (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was removed under reduced pressure and the remaining crude product was purified by flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152l** (204 mg, 0.71 mmol, 71%, 96% *ee*) as white solid.

(*S*)-2-Methyl-3-(3-(methylthio)phenyl)-*N*-((*S*)-1-phenylethyl)propanamide (3*S*,2'*S*-152m):



(3*S*,2'*S*)-**152m**

The amide (3*S*,2'*S*)-**152m** was prepared according to **TP8** from the iodide (*S*)-**142g** (29.2 mg, 0.1 mmol, 1.0 equiv) and (*S*)-(−)-α-methylbenzyl isocyanate (*S*-**151i**, 28 µL, 29.4 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (3*S*,2'*S*)-**152m** (22.3 mg, 0.071 mmol, 71%, dr = 96:4) as a colorless oil.

A scale-up of this reaction on 0.5 mmol scale was performed while doubling the amount of solvent used for the reaction (from 0.083 M to 0.42 M). Thus, the iodide (*S*)-**142g** (146.1 mg, 0.5 mmol, 91% *ee*, 1.0 equiv) was dissolved in pentane (7.4 mL) and diethyl ether (3.3 mL) before addition of Me_3SiCH_2MgCl (1 M, 0.75 mL, 0.75 mmol, 1.5 equiv). The reaction mixture was cooled to −78 °C and *t*-BuLi (2.2 equiv) was slowly added dropwise over two minutes. The resulting optically enriched secondaryl alkylmagnesium reagent was quenched with (*S*)-(−)-α-methylbenzyl isocyanate (*S*-**151i**, 141 µL, 147 mg, 1.0 mmol, 2.0 equiv). After work-up according to the typical procedure, the crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (3*S*,2'*S*)-**152m** (100.3 mg, 0.032 mmol, 63%, dr = 92:8) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.29–7.26 (m, 1H), 7.25–7.18 (m, 2H), 7.15–7.06 (m, 2H), 7.03 (dtd, *J* = 8.0, 1.5, 0.6 Hz, 3H), 6.88 (dt, *J* = 7.1, 1.6 Hz, 1H), 5.47 (d, *J* = 8.0 Hz, 1H), 5.12–5.01 (m, 1H), 2.92 (dd, *J* = 13.4, 8.8 Hz, 1H), 2.64 (dd, *J* = 13.4, 6.0 Hz, 1H), 2.50–2.38 (m, 4H), 1.43 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 174.5, 143.0, 140.7, 138.6, 129.0, 128.7, 127.3, 127.1, 126.2, 125.9, 124.5, 48.4, 44.1, 40.5, 21.7, 18.1, 15.8.

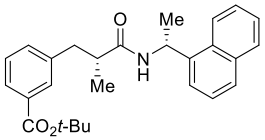
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3298 (m), 3061 (w), 3030 (w), 2966 (w), 2923 (m), 2870 (w), 2854 (w), 1639 (vs), 1591 (m), 1571 (w), 1536 (s), 1494 (m), 1474 (m), 1448 (m), 1420 (m), 1376 (m), 1281 (w), 1242 (m), 1210 (m), 1182 (w), 1169 (w), 1131 (w), 1098 (w), 1089 (m), 1076 (w), 1031 (w), 1016 (m), 966 (w), 949 (w), 905 (w), 880 (w), 854 (vw), 782 (m), 774 (m), 761 (m), 746 (w), 697 (vs).

MS (70 eV, EI): m/z (%): 313 (27), 176 (38), 165 (24), 137 (64), 120 (62) 117 (60), 105 (100), 91 (61), 79 (30).

HRMS (EI) for $C_{19}H_{23}ONS$: calc. $[M]^{+\bullet}$: 313.1500, found: 313.1495.

[α]$_D^{20}$: −3.1 (c = 1.39, $CHCl_3$).

***tert*-Butyl 3-((*R*)-2-methyl-3-(((*R*)-1-(naphthalen-1-yl)ethyl)amino)-3-oxopropyl)benzoate (3*R*,2'*R*-152n):**



(3*R*,2'*R*)-**152n**

The amide (3*R*,2'*R*)-**152n** was prepared according to **TP8** from the iodide (*R*)-**142i** (34.6 mg, 0.1 mmol, 1.0 equiv) and (*R*)-(−)-1-(1-naphthyl)ethyl isocyanate (*R*-**151j**, 35 µL, 39.5 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (3*R*,2'*R*)-**152n** (22.1 mg, 0.053 mmol, 53%, dr = 97:3) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.98–7.92 (m, 1H), 7.86–7.81 (m, 1H), 7.77–7.71 (m, 3H), 7.50–7.41 (m, 2H), 7.35 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.23–7.18 (m, 2H), 7.10 (td, *J* = 7.6, 0.8 Hz, 1H), 5.85 (p, *J* = 6.9 Hz, 1H), 5.56 (d, *J* = 8.0 Hz, 1H), 2.98 (dd, *J* = 13.6, 8.2 Hz, 1H), 2.70 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.52–2.41 (m, 1H), 1.60 (d, *J* = 6.8 Hz, 3H), 1.57 (s, 9H), 1.19 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 174.3, 166.0, 139.9, 138.3, 134.0, 133.5, 132.1, 131.1, 129.8, 128.8, 128.3, 128.3, 127.5, 126.6, 125.9, 125.3, 123.5, 122.5, 81.1, 44.6, 43.7, 40.0, 28.3, 20.9, 18.0.

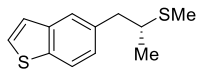
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3298 (vw), 3051 (vw), 2975 (w), 2930 (w), 2361 (vw), 1710 (m), 1641 (m), 1600 (w), 1588 (w), 1537 (m), 1511 (w), 1477 (w), 1450 (w), 1393 (w), 1368 (m), 1294 (m), 1256 (w), 1215 (w), 1160 (s), 1111 (m), 1085 (w), 1034 (vw), 1000 (vw), 932 (vw), 850 (w), 799 (w), 777 (m), 748 (vs), 696 (w), 666 (w).

MS (70 eV, EI): m/z (%): 361 (31), 170 (100), 155 (75), 135 (22).

HRMS (EI) for $C_{27}H_{31}NO_3$: calc. $[M]^{+\bullet}$: 417.2304, found: 417.2291

[α]$_D^{20}$: −19.1 (c = 1.45, $CHCl_3$).

(*R*)-5-(2-(methylthio)propyl)benzo[*b*]thiophene (*R*-152o):



(*R*)-**152o**

The thioether (*R*)-**152o** was prepared according to **TP8** from the iodide (*R*)-**142l** (30.2 mg, 0.1 mmol, 1.0 equiv) and *S*-Methyl methanethiosulfonate (**151k**, 25.2 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1) to afford (*R*)-**152o** (17.6 mg, 0.79 mmol, 79%, 71% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.80 (dt, *J* = 8.3, 0.8 Hz, 1H), 7.64 (dd, *J* = 1.6, 0.7 Hz, 1H), 7.43 (dd, *J* = 5.5, 0.5 Hz, 1H), 7.29 (dd, *J* = 5.5, 0.8 Hz, 1H), 7.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.10 (dd, *J* = 13.4, 5.9 Hz, 1H), 3.01–2.92 (m, 1H), 2.79 (dd, *J* = 13.4, 8.3 Hz, 1H), 2.12 (s, 3H), 1.26 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 138.0, 135.8, 126.8, 126.0, 124.1, 123.8, 122.4, 43.3, 43.2, 20.4, 13.9.

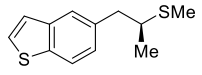
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2958 (m), 2918 (m), 2853 (w), 1436 (m), 1421 (m), 1373 (w), 1318 (w), 1261 (w), 1222 (w), 1186 (w), 1160 (w), 1145 (w), 1089 (m), 1067 (w), 1050 (m), 1019 (w), 953 (w), 891 (m), 832 (m), 808 (s), 769 (m), 754 (s), 731 (m), 713 (m), 703 (s), 690 (vs).

MS (70 eV, EI): m/z (%): 222 (48), 174 (13), 147 (100), 121 (9), 115 (9), 75 (74)

HRMS (EI) for $C_{12}H_{14}S_2$: calc. $[M]^{+\bullet}$: 222.0537, found: 222.0529

$[\alpha]_D^{20}$: −3.4 (c = 0.68, $CHCl_3$).

(*S*)-5-(2-(methylthio)propyl)benzo[*b*]thiophene (*S*-152o):



(*S*)-**152o**

The thioether (*S*)-**152o** was prepared according to **TP8** from the iodide (*S*)-**142l** (30.2 mg, 0.1 mmol, 1.0 equiv) and *S*-Methyl methanethiosulfonate (**151k**, 25.2 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (9:1) to afford (*S*)-**152o** (18.9 mg, 0.085 mmol, 85%, 78% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.81 (d, *J* = 8.3 Hz, 1H), 7.64 (d, *J* = 1.7 Hz, 1H), 7.43 (d, *J* = 5.4 Hz, 1H), 7.30 (dd, *J* = 5.5, 0.8 Hz, 1H), 7.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.10 (dd, *J* = 13.4, 5.9 Hz, 1H), 3.01–2.92 (m, 1H), 2.79 (dd, *J* = 13.4, 8.3 Hz, 1H), 2.12 (s, 3H), 1.26 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 138.0, 135.8, 126.8, 126.0, 124.1, 123.8, 122.4, 43.3, 43.2, 20.4, 13.9.

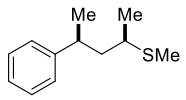
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2968 (s), 2916 (s), 2362 (s), 2360 (s), 2358 (s), 2357 (s), 2354 (s), 2172 (s), 2169 (vs), 2164 (vs), 2160 (s), 2151 (s), 1445 (s), 1440 (s), 1436 (s), 1422 (s), 1379 (s), 1366 (s), 1198 (s), 1153 (s), 1089 (s), 1050 (s), 946 (m), 825 (m), 804 (s), 722 (vs).

MS (70 eV, EI): m/z (%): 222 (37), 174 (13), 147 (100), 121 (11), 115 (11), 75 (57)

HRMS (EI) for $C_{12}H_{14}S_2$: calc. $[M]^{+\bullet}$: 222.0537, found: 222.0529

$[\alpha]_D^{20}$: +4.4 (c = 0.67, $CHCl_3$).

Methyl(*syn*-4-phenylpentan-2-yl)sulfane (*syn*-152p):



syn-**152p**

The thioether *syn*-**152p** was prepared according to **TP8** from the iodide *syn*-**142a** (27.4 mg, 0.1 mmol, 1.0 equiv) and *S*-Methyl methanethiosulfonate (**151k**, 25.2 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (20:1) to afford *syn*-**152p** (12.1 mg, 0.062 mmol, 62%, dr = 93:7) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.33–7.28 (m, 2H), 7.20 (dtd, *J* = 7.1, 3.8, 2.0 Hz, 3H), 2.92 (dp, *J* = 9.0, 6.8 Hz, 1H), 2.48 (dq, *J* = 8.5, 6.5 Hz, 1H), 2.01 (s, 3H), 1.97–1.90 (m, 1H), 1.68–1.61 (m, 1H), 1.26 (dd, *J* = 6.8, 1.8 Hz, 6H).

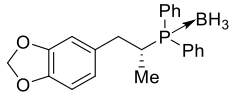
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 146.8, 128.6, 127.1, 126.2, 45.0, 38.7, 37.5, 22.8, 20.6, 12.9.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3086 (vw), 2975 (m), 2932 (w), 2861 (m), 2369 (vw), 1611 (w), 1511 (s), 1464 (w), 1444 (w), 1381 (m), 1350 (w), 1299 (w), 1246 (s), 1176 (m), 1151 (m), 1117 (vs), 1075 (m), 1038 (m), 1023 (m), 997 (m), 977 (m), 929 (w), 914 (w), 844 (m), 833 (m), 806 (m), 758 (w), 668 (w).

MS (70 eV, EI): m/z (%): 194 (13). 143 (19), 131 (100), 105 (21), 91 (11).

HRMS (EI) for $C_{12}H_{18}S$: calc. $[M]^{+\bullet}$: 194.1129, found: 194.1124.

(*R*)-(1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)diphenylphosphane (*R*-152q):



(*R*)-**152q**

The BH_3-phosphine complex (*R*)-**152q** was prepared according to **TP8** from the iodide (*R*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and chlorodiphenylphosphine (**151l**, 36 µL, 44.2 mg, 0.2 mmol, 2.0 equiv). After stirring the reaction mixture at −20 °C for 30 minutes, $BH_3{\cdot}SMe_2$ (2.0 M in THF, 0.15 mL, 3.0 equiv) was added and the reaction was further stirred at 0 °C for 1 h. The reaction was quenched with sat. aq. NH_4Cl and extracted with Et_2O (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (*R*)-**152q** (25.4 mg, 0.070 mmol, 70%, 90% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.90–7.74 (m, 4H), 7.56–7.40 (m, 6H), 6.70 (d, *J* = 7.8 Hz, 1H), 6.60–6.53 (m, 2H), 5.92 (s, 2H), 2.88–2.78 (m, 1H), 2.78–2.66 (m, 1H), 2.52–2.41 (m, 1H), 1.04 (dd, *J* = 16.3, 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.8, 146.2, 133.5 (*J* = 14.3 Hz), 132.7 (*J* = 3.3 Hz), 131.4 (*J* = 3.8 Hz), 129.0 (*J* = 10.2 Hz), 128.4 (*J* = 3.5 Hz), 122.1, 109.3, 108.3, 101.04 36.6 (*J* = 4.2 Hz), 31.4 (*J* = 34.5 Hz), 13.3 (*J* = 2.1 Hz).

^{11}B-NMR ($CDCl_3$, 128 MHz): δ [ppm] = −42.4 (d, *J* = 56.3 Hz).

^{31}P-NMR ($CDCl_3$, 162 MHz): δ [ppm] = 23.7 (d, *J* = 79.0 Hz).

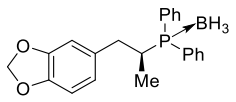
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3058 (vw), 2929 (w), 2892 (w), 2380 (m), 2345 (w), 1608 (vw), 1502 (m), 1488 (s), 1455 (w), 1437 (s), 1378 (w), 1364 (w), 1248 (s), 1218 (w), 1188 (m), 1136 (w), 1106 (m), 1063 (m), 1037 (s), 1008 (w), 1000 (m), 940 (w), 928 (m), 872 (w), 852 (w), 808 (m), 779 (m), 752 (s), 736 (vs), 719 (m), 692 (vs), 667 (m).

MS (70 eV, EI): m/z (%): 347 (100), 213 (89), 183 (81), 162 (72), 135 (51), 109 (70).

HRMS (EI) for $C_{22}H_{21}O_2P$: calc. $[M-H]^{+\bullet}$: 347.1195, found: 347.1196.

$[\alpha]_D^{20}$: −17.3 (c = 1.68, $CHCl_3$).

(*S*)-(1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)diphenylphosphane (*S*-152q):



(*S*)-**152q**

The BH_3-phosphine complex (*S*)-**152q** was prepared according to **TP8** from the iodide (*S*)-**142l** (29.0 mg, 0.1 mmol, 1.0 equiv) and chlorodiphenylphosphine (**151l**, 36 µL, 44.2 mg, 0.2 mmol, 2.0 equiv). After stirring the reaction mixture at −20 °C for 30 minutes, $BH_3{\cdot}SMe_2$ (2.0 M in THF, 0.15 mL, 3.0 equiv) was added and the reaction was further stirred at 0 °C for 1 h. The reaction was

quenched with sat. aq. NH_4Cl and extracted with Et_2O (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (*S*)-**152q** (27.2 mg, 0.075 mmol, 75%, 90% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.89–7.75 (m, 4H), 7.55–7.40 (m, 6H), 6.70 (d, *J* = 7.8 Hz, 1H), 6.60–6.52 (m, 2H), 5.92 (s, 2H), 2.87–2.78 (m, 1H), 2.78–2.66 (m, 1H), 2.52–2.40 (m, 1H), 1.05 (dd, *J* = 16.3, 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.6, 146.1, 133.3 (*J* = 14.3 Hz), 132.6 (*J* = 4.4 Hz), 131.2 (*J* = 3.8 Hz), 128.8 (*J* = 10.1 Hz), 122.0, 109.14, 108.17, 100.87, 36.4 (*J* = 4.3 Hz), 31.2 (*J* = 34.8 Hz), 13.1 (*J* = 2.3 Hz).

^{11}B-NMR ($CDCl_3$, 128 MHz): δ [ppm] = −42.5 (d, *J* = 57.1 Hz).

^{31}P-NMR ($CDCl_3$, 162 MHz): δ [ppm] = 23.8 (d, *J* = 80.2 Hz).

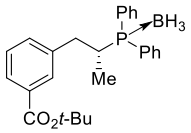
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3355 (vs), 2925 (w), 2384 (w), 2349 (vw), 1643 (m), 1634 (m), 1538 (vw), 1502 (w), 1489 (m), 1454 (w), 1437 (m), 1375 (w), 1365 (w), 1249 (m), 1189 (w), 1106 (w), 1064 (w), 1038 (w), 928 (w), 807 (vw), 778 (w), 736 (w), 718 (w), 692 (m).

MS (70 eV, EI): m/z (%): 347 (100), 213 (73), 183 (52), 162 (55), 135 (39), 109 (47).

HRMS (EI) for $C_{22}H_{21}O_2P$: calc. $[M-H]^{+\bullet}$: 347.1195, found: 347.1194.

$[\alpha]_D^{20}$: +20.7 (c = 1.08, $CHCl_3$).

***tert*-Butyl (*R*)-3-(2-(diphenylphosphaneyl)propyl)benzoate (*R*-152r):**



(*R*)-**152r**

The BH_3-phosphine complex (*R*)-**152r** was prepared according to **TP8** from the iodide (*S*)-**142i** (34.6 mg, 0.1 mmol, 1.0 equiv) and chlorodiphenylphosphine (**6l**, 36 µL, 44.2 mg, 0.2 mmol, 2.0 equiv). After stirring the reaction mixture at −20 °C for 30 minutes, $BH_3{\cdot}SMe_2$ (2.0 M in THF, 0.15 mL, 3.0 equiv) was added and the reaction was further stirred at 0 °C for 1 h. The reaction was quenched with sat. aq. NH_4Cl and extracted with Et_2O (3 × 50 mL). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (*R*)-**152r** (26.4 mg, 0.063 mmol, 63%, 88% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.91–7.84 (m, 2H), 7.84–7.77 (m, 3H), 7.74 (d, *J* = 1.8 Hz, 1H), 7.54–7.42 (m, 6H), 7.34–7.25 (m, 2H), 2.98–2.90 (m, 1H), 2.89–2.74 (m, 1H), 2.67–2.58 (m, 1H), 1.60 (s, 9H), 1.03 (dd, *J* = 16.3, 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 165.7, 139.7 (*J* = 14.2 Hz), 133.3, 132.6 (*J* = 4.2 Hz), 132.2, 131.3 (*J* = 4.3 Hz), 129.6, 128.9 (*J* = 7.5 Hz), 128.6 (*J* = 4.1 Hz), 128.3, 128.1 (*J* = 4.4 Hz), 127.6, 81.1, 36.4 (*J* = 4.4 Hz), 30.8 (*J* = 35.2 Hz), 28.2, 13.1 (*J* = 2.2 Hz).

^{11}B-NMR ($CDCl_3$, 128 MHz): δ [ppm] = −42.5 (d, *J* = 58.4 Hz).

^{31}P-NMR ($CDCl_3$, 162 MHz): δ [ppm] = 24.0 (d, *J* = 71.4 Hz).

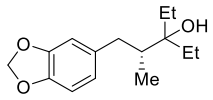
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3060 (vw), 3007 (vw), 2977 (w), 2931 (w), 2384 (w), 1708 (m), 1588 (vw), 1478 (w), 1457 (w), 1437 (m), 1393 (w), 1378 (vw), 1368 (w), 1296 (m), 1256 (w), 1215 (w), 1159 (s), 1107 (m), 1079 (w), 1063 (m), 1029 (vw), 1008 (vw), 1000 (w), 935 (vw), 890 (vw), 849 (w), 812 (vw), 747 (vs), 736 (vs), 692 (s), 667 (m).

MS (70 eV, EI): m/z (%): 404 (100), 347 (81), 213 (74), 186 (47), 109 (51).

HRMS (EI) for $C_{26}H_{29}O_2P$: calc. $[M]^{+\bullet}$: 404.1905, found: 404.1896.

$[\alpha]_D^{20}$: −17.2 (c = 1.37, $CHCl_3$).

(*R*)-1-(benzo[*d*][1,3]dioxol-5-yl)-3-ethyl-2-methylpentan-3-ol (*R*-152s):



(*R*)-**152s**

The alcohol (*R*)-**152s** was prepared according to **TP11** from the iodide (*R*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and pentan-3-one (**151m**, 27 µL, 21.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*R*)-**152s** (15.1 mg, 0.060 mmol, 60%, 93% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.73 (d, *J* = 7.9 Hz, 1H), 6.66 (d, *J* = 1.6 Hz, 1H), 6.61 (dd, *J* = 8.0, 1.7 Hz, 1H), 5.92 (s, 2H), 2.92 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.10 (dd, *J* = 13.2, 11.2 Hz, 1H), 1.80 (m, 1H), 1.67–1.49 (m, 4H), 1.14 (s, 1H), 0.91 (td, *J* = 7.5, 3.0 Hz, 6H), 0.77 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.6, 145.6, 136.1, 122.1, 109.6, 108.1, 100.9, 76.2, 41.9, 37.0, 28.3, 28.2, 13.2, 7.7, 7.6.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2967 (s), 2937 (m), 2893 (m), 2887 (m), 2880 (m), 2358 (w), 2215 (w), 2187 (w), 2170 (w), 2146 (w), 1502 (s), 1490 (vs), 1457 (m), 1446 (m), 1441 (m), 1358 (w), 1245 (vs), 1209 (m),

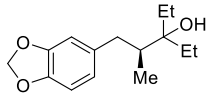
1187 (m), 1123 (w), 1113 (w), 1096 (w), 1076 (w), 1039 (s), 939 (m), 929 (m), 860 (vw), 809 (m), 779 (w).

MS (70 eV, EI): m/z (%): 232 (11), 203 (24), 173 (11), 135 (100), 87 (10).

HRMS (EI) for $C_{15}H_{22}O_3$: calc. $[M]^{+\bullet}$: 250.1569, found: 250.1565.

$[\alpha]_D^{20}$: +12.3 (c = 0.92, $CHCl_3$).

(*S*)-1-(benzo[*d*][1,3]dioxol-5-yl)-3-ethyl-2-methylpentan-3-ol (*S*-152s):



(*S*)-**152s**

The alcohol (*S*)-**152s** was prepared according to **TP11** from the iodide (*S*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and pentan-3-one (**151m**, 27 µL, 21.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica with diethyl ether/pentane = 1:4 to afford (*S*)-**152s** (17.0 mg, 0.068 mmol, 68%, 90% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.73 (d, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 1.7 Hz, 1H), 6.61 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.92 (s, 2H), 2.92 (dd, *J* = 13.3, 2.9 Hz, 1H), 2.10 (dd, *J* = 13.2, 11.3 Hz, 1H), 1.85–1.75 (m, 1H), 1.68–1.50 (m, 4H), 1.12 (s, 1H), 0.91 (td, *J* = 7.5, 3.0 Hz, 6H), 0.77 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): 147.6, 145.6, 136.1, 122.1, 109.6, 108.1, 100.9, 76.2, 41.9, 37.0, 28.3, 28.2, 13.2, 7.8, 7.6.

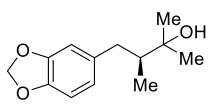
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2968 (s), 2945 (m), 2938 (m), 2930 (m), 2924 (m), 2881 (m), 2217 (m), 2179 (m), 2156 (m), 2129 (m), 1502 (s), 1490 (vs), 1460 (m), 1456 (m), 1447 (m), 1440 (s), 1364 (m), 1245 (vs), 1208 (m), 1187 (m), 1127 (m), 1094 (m), 1039 (s), 940 (s), 929 (m), 817 (m), 806 (m), 765 (w), 722 (m).

MS (70 eV, EI): m/z (%): 232 (15), 203 (41), 173 (20), 135 (100), 77 (7).

HRMS (EI) for $C_{15}H_{22}O_3$: calc. $[M]^{+\bullet}$: 250.1569, found: 250.1563.

$[\alpha]_D^{20}$: −11.8 (c = 0.88, $CHCl_3$).

(*S*)-4-(benzo[*d*][1,3]dioxol-5-yl)-2,3-dimethylbutan-2-ol (*S*-152t):



(*S*)-**152t**

The alcohol (*S*)-**152t** was prepared according to **TP11** from the iodide (*S*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and acetone (**151n**, 18 µL, 14.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152t** (10.0 mg, 0.045 mmol, 45%, 91% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.73 (d, *J* = 7.9 Hz, 1H), 6.67 (d, *J* = 1.7 Hz, 1H), 6.61 (dd, *J* = 8.0, 1.7 Hz, 1H), 5.92 (s, 2H), 3.00 (dd, *J* = 13.3, 3.1 Hz, 1H), 2.06 (dd, *J* = 13.3, 11.1 Hz, 1H), 1.72–1.64 (m, 1H), 1.28 (s, 1H), 1.24 (d, *J* = 5.1 Hz, 6H), 0.81 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.6, 145.7, 135.8, 122.0, 109.6, 108.2, 100.9, 73.4, 46.9, 37.9, 27.9, 26.2, 14.3.

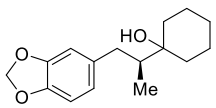
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3380 (w), 2966 (s), 2925 (s), 1503 (s), 1490 (vs), 1462 (m), 1441 (s), 1377 (m), 1372 (m), 1246 (vs), 1189 (m), 1144 (m), 1098 (m), 1040 (s), 942 (m), 931 (m), 808 (m), 778 (w).

MS (70 eV, EI): m/z (%): 222 (6), 204 (13), 189 (22), 159 (24), 135 (100), 122 (9), 77 (18), 59 (14).

HRMS (EI) for $C_{13}H_{18}O_3$: calc. $[M]^{+\bullet}$: 222.1256, found: 222.1250.

$[\alpha]_D^{20}$: + 29.6 (c = 0.92, $CHCl_3$).

(*S*)-1-(1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)cyclohexan-1-ol (*S*-152u):



(*S*)-**152u**

The alcohol (*S*)-**152u** was prepared according to **TP11** from the iodide (*S*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and cyclohexanone (**151o**, 26 µL, 24.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152u** (16.0 mg, 0.061 mmol, 61%, 92% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.72 (d, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 1.6 Hz, 1H), 6.60 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.92 (s, 2H), 3.00 (dd, *J* = 13.2, 3.0 Hz, 1H), 2.08 (dd, *J* = 13.3, 11.1 Hz, 1H), 1.74–1.42 (m, 11H), 1.25 (s, 1H), 0.79 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.6, 145.6, 136.2, 122.1, 109.6, 108.1, 100.8, 73.5, 45.8, 36.9, 35.1, 33.9, 26.0, 22.1, 22.0, 13.2.

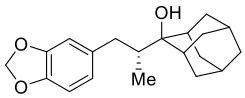
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3463 (vw), 2929 (m), 2860 (m), 1698 (w), 1503 (m), 1489 (vs), 1441 (s), 1381 (w), 1351 (w), 1310 (w), 1244 (vs), 1210 (m), 1187 (m), 1160 (m), 1117 (s), 1038 (vs), 957 (m), 939 (s), 928 (s), 904 (w), 871 (w), 846 (w), 835 (w), 806 (m), 780 (m), 731 (w), 714 (vw).

MS (70 eV, EI): m/z (%): 135 (100), 109 (11), 77 (16).

HRMS (EI) for $C_{16}H_{22}O_3$: calc. $[M]^{+\bullet}$: 262.1569, found: 262.1563.

$[\alpha]_D^{20}$: +11.6 (c = 1.07, $CHCl_3$).

(1*R*,3*S*,5*R*,7*R*)-2-((*R*)-1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)adamantan-2-ol (*R*-152v):



(*R*)-**152v**

The alcohol (*R*)-**152v** was prepared according to **TP11** from the iodide (*R*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and adamantanone (**151p**, 45.0 mg, 0.3 mmol, 3.0 equiv) at −40 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*R*)-**152v** (22.6 mg, 0.072 mmol, 72%, 94% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.73 (d, *J* = 7.8 Hz, 1H), 6.65 (d, *J* = 1.7 Hz, 1H), 6.60 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.92 (t, *J* = 1.3 Hz, 2H), 2.85 (dd, *J* = 13.3, 2.8 Hz, 1H), 2.35–2.23 (m, 1H), 2.20–2.11 (m, 4H), 1.99 (dd, *J* = 12.8, 3.2 Hz, 1H), 1.92 (q, *J* = 2.9 Hz, 1H), 1.85–1.74 (m, 4H), 1.73–1.56 (m, 5H), 1.43 (s, 1H), 0.74 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.5, 145.5, 136.3, 122.2, 109.7, 108.1, 100.8, 76.1, 38.4, 38.0, 35.7, 34.9, 34.2, 34.1, 33.8, 33.3, 33.2, 27.1, 27.1, 11.3.

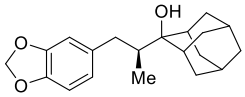
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3533 (w), 3445 (w), 2977 (w), 2914 (s), 2903 (s), 2853 (m), 1503 (m), 1490 (s), 1472 (m), 1452 (m), 1437 (m), 1396 (w), 1376 (w), 1358 (w), 1350 (m), 1329 (w), 1317 (w), 1306 (w), 1244 (s), 1222 (m), 1202 (m), 1186 (s), 1166 (w), 1143 (w), 1135 (m), 1108 (w), 1099 (m), 1082 (m), 1060 (w), 1034 (vs), 976 (s), 927 (vs), 878 (w), 860 (m), 840 (w), 807 (vs), 774 (s), 724 (w), 670 (w).

MS (70 eV, EI): m/z (%): 296 (83), 281 (74), 151 (64), 135 (100), 105 (18), 91 (25), 77 (30).

HRMS (EI) for $C_{20}H_{26}O_3$: calc. $[M]^{+\bullet}$: 314.1882, found: 314.1876.

$[\alpha]_D^{20}$: +28.9 (c = 1.54, $CHCl_3$).

(1*R*,3*S*,5*R*,7*R*)-2-((*S*)-1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)adamantan-2-ol (*S*-152v):

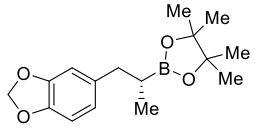


(*S*)-**152v**

A solution of alkyl iodide (*S*-**142k**, 0.08 M, 1.00 equiv) and adamantanone (**151p**, 0.20 M, 2.50 equiv) in hexane:Et_2O (2:1) and a solution of *t*-BuLi (ca. 0.20 M in hexane, 2.85 equiv) were prepared. The

solution of *t*-BuLi was pumped by pump A (flow rate A: 5.7 mL/min) into a precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The solution of the alkyl iodide was pumped by pump B (flow rate B: 5.0 mL/min) into a second precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The precooled solutions were mixed in a T-shaped mixer and passed within a residence time of (t^1 = 5.5 to 5.6 s) through a coil reactor (V_R = 1.0 mL) at the corresponding temperature (T^1 = –20 to 25 °C). The stream was subsequently upon reaching steady state injected for 10 min 30 s into a flask charged with sat. aq. NH_4Cl. The aqueous phase was extracted Et_2O (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was removed under reduced pressure and the remaining crude product was purified by flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152v** (720 mg, 2.3 mmol, 55%, 94% *ee*) as white solid.

(*R*)-2-(1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (*R*-152w):



(*R*)-**152w**

The boronate (*R*)-**152w** was prepared according to **TP11** from the iodide (*R*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and methoxy boronic acid pinacol ester (**151q**, 41 µL, 39.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:9 to afford (*R*)-**152w** (24.1 mg, 0.083 mmol, 83%, 92% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.72–6.68 (m, 2H), 6.64 (dd, *J* = 7.9, 1.5 Hz, 1H), 5.90 (s, 2H), 2.72 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.46 (dd, *J* = 13.6, 8.2 Hz, 1H), 1.35–1.24 (m, 1H), 1.20 (d, *J* = 3.2 Hz, 12H), 0.95 (d, *J* = 7.4 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.4, 145.5, 136.4, 121.8, 109.5, 107.9, 100.7, 83.2, 38.8, 24.9, 24.9, 15.2.

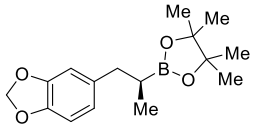
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3373 (w), 2969 (w), 2926 (w), 2883 (w), 1502 (s), 1488 (s), 1440 (s), 1391 (w), 1372 (m), 1346 (w), 1328 (w), 1290 (w), 1243 (vs), 1187 (m), 1169 (w), 1148 (w), 1121 (m), 1098 (m), 1075 (m), 1035 (vs), 937 (s), 927 (s), 864 (w), 852 (w), 838 (w), 803 (s), 777 (w), 771 (w), 757 (w), 672 (w).

MS (70 eV, EI): m/z (%): 290 (23), 162 (14), 135 (100), 84 (7).

HRMS (EI) for $C_{16}H_{23}BO_4$: calc. $[M]^+$: 290.1689, found: 290.1681.

$[\alpha]_D^{20}$: −6.7 (c = 1.04, $CHCl_3$).

(*S*)-2-(1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (*S*-152w):



(*S*)-**152w**

The boronate (*S*)-**152w** was prepared according to **TP11** from the iodide (*S*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and methoxy boronic acid pinacol ester (**151q**, 41 µL, 39.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:9 to afford (*S*)-**152w** (23.2 mg, 0.080 mmol, 80%, 91% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.72–6.67 (m, 2H), 6.64 (dd, *J* = 7.9, 1.6 Hz, 1H), 5.90 (s, 2H), 2.72 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.46 (dd, *J* = 13.6, 8.3 Hz, 1H), 1.34–1.26 (m, 1H), 1.20 (d, *J* = 3.2 Hz, 12H), 0.95 (d, *J* = 7.4 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.4, 145.5, 136.4, 121.8, 109.5, 107.9, 100.7, 83.2, 38.9, 24.9, 24.9, 15.2.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3373 (w), 2969 (w), 2926 (w), 2883 (w), 1502 (s), 1488 (s), 1440 (s), 1391 (w), 1372 (m), 1346 (w), 1328 (w), 1290 (w), 1243 (vs), 1187 (m), 1169 (w), 1148 (w), 1121 (m), 1098 (m), 1075 (m), 1035 (vs), 937 (s), 927 (s), 864 (w), 852 (w), 838 (w), 803 (s), 777 (w), 771 (w), 757 (w), 672 (w).

MS (70 eV, EI): m/z (%): 290 (24), 162 (17), 135 (100), 43 (11).

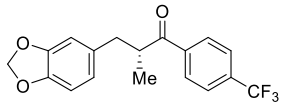
HRMS (EI) for $C_{16}H_{23}BO_4$: calc. $[M]^+$: 290.1689, found: 290.1686.

$[\alpha]_D^{20}$: +3.33 (c = 0.69, $CHCl_3$).

A solution of alkyl iodide (*S*-**142k**, 0.08 M, 1.00 equiv) and methoxy boronic acid pinacol ester (**151q**, 0.20 M, 2.50 equiv) in hexane:Et_2O (2:1) and a solution of *t*-BuLi (ca. 0.20 M in hexane, 3.0 equiv) were prepared. The solution of *t*-BuLi was pumped by pump A (flow rate A: 6.0 mL/min) into a precooling loop (V_{pre} = 2.0 mL) at T^1 = 0 to 25 °C. The solution of the alkyl iodide was pumped by pump B (flow rate B: 5.0 mL/min) into a second precooling loop (V_{pre} = 2.0 mL) at T^1 = 0 to 25 °C. The precooled solutions were mixed in a T-shaped mixer and passed within a residence time of (t^1 = 5.5 to 5.6 s) through a coil reactor (V_R = 1.0 mL) at the corresponding temperature (T^1 = 0 to 25 °C). The stream was subsequently upon reaching steady state injected for 1 min 24 s into a flask charged with sat. aq. NH_4Cl. The aqueous phase was extracted three times with Et_2O (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was removed under reduced pressure and the remaining

crude product was purified by flash column chromatography on silica gel to afford afford (*S*)-**152w** (76 mg, 0.47 mmol, 54%, 88% *ee*) as white solid.

(*R*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-2-methyl-1-(4-(trifluoromethyl)phenyl)propan-1-one (*R*-152x):



(*R*)-**152x**

The ketone (*R*)-**152x** was prepared according to **TP11** from the iodide (*R*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and the weinreb amide **151r** (70.0 mg, 0.3 mmol, 3.0 equiv) at −40 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:9 to afford (*R*)-**152x** (18.8 mg, 0.056 mmol, 56%, 94% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.02–7.95 (m, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 6.73–6.59 (m, 3H), 5.90 (q, *J* = 1.4 Hz, 2H), 3.68 (h, *J* = 7.0 Hz, 1H), 3.07 (dd, *J* = 13.8, 6.8 Hz, 1H), 2.64 (dd, *J* = 13.8, 7.3 Hz, 1H), 1.21 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 202.9, 146.8 (d, *J* = 158.1 Hz), 139.3, 134.2 (d, *J* = 32.6 Hz), 133.3, 128.6, 125.7 (q, *J* = 3.7 Hz), 123.6 (d, *J* = 272.6 Hz), 122.0, 109.4, 108.2, 100.9, 43.5, 39.1, 17.4.

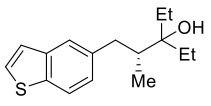
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2969 (vw), 2932 (w), 1744 (w), 1686 (m), 1504 (m), 1489 (m), 1458 (w), 1442 (m), 1410 (m), 1322 (vs), 1247 (s), 1227 (m), 1167 (s), 1125 (vs), 1066 (vs), 1039 (s), 1017 (m), 976 (s), 940 (w), 929 (m), 853 (m), 810 (m), 795 (m), 780 (w), 773 (w), 766 (w), 725 (w), 715 (w), 698 (w).

MS (70 eV, EI): m/z (%): 145 (17), 135 (100), 77 (11).

HRMS (EI) for $C_{18}H_{15}F_3O_3$: calc. $[M]^{+\bullet}$: 336.0973, found: 336.0961.

$[\alpha]_D^{20}$: +48.8 (c = 0.84, $CHCl_3$).

(*R*)-1-(Benzo[*b*]thiophen-5-yl)-3-ethyl-2-methylpentan-3-ol (*R*-152y):



(*R*)-**152y**

The alcohol (*R*)-**152y** was prepared according to **TP11** from the iodide (*R*)-**142l** (30.0 mg, 0.1 mmol, 1.0 equiv) and pentan-3-one (**151m**, 27 µL, 21.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*R*)-**152y** (16.5 mg, 0.063 mmol, 63%, 91% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.79 (d, *J* = 8.2 Hz, 1H), 7.63–7.60 (m, 1H), 7.42 (d, *J* = 5.4 Hz, 1H), 7.28 (dd, *J* = 5.5, 0.8 Hz, 1H), 7.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.13 (dd, *J* = 13.2, 2.9 Hz, 1H),

2.30 (dd, *J* = 13.2, 11.3 Hz, 1H), 1.97–1.89 (m, 1H), 1.72–1.56 (m, 4H), 1.17 (s, 1H), 0.95 (m, 6H), 0.79 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 138.4, 137.4, 126.6, 126.1, 124.0, 123.7, 122.3, 76.3, 42.1, 37.2, 28.4, 28.2, 13.3, 7.8, 7.7.

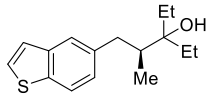
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2959 (m), 2955 (m), 2921 (m), 2873 (w), 2869 (w), 2852 (m), 1699 (w), 1695 (w), 1683 (w), 1456 (m), 1436 (m), 1420 (m), 1375 (m), 1326 (w), 1260 (w), 1231 (w), 1160 (w), 1147 (m), 1140 (m), 1100 (w), 1089 (m), 1061 (m), 1050 (m), 988 (w), 949 (w), 940 (w), 891 (m), 831 (m), 806 (s), 767 (m), 753 (s), 703 (vs), 689 (vs), 668 (m).

MS (70 eV, EI): m/z (%): 207 (4), 174 (6), 147 (100), 121 (5).

HRMS (EI) for $C_{16}H_{20}S$: calc. $[M\text{-}H_2O]^{+\bullet}$: 244.1280, found: 244.1283.

$[\alpha]_D^{20}$: −35.3 (c = 0.76, $CHCl_3$).

(*S*)-1-(Benzo[*b*]thiophen-5-yl)-3-ethyl-2-methylpentan-3-ol (*S*-152y):



(*S*)-**152y**

The alcohol (*S*)-**152y** was prepared according to **TP11** from the iodide (*S*)-**142l** (30.0 mg, 0.1 mmol, 1.0 equiv) and pentan-3-one (**151m**, 27 µL, 21.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152y** (17.6 mg, 0.067 mmol, 67%, 96% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.79 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 1.6 Hz, 1H), 7.42 (d, *J* = 5.4 Hz, 1H), 7.28 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.13 (dd, *J* = 13.1, 2.8 Hz, 1H), 2.30 (dd, *J* = 13.2, 11.3 Hz, 1H), 1.93 (m, 1H), 1.73–1.57 (m, 4H), 1.18 (s, 1H), 0.95 (m, 6H), 0.79 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 138.4, 137.3, 126.6, 126.1, 124.0, 123.7, 122.3, 76.3, 42.0, 37.2, 28.4, 28.2, 13.3, 7.8, 7.7.

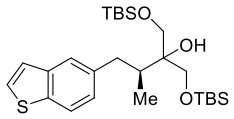
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3486 (w), 2967 (vs), 2938 (s), 2880 (m), 1460 (m), 1437 (m), 1421 (w), 1379 (w), 1260 (w), 1159 (w), 1145 (w), 1125 (w), 1090 (w), 1050 (w), 940 (s), 893 (w), 833 (w), 810 (m), 754 (m), 720 (w), 692 (s).

MS (70 eV, EI): m/z (%): 244 (10), 215 (29), 173 (10), 147 (100), 134 (6).

HRMS (EI) for $C_{16}H_{22}OS$: calc. $[M]^{+\bullet}$: 262.1391, found: 262.1389.

$[\alpha]_D^{20}$: +43.4 (c = 0.78, $CHCl_3$).

(*S*)-6-(1-(Benzo[*b*]thiophen-5-yl)propan-2-yl)-2,2,3,3,9,9,10,10-octamethyl-4,8-dioxa-3,9-disilaundecan-6-ol (*S*-152z):



(*S*)-**152z**

The alcohol (*S*)-**152z** was prepared according to **TP11** from the iodide (*S*)-**142l** (30.0 mg, 0.1 mmol, 1.0 equiv) and ketone **151s** (95.6 mg, 0.3 mmol, 3.0 equiv) at −40 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152z** (35.6 mg, 0.072 mmol, 72%, 98% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.78 (d, *J* = 8.2 Hz, 1H), 7.63–7.60 (m, 1H), 7.41 (d, *J* = 5.5 Hz, 1H), 7.27 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.71 (dd, *J* = 11.5, 9.6 Hz, 2H), 3.59 (d, *J* = 9.5 Hz, 2H), 3.19 (dd, *J* = 13.3, 3.0 Hz, 1H), 2.64 (s, 1H), 2.42 (dd, *J* = 13.3, 11.5 Hz, 1H), 2.02 (m, 1H), 0.93 (d, *J* = 4.6 Hz, 18H), 0.83 (d, *J* = 6.9 Hz, 3H), 0.11–0.08 (m, 12H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 138.4, 137.3, 126.5, 126.1, 124.1, 123.8, 122.2, 75.3, 64.1, 63.9, 39.3, 37.1, 26.0, 18.4, 13.1, -5.3, -5.3, -5.4, -5.4.

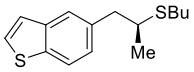
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3555 (vw), 2953 (m), 2927 (m), 2903 (w), 2894 (w), 2856 (m), 1736 (vw), 1683 (vw), 1669 (vw), 1471 (w), 1463 (w), 1437 (vw), 1389 (w), 1361 (w), 1328 (vw), 1291 (vw), 1251 (m), 1144 (w), 1087 (m), 1063 (m), 1027 (w), 1005 (w), 939 (w), 913 (vw), 890 (vw), 888 (vw), 834 (vs), 814 (m), 774 (s), 753 (w), 732 (vw), 725 (vw), 722 (vw), 715 (vw), 698 (w), 690 (w), 667 (w).

MS (70 eV, EI): m/z (%): 331 (24), 261 (21), 213 (100), 199 (21), 147 (74), 105 (13), 89 (27), 73 (39).

HRMS (EI) for $C_{24}H_{39}O_2SSi_2$: calc. $[M-C_2H_7O]^+$: 447.2209, found: 447.2204.

$[\alpha]_D^{20}$: −18.4 (c = 0.78, $CHCl_3$).

(*S*)-5-(2-(Butylthio)propyl)benzo[*b*]thiophene (*S*-152aa):



(*S*)-**152aa**

The sulfide (*S*)-**152aa** was prepared according to **TP11** from the iodide (*S*)-**142l** (30.0 mg, 0.1 mmol, 1.0 equiv) and dibutyl disulfide (**151t**, 48 µL, 44.6 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:100 to afford (*S*)-**152aa** (16.7 mg, 0.063 mmol, 63%, 93% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.80 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.43 (d, *J* = 5.5 Hz, 1H), 7.30 (dd, *J* = 5.5, 0.8 Hz, 1H), 7.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.12 (dd, *J* = 13.2, 5.6 Hz, 1H), 3.09–2.99 (m, 1H), 2.77 (dd, *J* = 13.2, 8.4 Hz, 1H), 2.60–2.53 (m, 2H), 1.63–1.52 (m, 2H), 1.48–1.35 (m, 2H), 1.24 (d, *J* = 6.6 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 137.9, 135.9, 126.7, 126.0, 124.1, 123.8, 122.3, 43.8, 41.7, 32.0, 30.6, 22.3, 20.8, 13.8.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2956 (m), 2924 (m), 2870 (w), 2861 (w), 1454 (m), 1436 (m), 1421 (m), 1373 (w), 1364 (w), 1327 (w), 1274 (w), 1261 (w), 1221 (w), 1183 (w), 1160 (w), 1145 (w), 1089 (m), 1065 (w), 1050 (m), 1012 (w), 891 (m), 832 (m), 808 (m), 769 (m), 753 (s), 725 (m), 689 (vs), 668 (w).

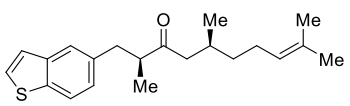
MS (70 eV, EI): m/z (%): 147 (50), 117 (53), 75 (100).

HRMS (EI) for $C_{15}H_{20}S_2$: calc. $[M]^{+\bullet}$: 264.1006, found: 264.0997.

$[\alpha]_D^{20}$: +6.8 (c = 1.99, $CHCl_3$).

A solution of alkyl iodide (*S*-**142l**, 0.08 M, 1.00 equiv) and dibutyl disulfide (**151t**, 0.20 M, 2.50 equiv) in hexane:Et_2O (2:1) and a solution of *t*-BuLi (ca. 0.20 M in hexane, 2.85 equiv) were prepared. The solution of *t*-BuLi was pumped by pump A (flow rate A: 5.7 mL/min) into a precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The solution of the alkyl iodide was pumped by pump B (flow rate B: 5.0 mL/min) into a second precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The precooled solutions were mixed in a T-shaped mixer and passed within a residence time of (t^1 = 5.5 to 5.6 s) through a coil reactor (V_R = 1.0 mL) at the corresponding temperature (T^1 = –20 to 25 °C). The stream was subsequently upon reaching steady state injected for 3 min 12 s into a flask charged with sat. aq. NH_4Cl. The aqueous phase was extracted Et_2O (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was removed under reduced pressure and the remaining crude product was purified by flash column chromatography on silica gel with diethyl ether/pentane = 1:100 to afford (*S*)-**152aa** (209 mg, 0.8 mmol, 63%, 86% *ee*) as white solid.

(2*S*,5*S*)-1-(Benzo[*b*]thiophen-5-yl)-2,5,9-trimethyldec-8-en-3-one (2*S*,5*S*-152ab):



(2*S*,5*S*)-**152ab**

The ketone (2*S*,5*S*)-**152ab** was prepared according to **TP11** from the iodide (*S*)-**142l** (30.0 mg, 0.1 mmol, 1.0 equiv) and (*S*)-citronellal (*S*-**151d**, 45 µL, 38.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude alcohol was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:9 (ca. 0.05 mmol, 50% yield). Both diastertereoisomers of the alcohol were then dissolved in DCM (0.8 mL) and oxidized using Dess-Martin-Periodinane[118] (31.8 mg, 0.075 mmol) and

stirred at ambient temperature for 10 min before quenching with sat. aq. NH_4Cl. The reaction mixture was extracted with Et_2O (3 x 20 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (2*S*,5*S*)-**152ab** (15.8 mg, 0.048 mmol, 48%, dr = 92:8, 96% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.78 (d, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 1.7 Hz, 1H), 7.42 (d, *J* = 5.4 Hz, 1H), 7.27 (s, 1H), 7.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 5.07–4.98 (m, 1H), 3.10 (dd, *J* = 13.5, 7.1 Hz, 1H), 2.86 (h, *J* = 7.0 Hz, 1H), 2.65 (dd, *J* = 13.5, 7.5 Hz, 1H), 2.33–2.16 (m, 2H), 2.03–1.72 (m, 4H), 1.66 (d, *J* = 1.6 Hz, 3H), 1.55 (s, 3H), 1.24–1.14 (m, 1H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 214.2, 140.0, 137.8, 136.1, 131.5, 126.7, 125.8, 124.5, 124.0, 123.8, 122.5, 49.7, 48.8, 38.9, 37.0, 28.6, 25.9, 25.6, 19.9, 17.8, 16.6.

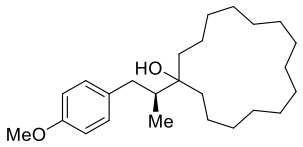
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2960 (m), 2926 (m), 2872 (m), 2857 (m), 1716 (s), 1457 (m), 1438 (m), 1422 (w), 1408 (w), 1376 (m), 1267 (vs), 1249 (s), 1146 (w), 1116 (s), 1102 (s), 1051 (w), 1034 (w), 1019 (m), 892 (w), 874 (w), 831 (w), 812 (w), 768 (w), 754 (m), 731 (s), 702 (m), 691 (m).

MS (70 eV, EI): m/z (%): 175 (12), 147 (100).

HRMS (EI) for $C_{21}H_{28}OS$: calc. $[M]^{+\bullet}$: 328.1861, found: 328.1852.

$[\alpha]_D^{20}$: +10.6 (c = 0.94, $CHCl_3$).

(*S*)-1-(1-(4-Methoxyphenyl)propan-2-yl)cyclopentadecan-1-ol (*S*-152ac):



(*S*)-**152ac**

The alcohol (*S*)-**152ac** was prepared according to **TP11** from the iodide (*S*)-**142f** (27.6 mg, 0.1 mmol, 1.0 equiv) and cyclopentadecanone (**151u**, 67.3 mg, 0.3 mmol, 3.0 equiv) at −40 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152ac** (19.9 mg, 0.053 mmol, 53%, 92% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.11–7.03 (m, 2H), 6.86–6.80 (m, 2H), 3.79 (s, 3H), 2.97 (dd, *J* = 13.3, 3.0 Hz, 1H), 2.17 (dd, *J* = 13.4, 11.2 Hz, 1H), 1.75–1.67 (m, 1H), 1.67–1.57 (m, 2H), 1.56–1.49 (m, 2H), 1.46–1.26 (m, 24H), 1.10 (s, 1H), 0.78 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.8, 134.3, 130.2, 113.7, 76.4, 55.4, 42.7, 37.0, 36.8, 36.0, 28.1, 28.0, 27.0, 26.9, 26.9, 26.8, 26.7, 26.1, 22.2, 22.1, 12.8.

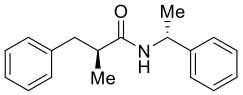
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3401 (s), 3244 (m), 3067 (w), 2927 (s), 2925 (s), 2854 (m), 1705 (vs), 1652 (m), 1643 (m), 1637 (m), 1611 (m), 1511 (s), 1458 (m), 1456 (m), 1441 (m), 1429 (w), 1421 (w), 1419 (w), 1362 (s), 1361 (s), 1299 (w), 1245 (vs), 1223 (m), 1220 (m), 1175 (w), 1091 (w), 1036 (m), 819 (w), 816 (m), 814 (m), 812 (m), 807 (m), 799 (w), 771 (w), 710 (w).

MS (70 eV, EI): m/z (%): 281 (4), 234 (5), 207 (12), 121 (100), 91 (4).

HRMS (EI) for $C_{25}H_{40}O$: calc. $[M-H_2O]^{+\bullet}$: 356.3074, found: 356.3075.

[α]$_D^{20}$: −7.5 (c = 1.17, $CHCl_3$).

(*S*)-2-Methyl-3-phenyl-*N*-((*R*)-1-phenylethyl)propanamide (2'*S*,3*R*-152ad):



(2'*S*,3*R*)-**152ad**

The amide (2'*S*,3*R*)-**152ad** was prepared according to **TP11** from the iodide (*S*)-**142m** (24.6 mg, 0.1 mmol, 1.0 equiv) and (*R*)-(+)-1-phenylethyl isocyanate (*R*-**151i**, 35 µL, 36.8 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (2'*S*,3*R*)-**152ad** (19.3 mg, 0.072 mmol, 72%, dr = 2:98, 96% *ee*) as white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.33–7.27 (m, 4H), 7.25–7.16 (m, 6H), 5.32 (d, *J* = 8.0 Hz, 1H), 5.02 (p, *J* = 7.1 Hz, 1H), 2.94 (dd, *J* = 13.4, 9.1 Hz, 1H), 2.71 (dd, *J* = 13.4, 6.0 Hz, 1H), 2.46–2.36 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.19 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 174.5, 143.3, 140.1, 129.1, 128.7, 128.6, 127.4, 126.5, 126.3, 48.5, 44.2, 40.9, 21.5, 17.9.

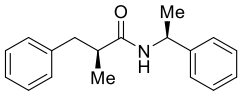
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3306 (w), 2976 (w), 2932 (w), 1639 (s), 1537 (s), 1494 (w), 1446 (w), 1382 (w), 1366 (w), 1245 (m), 1207 (w), 1177 (w), 1130 (w), 1094 (w), 1081 (w), 1031 (w), 1015 (w), 946 (w), 914 (w), 742 (m), 697 (vs).

MS (70 eV, EI): m/z (%): 176 (13), 120 (18), 105 (34), 91 (100), 77 (20).

HRMS (EI) for $C_{18}H_{21}NO$: calc. $[M]^{+\bullet}$: 267.1623, found: 267.1618.

[α]$_D^{20}$: −3.9 (c = 0.94, $CHCl_3$).

(*S*)-2-Methyl-3-phenyl-*N*-((*S*)-1-phenylethyl)propanamide (2'*S*,3*S*-152ad):



(2'*S*,3*S*)-**152ad**

A solution of alkyl iodide (*S*-**142m**, 0.08 M, 1.00 equiv) and (*S*)-(−)-1-phenylethyl isocyanate (*S*-**151i**, 0.20 M, 2.50 equiv) in hexane:Et_2O (2:1) and a solution of *t*-BuLi (ca. 0.20 M in hexane, 2.85 equiv) were prepared. The solution of *t*-BuLi was pumped by pump A (flow rate A: 5.7 mL/min) into a precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The solution of the alkyl iodide was pumped by pump B (flow rate B: 5.0 mL/min) into a second precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The precooled solutions were mixed in a T-shaped mixer and passed within a residence time of (t^1 = 5.5 to 5.6 s) through a coil reactor (V_R = 1.0 mL) at the corresponding temperature (T^1 = –20 to 25 °C). The stream was subsequently upon reaching steady state injected for 3 min 30 s into a flask charged with sat. aq. NH_4Cl. The aqueous phase was extracted Et_2O (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was removed under reduced pressure and the remaining crude product was purified by flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (1'*S*,2*S*)-**152ad** (217 mg, 0.81 mmol, 58%, dr = 98:2, 96% *ee*) as white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.25–7.16 (m, 6H), 7.14–7.08 (m, 2H), 7.03–6.98 (m, 2H), 5.46–5.34 (m, 1H), 5.10–5.00 (m, 1H), 2.94 (dd, *J* = 13.4, 8.8 Hz, 1H), 2.67 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.49–2.36 (m, 1H), 1.41 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 174.6, 143.0, 139.9, 129.1, 128.6, 128.6, 127.2, 126.4, 126.3, 48.4, 44.2, 40.6, 21.6, 18.1.

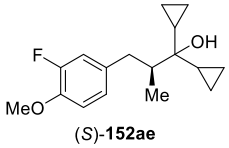
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3305 (w), 2975 (w), 2932 (vw), 2922 (vw), 1639 (m), 1606 (vw), 1537 (m), 1494 (w), 1444 (w), 1382 (w), 1366 (w), 1245 (w), 1207 (w), 1177 (vw), 1130 (w), 1081 (w), 1031 (vw), 1015 (vw), 946 (vw), 914 (vw), 742 (m), 697 (vs).

MS (70 eV, EI): m/z (%): 176 (13), 120 (17), 105 (32), 91 (100), 77 (20).

HRMS (EI) for $C_{18}H_{21}NO$: calc. $[M]^{+\bullet}$: 267.1623, found: 267.1617.

$[\alpha]_D^{20}$: −4.2 (c = 0.98, $CHCl_3$).

(*S*)-1,1-Dicyclopropyl-3-(3-fluoro-4-methoxyphenyl)-2-methylpropan-1-ol (*S*-152ae):



(*S*)-**152ae**

The alcohol (*S*)-**152ae** was prepared according to **TP11** from the iodide (*S*)-**142n** (29.4 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 28 µL, 27.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152ae** (21.7 mg, 0.078 mmol, 78%, 94% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.95–6.87 (m, 3H), 3.87 (s, 3H), 3.18 (dd, *J* = 13.3, 2.9 Hz, 1H), 2.24 (dd, *J* = 13.3, 11.4 Hz, 1H), 1.90–1.85 (m, 1H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 6.4 Hz, 2H), 0.50–0.39 (m, 7H), 0.35–0.26 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 244.7 Hz), 145.6 (d, *J* = 10.7 Hz), 135.6 (d, *J* = 5.9 Hz), 124.7 (d, *J* = 3.4 Hz), 116.8 (d, *J* = 17.6 Hz), 113.3 (d, *J* = 2.1 Hz), 72.7, 56.5, 47.8, 37.3 (d, *J* = 1.4 Hz), 16.9, 15.8, 14.2, 1.7, 1.4, -0.9, -1.0.

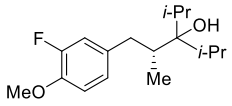
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2960 (m), 2958 (m), 2931 (m), 2903 (w), 1517 (vs), 1463 (m), 1443 (m), 1429 (m), 1375 (w), 1311 (m), 1304 (w), 1276 (s), 1275 (s), 1224 (m), 1181 (w), 1127 (s), 1027 (s), 993 (m), 977 (m), 955 (w), 913 (w), 807 (m), 762 (m), 668 (w).

MS (70 eV, EI): m/z (%): 139 (100), 111 (96), 69 (86).

HRMS (EI) for $C_{17}H_{23}FO_2$: calc. $[M]^{+\bullet}$: 278.1682, found: 278.1677.

$[\alpha]_D^{20}$: −17.8 (c = 0.54, $CHCl_3$).

(*R*)-1-(3-Fluoro-4-methoxyphenyl)-3-isopropyl-2,4-dimethylpentan-3-ol (*R*-152af):



(*R*)-**152af**

The alcohol (*R*)-**152af** was prepared according to **TP11** from the iodide (*R*)-**142n** (29.4 mg, 0.1 mmol, 1.0 equiv) and diisopropyl ketone (**151v**, 35 µL, 28.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:9 to afford (*R*)-**152af** (18.6 mg, 0.066 mmol, 66%, 90% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.95–6.83 (m, 3H), 3.87 (s, 3H), 3.07 (dd, *J* = 13.1, 2.5 Hz, 1H), 2.23–2.11 (m, 3H), 2.04 (m, 1H), 1.18 (s, 1H), 1.06–0.98 (m, 12H), 0.85 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 244.9 Hz), 145.6 (d, *J* = 10.7 Hz), 135.9 (d, *J* = 5.9 Hz), 124.7 (d, *J* = 3.5 Hz), 116.7 (d, *J* = 17.6 Hz), 113.3 (d, *J* = 2.2 Hz), 78.2, 56.5, 41.7, 37.9, 33.1, 33.0, 18.9, 18.8, 18.7, 18.6, 14.9.

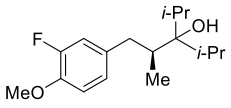
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2964 (m), 2879 (w), 1515 (vs), 1464 (m), 1443 (m), 1429 (w), 1382 (w), 1310 (w), 1275 (s), 1224 (m), 1126 (m), 1031 (m), 988 (w), 949 (m), 808 (w), 762 (w).

MS (70 eV, EI): m/z (%): 221 (12), 140 (9), 139 (100), 115 (4), 71 (8).

HRMS (EI) for $C_{14}H_{20}FO_2$: calc. $[M-(i\text{-Pr})]^{+\bullet}$: 239.1447, found: 239.1440.

$[\alpha]_D^{20}$: +62.5 (c = 0.80, $CHCl_3$).

(*S*)-1-(3-Fluoro-4-methoxyphenyl)-3-isopropyl-2,4-dimethylpentan-3-ol (*S*-152af):



(*S*)-**152af**

The alcohol (*S*)-**152af** was prepared according to **TP11** from the iodide (*S*)-**142n** (29.4 mg, 0.1 mmol, 1.0 equiv) and diisopropyl ketone (**151v**, 35 µL, 28.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:9 to afford (*S*)-**152af** (18.1 mg, 0.064 mmol, 64%, 96% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.94–6.83 (m, 3H), 3.87 (s, 3H), 3.07 (dd, *J* = 13.1, 2.5 Hz, 1H), 2.22–2.11 (m, 3H), 2.04 (m, 1H), 1.18 (s, 1H), 1.06–0.97 (m, 12H), 0.85 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 244.9 Hz), 145.6 (d, *J* = 10.7 Hz), 135.9 (d, *J* = 5.9 Hz), 124.7 (d, *J* = 3.4 Hz), 116.7 (d, *J* = 17.6 Hz), 113.3 (d, *J* = 2.2 Hz), 78.2, 56.5, 41.7, 37.9, 33.1, 33.0, 18.9, 18.8, 18.7, 18.6, 14.9.

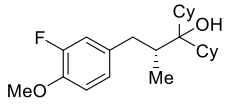
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3613 (vw), 2960 (m), 2931 (m), 2915 (m), 2911 (m), 2889 (m), 2862 (w), 2836 (w), 2248 (m), 2220 (m), 2194 (m), 2190 (m), 2167 (vs), 2122 (w), 2115 (m), 2084 (m), 1521 (m), 1515 (m), 1453 (w), 1445 (m), 1383 (w), 1278 (m), 1275 (m), 1224 (w), 1127 (w), 1029 (w), 945 (w), 808 (w), 723 (s), 690 (w).

MS (70 eV, EI): m/z (%): 221 (11), 139 (100), 115 (5), 71 (8).

HRMS (EI) for $C_{14}H_{20}FO_2$: calc. $[M-(i\text{-Pr})]^{+\bullet}$: 239.1447, found: 239.1440.

$[\alpha]_D^{20}$: −67.8 (c = 0.72, $CHCl_3$).

(*R*)-1,1-Dicyclohexyl-3-(3-fluoro-4-methoxyphenyl)-2-methylpropan-1-ol (*R*-152ag):



(*R*)-**152ag**

The alcohol (*R*)-**152ag** was prepared according to **TP11** from the iodide (*R*)-**142n** (29.4 mg, 0.1 mmol, 1.0 equiv) and dicyclohexyl ketone (**151w**, 28.5 mg, 0.25 mmol, 2.5 equiv) at −40 °C. The crude

product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:9 to afford (*R*)-**152ag** (25.0 mg, 0.069 mmol, 69%, 94% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.95–6.81 (m, 3H), 3.87 (s, 3H), 3.04 (dd, *J* = 13.0, 2.4 Hz, 1H), 2.21–2.04 (m, 2H), 1.85–1.67 (m, 12H), 1.27–1.17 (m, 11H), 0.81 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 245.0 Hz), 145.6 (d, *J* = 10.8 Hz), 136.0 (d, *J* = 5.9 Hz), 124.7 (d, *J* = 3.3 Hz), 116.7 (d, *J* = 17.6 Hz), 113.4 (d, *J* = 2.2 Hz), 78.2, 56.5, 44.6, 44.3, 40.9, 37.7, 28.7, 28.6, 28.6, 28.5, 27.6, 27.6, 27.5, 27.5, 26.9, 26.9, 14.7.

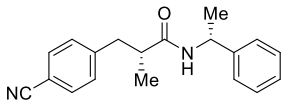
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2924 (vs), 2851 (s), 1585 (w), 1516 (vs), 1463 (m), 1445 (m), 1429 (w), 1379 (w), 1366 (w), 1310 (w), 1275 (s), 1224 (m), 1184 (w), 1127 (s), 1066 (w), 1031 (m), 981 (w), 954 (m), 893 (w), 876 (w), 819 (w), 805 (m), 759 (m).

MS (70 eV, EI): m/z (%): 279 (17), 195 (23), 139 (100), 95 (10).

HRMS (EI) for $C_{23}H_{36}FO_2$: calc. $[M+H]^+$: 363.2694, found: 363.2694.

$[\alpha]_D^{20}$: +4.3 (c = 0.83, $CHCl_3$).

(*R*)-3-(4-Cyanophenyl)-2-methyl-*N*-((*R*)-1-phenylethyl)propanamide (2'*R*,3*R*-152ah):



(2'*R*,3*R*)-**152ah**

The amide (2'*R*,3*R*)-**152ah** was prepared according to **TP11** from the iodide (*R*)-**142o** (27.1 mg, 0.1 mmol, 1.0 equiv) and (*R*)-(+)-1-phenylethyl isocyanate (*R*-**151i**, 35 µL, 36.8 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:3 to afford (2'*R*,3*R*)-**152ah** (21.9 mg, 0.075 mmol, 75%, dr = 94:6, 96% *ee*) as white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.44–7.38 (m, 2H), 7.27 (d, *J* = 3.8 Hz, 2H), 7.19–7.13 (m, 2H), 7.02–6.95 (m, 2H), 5.38 (d, *J* = 8.2 Hz, 1H), 5.03 (p, *J* = 7.2 Hz, 1H), 2.98 (dd, *J* = 13.3, 9.6 Hz, 1H), 2.69 (dd, *J* = 13.3, 5.4 Hz, 1H), 2.44–2.32 (m, 1H), 1.41 (d, *J* = 6.9 Hz, 3H), 1.25 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 173.7, 145.5, 142.9, 132.3, 129.9, 128.7, 127.6, 126.1, 119.1, 110.3, 48.5, 44.1, 40.6, 21.6, 18.4.

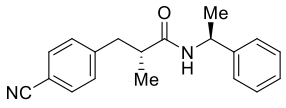
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3265 (m), 2972 (w), 2960 (w), 2930 (w), 2872 (w), 2853 (w), 2226 (w), 1638 (vs), 1608 (w), 1540 (m), 1505 (w), 1496 (w), 1470 (w), 1452 (m), 1418 (w), 1375 (w), 1365 (w), 1246 (w), 1108 (w), 1024 (w), 850 (w), 823 (w), 743 (w), 716 (w), 692 (s).

MS (70 eV, EI): m/z (%): 293 (16), 176 (52), 116 (44), 105 (100).

HRMS (EI) for $C_{19}H_{20}N_2O$: calc. $[M+H]^{+\bullet}$: 293.1654, found: 293.1650.

$[\alpha]_D^{20}$: −52.8 (c = 0.62, $CHCl_3$).

(*R*)-3-(4-Cyanophenyl)-2-methyl-*N*-((*S*)-1-phenylethyl)propanamide (2'*R*,3*S*-152ah):



(2'*R*,3*S*)-**152ah**

The amide (2'*R*,3*S*)-**152ah** was prepared according to **TP11** from the iodide (*R*)-**142o** (27.1 mg, 0.1 mmol, 1.0 equiv) and (*S*)-(−)-1-phenylethyl isocyanate (*S*-**151i**, 35 µL, 36.8 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:3 to afford (2'*R*,3*S*)-**152ah** (24.0 mg, 0.082 mmol, 82%, dr = 8:92, 96% *ee*) as white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.59–7.52 (m, 2H), 7.36–7.24 (m, 6H), 7.21 (dd, *J* = 7.0, 1.8 Hz, 2H), 5.40 (d, *J* = 8.0 Hz, 1H), 5.03 (p, *J* = 7.1 Hz, 1H), 3.04 (dd, *J* = 13.4, 9.0 Hz, 1H), 2.74 (dd, *J* = 13.4, 5.8 Hz, 1H), 2.48–2.31 (m, 1H), 1.28 (d, *J* = 6.9 Hz, 3H), 1.19 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 173.7, 145.7, 142.9, 132.3, 130.0, 128.9, 127.6, 126.2, 119.1, 110.4, 48.6, 43.7, 40.5, 21.6, 18.1.

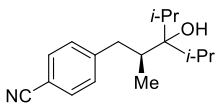
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3345 (w), 3324 (w), 2978 (w), 2966 (w), 2953 (w), 2930 (w), 2226 (m), 1646 (vs), 1606 (w), 1527 (vs), 1506 (m), 1494 (w), 1449 (w), 1410 (w), 1376 (w), 1366 (w), 1306 (w), 1299 (w), 1282 (w), 1238 (m), 1227 (w), 1212 (w), 1193 (w), 1180 (w), 1131 (w), 1107 (w), 1013 (w), 942 (w), 868 (w), 848 (w), 818 (w), 756 (m), 697 (s).

MS (70 eV, EI): m/z (%): 292 (59), 176 (32), 116 (28), 105 (100).

HRMS (EI) for $C_{19}H_{20}N_2O$: calc. $[M]^{+\bullet}$: 292.1576, found: 292.1569.

$[\alpha]_D^{20}$: −56.0 (c = 0.67, $CHCl_3$).

(*S*)-4-(3-Hydroxy-3-isopropyl-2,4-dimethylpentyl)benzonitrile (*S*-152ai):



(*S*)-**152ai**

The alcohol (*S*)-**152ai** was prepared according to **TP11** from the iodide (*S*)-**142o** (27.1 mg, 0.1 mmol, 1.0 equiv) and diisopropyl ketone (**151v**, 35 µL, 28.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude

product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:9 to afford (*S*)-**152ai** (12.7 mg, 0.049 mmol, 49%, 95% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.60–7.54 (m, 2H), 7.31–7.26 (m, 2H), 3.23 (dd, *J* = 13.0, 2.6 Hz, 1H), 2.32 (dd, *J* = 13.0, 11.1 Hz, 1H), 2.20 – 2.06 (m, 3H), 1.20 (s, 1H), 1.08–1.02 (m, 9H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 7.0 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 148.9, 132.2, 130.0, 119.4, 109.6, 78.1, 41.6, 39.2, 33.2, 33.1, 19.0, 18.8, 18.5, 15.1, 1.2.

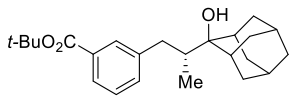
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3534 (w), 2965 (vs), 2926 (vs), 2880 (m), 2856 (m), 2228 (s), 1672 (w), 1607 (s), 1503 (m), 1468 (m), 1454 (m), 1414 (m), 1382 (m), 1266 (m), 1178 (m), 1160 (w), 1128 (w), 1094 (m), 990 (m), 950 (s), 842 (w), 815 (m).

MS (70 eV, EI): m/z (%): 216 (11), 198 (14), 172 (59), 157 (40), 146 (27), 142 (80), 130 (39), 116 (100), 89 (21), 71 (47).

HRMS (EI) for $C_{17}H_{25}NO$: calc. $[M]^{+\bullet}$: 260.2009, found: 260.2013.

$[\alpha]_D^{20}$: −22.7 (c = 0.93, $CHCl_3$).

***tert*-Butyl 3-((*R*)-2-((1*R*,3*S*,5*R*,7*R*)-2-hydroxyadamantan-2-yl)propyl)benzoate (*R*-152aj):**



(*R*)-**152aj**

The alcohol (*R*)-**152aj** was prepared according to **TP11** from the iodide (*R*)-**142i** (34.6 mg, 0.1 mmol, 1.0 equiv) and adamantanone (**151p**, 45.0 mg, 0.3 mmol, 3.0 equiv) at −40 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*R*)-**152aj** (19.6 mg, 0.053 mmol, 53%, 95% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.82–7.78 (m, 2H), 7.34–7.31 (m, 2H), 2.97 (dd, *J* = 12.9, 2.7 Hz, 1H), 2.43–2.32 (m, 1H), 2.26 (dd, *J* = 13.0, 11.2 Hz, 1H), 2.17 (t, *J* = 3.0 Hz, 3H), 2.02 (d, *J* = 3.1 Hz, 1H), 1.95–1.92 (m, 1H), 1.88–1.77 (m, 5H), 1.74–1.70 (m, 2H), 1.60 (s, 9H), 1.34 (s, 1H), 1.10 (d, *J* = 1.7 Hz, 1H), 1.08 (d, *J* = 1.4 Hz, 1H), 0.72 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.2, 142.8, 133.7, 132.1, 130.3, 128.2, 126.9, 81.1, 76.2, 38.4, 37.8, 35.8, 35.0, 34.2, 34.1, 33.9, 33.4, 33.3, 28.4, 27.1, 27.1, 11.3.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3521 (w), 2969 (w), 2965 (w), 2960 (w), 2910 (m), 2858 (w), 1739 (w), 1710 (vs), 1675 (w), 1604 (w), 1476 (w), 1455 (m), 1419 (w), 1392 (w), 1365 (s), 1331 (w), 1304 (m), 1292 (s), 1257 (m), 1219 (m), 1160 (s), 1111 (m), 1098 (m), 1091 (m), 1071 (w), 1058 (w), 1044 (w), 1032 (w),

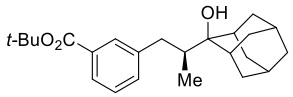
991 (w), 980 (m), 937 (w), 927 (m), 913 (w), 850 (w), 811 (w), 804 (w), 760 (m), 747 (m), 718 (w), 692 (w).

MS (70 eV, EI): m/z (%): 293 (11), 207 (6), 203 (6), 164 (14), 151 (100), 135 (15), 91 (18), 81 (10), 71 (13), 57 (49).

HRMS (EI) for $C_{24}H_{35}O_3$: calc. $[M+H]^{+\bullet}$: 371.2581, found: 371.2565.

$[\alpha]_D^{20}$: +9.70 (c = 0.93, $CHCl_3$).

***tert*-Butyl 3-((*S*)-2-((1*R*,3*S*,5*R*,7*R*)-2-hydroxyadamantan-2-yl)propyl)benzoate (*S*-152aj):**



(*S*)-**152aj**

The alcohol (*S*)-**152aj** was prepared according to **TP11** from the iodide (*S*)-**142i** (34.6 mg, 0.1 mmol, 1.0 equiv) and adamantanone (**151p**, 45.0 mg, 0.3 mmol, 3.0 equiv) at −40 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152aj** (18.9 mg, 0.051 mmol, 51%, 95% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.83–7.78 (m, 2H), 7.34–7.30 (m, 2H), 2.97 (dd, *J* = 13.0, 2.6 Hz, 1H), 2.43–2.33 (m, 1H), 2.26 (dd, *J* = 13.0, 11.2 Hz, 1H), 2.20–2.13 (m, 3H), 2.03 (dd, *J* = 13.2, 3.1 Hz, 1H), 1.93 (p, *J* = 2.6 Hz, 1H), 1.88–1.77 (m, 3H), 1.73–1.62 (m, 4H), 1.60 (s, 9H), 1.35 (d, *J* = 1.3 Hz, 1H), 1.09 (dd, *J* = 6.4, 1.5 Hz, 2H), 0.72 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.2, 142.8, 133.7, 132.1, 130.3, 128.2, 126.9, 81.1, 76.2, 38.4, 37.8, 35.8, 35.0, 34.2, 34.1, 33.9, 33.4, 33.3, 28.3, 27.1, 27.1, 11.3.

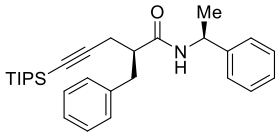
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3419 (m), 3226 (w), 3005 (w), 2952 (w), 2946 (w), 2913 (w), 2874 (w), 2858 (w), 1745 (w), 1706 (vs), 1660 (w), 1637 (w), 1608 (w), 1477 (w), 1471 (w), 1456 (w), 1436 (w), 1423 (w), 1421 (w), 1392 (w), 1364 (s), 1362 (s), 1304 (w), 1292 (m), 1258 (w), 1220 (m), 1161 (m), 1111 (w), 1097 (w), 1093 (w), 1091 (w), 1071 (w), 1065 (w), 1058 (w), 1032 (w), 991 (w), 981 (w), 927 (w), 851 (w), 849 (w), 809 (w), 804 (w), 798 (w), 760 (w), 747 (w), 719 (w).

MS (70 eV, EI): m/z (%): 297 (7), 164 (11), 151 (100), 135 (10), 97 (6), 91 (11), 57 (31).

HRMS (EI) for $C_{24}H_{35}O_3$: calc. $[M+H]^{+\bullet}$: 371.2581, found: 371.2584.

$[\alpha]_D^{20}$: −9.3 (c = 1.26, $CHCl_3$).

(*S*)-2-Benzyl-*N*-((*S*)-1-phenylethyl)-5-(tri*iso*propylsilyl)pent-4-ynamide (2'*S*,3*S*-152ak):



(2'*S*,3*S*)-**152ak**

The amide (2'*S*,3*S*)-**152ak** was prepared according to **TP11** from the iodide (*S*)-**142p** (42.6 mg, 0.1 mmol, 1.0 equiv) and (*S*)-(−)-1-phenylethyl isocyanate (*S*-**151i**, 35 µL, 36.8 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (2'*S*,3*S*)-**152ak** (34.5 mg, 0.077 mmol, 77%, dr = 94:6, 96% *ee*) as white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.40–7.29 (m, 9H), 7.26–7.24 (m, 1H), 5.61 (d, *J* = 7.8 Hz, 1H), 5.07 (p, *J* = 7.0 Hz, 1H), 3.17 (dd, *J* = 13.4, 5.4 Hz, 1H), 2.99 (dd, *J* = 13.4, 9.1 Hz, 1H), 2.63 (dd, *J* = 6.5, 2.3 Hz, 2H), 2.61–2.55 (m, 1H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.19–1.06 (m, 21H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 172.4, 143.0, 139.5, 129.2, 128.7, 128.7, 127.4, 126.7, 126.2, 106.2, 83.1, 49.4, 48.8, 38.2, 22.8, 21.6, 18.8, 11.4.

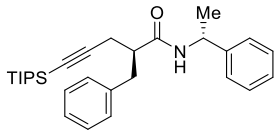
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3290 (w), 2974 (m), 2942 (m), 2892 (w), 2865 (m), 2174 (w), 2168 (w), 1642 (s), 1540 (m), 1506 (w), 1496 (m), 1463 (m), 1455 (m), 1382 (m), 1350 (w), 1280 (w), 1241 (w), 1210 (w), 1183 (w), 1152 (w), 1119 (s), 1075 (m), 1046 (w), 1029 (w), 1018 (m), 996 (w), 919 (w), 883 (m), 744 (m), 698 (vs), 676 (s), 661 (m).

MS (70 eV, EI): m/z (%): 105 (100), 91 (32), 78 (17).

HRMS (EI) for $C_{29}H_{41}NOSi$: calc. $[M]^{+\bullet}$: 447.2957, found: 447.2950

$[\alpha]_D^{20}$: +23.6 (c = 1.76, $CHCl_3$).

(*S*)-2-Benzyl-*N*-((*R*)-1-phenylethyl)-5-(tri*iso*propylsilyl)pent-4-ynamide (2'*S*,3*R*-152ak):



(2'*S*,3*R*)-**152ak**

The amide (2'*S*,3*R*)-**152ak** was prepared according to **TP11** from the iodide (*S*)-**142p** (42.6 mg, 0.1 mmol, 1.0 equiv) and (*R*)-(−)-1-phenylethyl isocyanate (*R*-**151i**, 35 µL, 36.8 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (2'*S*,3*R*)-**152ak** (31.8 mg, 0.071 mmol, 71%, dr = 4:96, 96% *ee*) as white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.25–7.19 (m, 6H), 7.14–7.11 (m, 2H), 6.99–6.96 (m, 2H), 5.64 (d, *J* = 7.8 Hz, 1H), 5.04 (p, *J* = 7.1 Hz, 1H), 2.98 (dd, *J* = 13.4, 5.4 Hz, 1H), 2.92 (dd, *J* = 13.5, 8.6 Hz, 1H), 2.65–2.58 (m, 1H), 2.55–2.47 (m, 2H), 1.41 (d, *J* = 6.9 Hz, 3H), 1.10–1.03 (m, 21H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 172.5, 142.9, 139.3, 129.2, 128.7, 128.6, 127.2, 126.5, 126.2, 106.2, 83.0, 49.6, 48.7, 38.2, 23.2, 21.7, 18.8, 11.4.

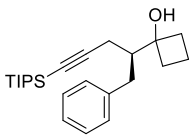
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3288 (w), 3064 (w), 3029 (w), 2942 (m), 2892 (w), 2864 (m), 2169 (w), 1638 (vs), 1605 (w), 1586 (w), 1543 (m), 1496 (m), 1462 (m), 1454 (m), 1427 (w), 1382 (m), 1367 (w), 1291 (w), 1240 (m), 1211 (w), 1128 (w), 1075 (w), 1062 (w), 1048 (w), 1030 (w), 1017 (m), 995 (m), 918 (w), 882 (s), 760 (w), 744 (m), 697 (vs), 676 (s), 660 (m).

MS (70 eV, EI): m/z (%): 404 (19), 300 (12), 105 (100), 91 (27), 79 (15).

HRMS (EI) for $C_{29}H_{41}NOSi$: calc. $[M]^{+\bullet}$: 447.2957, found: 447.2957

$[\alpha]_D^{20}$: +26.4 (c = 1.61, $CHCl_3$).

(*S*)-1-(1-Phenyl-5-(tri*iso*propylsilyl)pent-4-yn-2-yl)cyclobutan-1-ol (*S*-152al):



(*S*)-**152al**

The alcohol (*S*)-**152al** was prepared according to **TP11** from the iodide (*S*)-**142p** (42.6 mg, 0.1 mmol, 1.0 equiv) and cyclobutanone (**151x**, 19 µL, 17.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:6 to afford (*S*)-**152al** (22.2 mg, 0.060 mmol, 60%, 90% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.32–7.17 (m, 6H), 3.07 (s, 1H), 2.95–2.81 (m, 2H), 2.44 (dd, *J* = 17.4, 4.5 Hz, 1H), 2.25–2.01 (m, 5H), 2.00–1.89 (m, 2H), 1.68–1.54 (m, 1H), 1.10 (d, *J* = 3.4 Hz, 21H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 141.1, 129.3, 128.5, 126.2, 107.5, 85.0, 79.6, 46.9, 35.1, 34.8, 33.2, 18.8, 17.6, 12.9, 11.4.

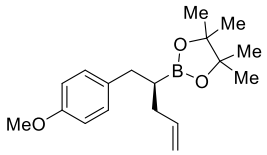
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3563 (vw), 3490 (vw), 3074 (vw), 2966 (m), 2935 (m), 2882 (w), 2835 (w), 1637 (w), 1611 (w), 1584 (w), 1511 (vs), 1462 (m), 1442 (m), 1418 (vw), 1380 (w), 1300 (m), 1244 (vs), 1177 (m), 1125 (w), 1106 (w), 1037 (m), 995 (w), 976 (w), 911 (m), 841 (w), 831 (w), 816 (m), 809 (m), 763 (w).

MS (70 eV, EI): m/z (%): 137 (12), (129 (17), 103 (39), 91 (76), 75 (100).

HRMS (EI) for $C_{21}H_{31}OSi$: calc. $[M-i\text{-}Pr]^{+\bullet}$: 327.2144, found: 327.2132.

$[\alpha]_D^{20}$: +26.3 (c = 3.8, $CHCl_3$).

(*S*)-2-(1-(4-Methoxyphenyl)pent-4-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (*S*-152am):



(*S*)-**152am**

The boronate (*S*)-**152am** was prepared according to **TP11** from the iodide (*S*)-**142q** (30.2 mg, 0.1 mmol, 1.0 equiv) and methoxy boronic acid pinacol ester (**151q**, 41 µL, 39.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:6 to afford (*S*)-**152am** (22.1 mg, 0.073 mmol, 73%, 90% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.14–7.09 (m, 2H), 6.82–6.77 (m, 2H), 5.82 (ddt, *J* = 17.0, 10.1, 6.9 Hz, 1H), 5.07–4.93 (m, 2H), 3.77 (s, 3H), 2.72–2.58 (m, 2H), 2.20–2.12 (m, 2H), 1.48–1.37 (m, 1H), 1.15 (d, *J* = 11.3 Hz, 12H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.8, 138.4, 134.3, 129.9, 115.3, 113.6, 83.2, 55.4, 36.0, 35.3, 24.9, 24.9.

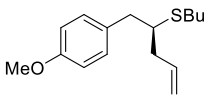
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2977 (w), 2930 (w), 2835 (w), 1640 (w), 1612 (w), 1584 (vw), 1512 (s), 1480 (w), 1465 (w), 1443 (w), 1407 (w), 1380 (s), 1372 (s), 1321 (m), 1301 (m), 1269 (m), 1243 (vs), 1214 (m), 1176 (m), 1166 (m), 1142 (vs), 1108 (w), 1037 (m), 992 (w), 967 (m), 910 (m), 854 (m), 835 (m), 806 (m), 760 (w), 752 (w), 712 (w), 691 (w), 670 (w).

MS (70 eV, EI): m/z (%): 260 (52), 174 (11), 121 (100).

HRMS (EI) for $C_{18}H_{27}O_3B$: calc. $[M]^{+\bullet}$: 302.2053, found: 302.2051.

$[\alpha]_D^{20}$: +8.4 (c = 2.82, $CHCl_3$).

(*S*)-Butyl(1-(4-methoxyphenyl)pent-4-en-2-yl)sulfane (*S*-152an):



(*S*)-**152an**

The sulfide (*S*)-**152an** was prepared according to **TP11** from the iodide (*S*)-**142q** (30.2 mg, 0.1 mmol, 1.0 equiv) and dibutyl disulfide (**151t**, 48 µL, 44.6 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude

product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:100 to afford (*S*)-**152an** (15.1 mg, 0.057 mmol, 57%, 91% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.14–7.09 (m, 2H), 6.87–6.81 (m, 2H), 5.89 (ddt, *J* = 17.2, 10.6, 7.0 Hz, 1H), 5.11–5.05 (m, 2H), 3.79 (s, 3H), 2.87 (dq, *J* = 7.5, 5.9 Hz, 1H), 2.79 (dd, *J* = 7.0, 4.6 Hz, 2H), 2.46 (t, *J* = 7.4 Hz, 2H), 2.39–2.21 (m, 2H), 1.54–1.47 (m, 2H), 1.41–1.33 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 158.1, 135.6, 131.6, 130.3, 117.1, 113.7, 55.3, 46.9, 40.4, 38.3, 31.8, 30.6, 22.1, 13.7.

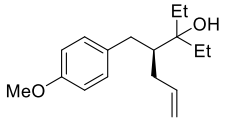
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3076 (vw), 2956 (m), 2929 (m), 2872 (w), 2860 (w), 2835 (w), 1640 (w), 1611 (w), 1584 (w), 1511 (vs), 1464 (m), 1439 (w), 1378 (vw), 1300 (w), 1245 (vs), 1200 (w), 1176 (m), 1117 (w), 1107 (w), 1036 (s), 1004 (w), 991 (w), 968 (vw), 913 (m), 831 (m), 815 (m), 809 (m), 753 (w), 721 (w), 695 (vw).

MS (70 eV, EI): m/z (%): 143 (39), 121 (100), 101 (18), 91 (23), 87 (49), 44 (14).

HRMS (EI) for $C_{13}H_{19}OS$: calc. $[M-C_3H_5]^{+\bullet}$: 223.1147, found: 223.1157.

$[\alpha]_D^{20}$: −6.5 (c = 1.24, $CHCl_3$).

(*S*)-3-Ethyl-4-(4-methoxybenzyl)hept-6-en-3-ol (*S*-152ao):



(*S*)-**152ao**

The alcohol (*S*)-**152ao** was prepared according to **TP11** from the iodide (*S*)-**142q** (30.2 mg, 0.1 mmol, 1.0 equiv) and pentan-3-one (**151m**, 27 µL, 21.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica with diethyl ether/pentane = 1:9 to afford (*S*)-**152ao** (20.5 mg, 0.078 mmol, 78%, 92% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.14–7.08 (m, 2H), 6.85–6.80 (m, 2H), 5.87–5.74 (m, 1H), 5.03–4.89 (m, 2H), 3.79 (s, 3H), 2.85 (dd, *J* = 14.0, 4.1 Hz, 1H), 2.42 (dd, *J* = 14.0, 9.7 Hz, 1H), 2.24–2.17 (m, 1H), 2.11–2.03 (m, 1H), 1.98–1.91 (m, 1H), 1.66–1.54 (m, 4H), 1.33 (s, 1H), 0.90 (dt, *J* = 8.4, 7.5 Hz, 6H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.9, 139.0, 134.0, 130.2, 115.9, 113.9, 55.4, 46.5, 34.4, 33.6, 28.9, 28.6, 7.8.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3564 (vw), 3493 (vw), 3073 (vw), 2967 (m), 2934 (m), 2882 (w), 2836 (w), 1637 (w), 1612 (w), 1584 (w), 1511 (vs), 1462 (m), 1442 (m), 1418 (vw), 1380 (w), 1300 (m), 1244 (vs),

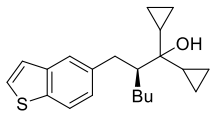
1177 (m), 1125 (w), 1106 (w), 1037 (m), 995 (w), 976 (w), 911 (m), 842 (w), 831 (w), 816 (m), 809 (m), 762 (w).

MS (70 eV, EI): m/z (%): 203 (59), 121 (100), 87 (60), 45 (31).

HRMS (EI) for $C_{17}H_{26}O_2$: calc. $[M]^{+\bullet}$: 262.1933, found: 262.1925.

$[\alpha]_D^{20}$: −43.7 (c = 0.7, $CHCl_3$).

(*S*)-2-(Benzo[*b*]thiophen-5-ylmethyl)-1,1-dicyclopropylhexan-1-ol (*S*-152ap):



(*S*)-**152ap**

The alcohol (*S*)-**152ap** was prepared according to **TP11** from the iodide (*S*)-**142r** (34.4 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 39 µL, 38.6 mg, 0.35 mmol, 3.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152ap** (16.4 mg, 0.05 mmol, 50%, 92% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.77 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 1.7 Hz, 1H), 7.40 (d, *J* = 5.4 Hz, 1H), 7.27 (d, *J* = 5.6 Hz, 1H), 7.24 (d, *J* = 1.6 Hz, 1H), 3.28 (dd, *J* = 14.0, 4.8 Hz, 1H), 2.64 (dd, *J* = 14.0, 8.2 Hz, 1H), 2.02–1.92 (m, 1H), 1.83–1.71 (m, 1H), 1.45–1.31 (m, 1H), 1.24–1.07 (m, 3H), 1.00–0.87 (m, 2H), 0.83 (s, 1H), 0.79–0.71 (m, 3H), 0.52–0.36 (m, 6H), 0.33–0.22 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 139.2, 137.2, 126.4, 126.1, 123.8, 123.8, 122.2, 73.5, 52.8, 37.3, 31.6, 30.5, 23.2, 17.5, 16.5, 14.1, 2.0, 1.5, -0.5, -0.8.

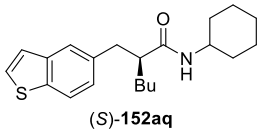
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3589 (w), 3084 (w), 3007 (m), 2954 (s), 2926 (s), 2868 (m), 2858 (m), 1464 (m), 1458 (m), 1436 (m), 1421 (m), 1377 (m), 1326 (w), 1306 (m), 1262 (w), 1222 (w), 1180 (w), 1160 (w), 1146 (m), 1115 (w), 1089 (m), 1050 (s), 1022 (s), 985 (s), 945 (w), 926 (m), 913 (m), 892 (m), 867 (w), 832 (m), 805 (m), 769 (m), 753 (m), 729 (w), 704 (m), 691 (vs).

MS (70 eV, EI): m/z (%): 225 (11), 197 (11), 147 (100), 111 (47), 69 (23).

HRMS (EI) for $C_{21}H_{26}S$: calc. $[M-H_2O]^{+\bullet}$: 310.1755, found: 310.1748.

$[\alpha]_D^{20}$: −6.9 (c = 0.72, $CHCl_3$).

(*S*)-2-(Benzo[*b*]thiophen-5-ylmethyl)-*N*-cyclohexylhexanamide (*S*-152aq):



(*S*)-**152aq**

The alcohol (*S*)-**152aq** was prepared according to **TP11** from the iodide (*S*)-**142r** (34.4 mg, 0.1 mmol, 1.0 equiv) and cyclohexyl isocyanate (**151h**, 45 µL, 43.8 mg, 0.35 mmol, 3.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:2 to afford (*S*)-**152aq** (21.0 mg, 0.061 mmol, 61%, 92% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.76 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 1.7 Hz, 1H), 7.40 (d, *J* = 5.4 Hz, 1H), 7.25 (d, *J* = 5.6 Hz, 1H), 7.15 (dd, *J* = 8.2, 1.7 Hz, 1H), 4.98 (d, *J* = 8.4 Hz, 1H), 3.76–3.62 (m, 1H), 3.01 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.81 (dd, *J* = 13.4, 5.2 Hz, 1H), 2.26–2.10 (m, 1H), 1.86–1.68 (m, 3H), 1.64–1.56 (m, 1H), 1.54–1.41 (m, 3H), 1.40–1.13 (m, 6H), 1.11–0.93 (m, 2H), 0.88 (t, *J* = 6.9 Hz, 3H), 0.73–0.63 (m, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 173.9, 140.0, 137.7, 136.4, 126.6, 125.7, 123.9, 123.7, 122.3, 51.3, 47.8, 39.5, 33.3, 33.0, 32.7, 30.0, 25.6, 24.9, 24.8, 22.9, 14.2.

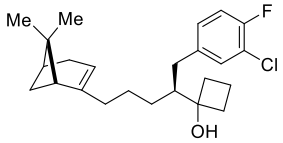
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3291 (m), 2931 (m), 2872 (w), 2853 (m), 1631 (vs), 1540 (s), 1506 (w), 1466 (w), 1446 (m), 1438 (m), 1421 (w), 1390 (w), 1346 (w), 1308 (w), 1250 (m), 1237 (m), 1092 (w), 1051 (w), 892 (m), 831 (w), 813 (m), 768 (w), 756 (m), 690 (s).

MS (70 eV, EI): m/z (%): 286 (15), 187 (22), 160 (10), 147 (100).

HRMS (EI) for $C_{21}H_{29}NOS$: calc. $[M]^{+\bullet}$: 343.1970, found: 343.1963.

$[\alpha]_D^{20}$: +33.1 (c = 1.05, $CHCl_3$).

1-((*S*)-1-(3-Chloro-4-fluorophenyl)-5-((1*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)pentan-2-yl)cyclobutan-1-ol (*R*,*S*,*S*-152ar):



(*R*,*S*,*S*)-**152ar**

The alcohol (*R*,*S*,*S*)-**152ar** was prepared according to **TP11** from the iodide (*S*)-**142s** (42.6 mg, 0.1 mmol, 1.0 equiv) and cyclobutanone (**151x**, 19 µL, 17.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:9 to afford (*R*,*S*,*S*)-**152ar** (23.1 mg, 0.059 mmol, 59%, dr = 92:8, 98% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.22 (dd, *J* = 7.3, 1.8 Hz, 1H), 7.08–6.99 (m, 2H), 5.12–5.04 (m, 1H), 2.75 (dd, *J* = 14.0, 5.0 Hz, 1H), 2.43 (dd, *J* = 14.0, 8.4 Hz, 1H), 2.35–2.27 (m, 1H), 2.24–1.69 (m, 10H), 1.67–1.58 (m, 1H), 1.50 (s, 1H), 1.45–1.36 (m, 1H), 1.24 (s, 8H), 1.05 (d, *J* = 8.4 Hz, 1H), 0.75 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 156.6 (d, *J* = 246.3 Hz), 148.1, 139.4 (d, *J* = 4.0 Hz), 131.0, 128.8 (d, *J* = 6.8 Hz), 120.5 (d, *J* = 17.5 Hz), 116.3 (d, *J* = 20.7 Hz), 116.1, 79.8, 48.6, 45.7, 41.0, 38.0, 37.3, 36.0, 35.7, 35.0, 31.8, 31.4, 29.2, 26.4, 26.3, 21.3, 13.3.

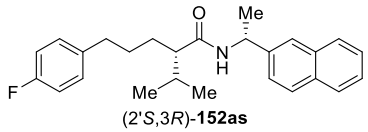
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3419 (vw), 2983 (w), 2924 (s), 2876 (m), 2833 (w), 1733 (vw), 1710 (w), 1500 (vs), 1459 (w), 1449 (w), 1435 (w), 1420 (w), 1406 (w), 1381 (w), 1364 (w), 1331 (w), 1264 (m), 1247 (s), 1221 (w), 1204 (w), 1166 (w), 1126 (w), 1094 (w), 1060 (m), 957 (vw), 943 (vw), 900 (w), 887 (w), 815 (m), 792 (w), 773 (w), 751 (vw), 703 (w), 688 (w).

MS (70 eV, EI): m/z (%): 162 (16), 145 (30), 131 (26), 119 (49), 105 (42), 91 (100).

HRMS (EI) for $C_{24}H_{32}ClFO$: calc. $[M]^{+\bullet}$: 390.2126, found: 390.2137.

$[\alpha]_D^{20}$: −14.3 (c = 1.3, $CHCl_3$).

(*S*)-5-(4-Fluorophenyl)-2-isopropyl-*N*-((*R*)-1-(naphthalen-2-yl)ethyl)pentanamide (2'*S*,3*R*-152as):



(2'*S*,3*R*)-**152as**

The amide (2'*S*,3*R*)-**152as** was prepared according to **TP11** from the iodide (*S*)-**142t** (32.0 mg, 0.1 mmol, 1.0 equiv) and (*R*)-(−)-1-(1-naphthyl)ethyl isocyanate (*R*-**151j**, 62 µL, 69 mg, 0.35 mmol, 3.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (2'*S*,3*R*)-**152as** (18.4 mg, 0.047 mmol, 47%, dr = 91:9, 95% *ee*) as white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = δ 8.20–8.05 (m, 1H), 7.92–7.76 (m, 2H), 7.56–7.42 (m, 4H), 7.07–6.99 (m, 2H), 6.97–6.83 (m, 2H), 5.98 (p, *J* = 7.0 Hz, 1H), 5.55 (d, *J* = 8.3 Hz, 1H), 2.55 (t, *J* = 7.4 Hz, 2H), 1.87–1.70 (m, 1H), 1.71–1.60 (m, 5H), 1.62–1.42 (m, 2H), 1.39–1.26 (m, 1H), 0.85 (dd, *J* = 6.6, 3.5 Hz, 6H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 174.1, 161.3 (d, *J* = 243.1 Hz), 138.3, 138.0 (d, *J* = 3.2 Hz), 134.0, 131.3, 129.7 (d, *J* = 7.7 Hz), 128.8, 128.6, 126.6, 126.1, 125.3, 123.9, 122.8, 115.1 (d, *J* = 21.0 Hz), 55.3, 44.4, 35.3, 31.0, 30.0, 29.9, 21.2, 20.6, 20.5.

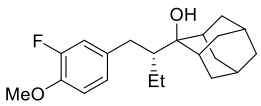
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3289 (w), 3050 (w), 2956 (m), 2926 (m), 2857 (w), 1684 (w), 1633 (s), 1600 (w), 1537 (m), 1509 (vs), 1458 (m), 1416 (w), 1397 (w), 1385 (w), 1374 (w), 1304 (w), 1260 (w), 1221 (s), 1172 (w), 1157 (w), 1123 (w), 1096 (w), 1016 (w), 848 (w), 832 (w), 821 (w), 799 (m), 777 (vs), 720 (vw), 701 (w).

MS (70 eV, EI): m/z (%): 391 (13), 170 (24), 155 (100), 109 (14).

HRMS (EI) for $C_{26}H_{30}FNO$: calc. $[M]^{+\bullet}$: 391.2311, found: 391.2314

$[\alpha]_D^{20}$: +5.7 (c = 1.05, $CHCl_3$).

(1*R*,3*S*,5*R*,7*R*)-2-((*R*)-1-(3-Fluoro-4-methoxyphenyl)butan-2-yl)adamantan-2-ol (*R*-152at):



(*R*)-**152at**

The alcohol (*R*)-**152at** was prepared according to **TP11** from the iodide (*R*)-**142u** (30.8 mg, 0.1 mmol, 1.0 equiv) and adamantanone (**151p**, 45.0 mg, 0.3 mmol, 3.0 equiv) at −40 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*R*)-**152at** (27.9 mg, 0.084 mmol, 84%, 92% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.96–6.82 (m, 3H), 3.86 (s, 3H), 2.82 (dd, *J* = 14.1, 3.8 Hz, 1H), 2.39 (dd, *J* = 14.1, 9.2 Hz, 1H), 2.23–2.11 (m, 3H), 2.08–1.96 (m, 2H), 1.88–1.77 (m, 4H), 1.73–1.56 (m, 6H), 1.55–1.42 (m, 1H), 1.37–1.20 (m, 2H), 0.81 (t, *J* = 7.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 244.9 Hz), 145.5 (d, *J* = 10.8 Hz), 136.0 (d, *J* = 5.9 Hz), 124.8 (d, *J* = 3.4 Hz), 116.8 (d, *J* = 17.6 Hz), 113.3 (d, *J* = 2.1 Hz), 77.4, 56.4, 43.8, 38.3, 35.0, 34.7, 34.3, 34.2, 33.3, 33.2, 33.2, 27.1, 27.0, 20.5, 13.2.

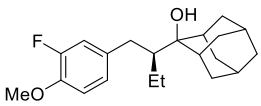
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2905 (s), 2857 (m), 1624 (vw), 1584 (w), 1515 (vs), 1462 (m), 1454 (m), 1442 (m), 1428 (w), 1377 (w), 1363 (w), 1352 (w), 1308 (m), 1271 (vs), 1224 (s), 1201 (w), 1182 (w), 1125 (s), 1099 (m), 1067 (w), 1059 (w), 1030 (m), 1015 (m), 987 (m), 956 (m), 930 (m), 914 (w), 870 (w), 838 (vw), 803 (w), 791 (m), 775 (w), 760 (m).

MS (70 eV, EI): m/z (%): 285 (62), 151 (100), 139 (41), 107 (7), 91 (25).

HRMS (EI) for $C_{21}H_{27}FO$: calc. $[M-H_2O]^{+\bullet}$: 314.2046, found: 314.2042.

$[\alpha]_D^{20}$: −9.10 (c = 0.76, $CHCl_3$).

(1*R*,3*S*,5*R*,7*R*)-2-((*S*)-1-(3-Fluoro-4-methoxyphenyl)butan-2-yl)adamantan-2-ol (*S*-152at):



(*S*)-**152at**

The alcohol (*S*)-**152at** was prepared according to **TP11** from the iodide (*S*)-**142u** (30.8 mg, 0.1 mmol, 1.0 equiv) and adamantanone (**151p**, 45.0 mg, 0.3 mmol, 3.0 equiv) at −40 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152at** (26.9 mg, 0.081 mmol, 81%, 90% *ee*) as colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.96–6.83 (m, 3H), 3.87 (s, 3H), 2.83 (dd, *J* = 14.1, 3.8 Hz, 1H), 2.39 (dd, *J* = 14.0, 9.2 Hz, 1H), 2.22–2.12 (m, 3H), 2.08–1.98 (m, 2H), 1.87–1.76 (m, 4H), 1.73–1.58 (m, 6H), 1.55–1.42 (m, 1H), 1.37–1.20 (m, 2H), 0.81 (t, *J* = 7.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 244.7 Hz), 145.5 (d, *J* = 10.7 Hz), 136.0 (d, *J* = 5.9 Hz), 124.8 (d, *J* = 3.3 Hz), 116.8 (d, *J* = 17.6 Hz), 113.3 (d, *J* = 2.2 Hz), 77.4, 56.5, 43.8, 38.4, 35.0, 34.8, 34.3, 34.2, 33.3, 33.3, 33.2, 27.2, 27.0, 20.5, 13.2.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3482 (vw), 2907 (vs), 2856 (s), 1732 (w), 1720 (m), 1702 (m), 1676 (w), 1624 (vw), 1584 (w), 1517 (vs), 1454 (m), 1444 (m), 1378 (w), 1353 (w), 1310 (w), 1273 (s), 1225 (m), 1182 (w), 1126 (m), 1100 (w), 1059 (w), 1031 (m), 1020 (m), 998 (w), 988 (w), 956 (w), 932 (w), 874 (w), 803 (w), 793 (w), 774 (vw), 760 (w), 722 (w), 696 (vw).

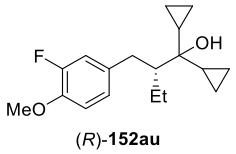
MS (70 eV, EI): m/z (%): 314 (9), 285 (29), 182 (6), 151 (100), 139 (28).

HRMS (EI) for $C_{21}H_{29}FO_2$: calc. $[M]^{+\bullet}$: 332.2119, found: 332.2111.

$[\alpha]_D^{20}$: +11.6 (c = 0.86, $CHCl_3$).

A solution of alkyl iodide (*S*-**142u**, 0.08 M, 1.00 equiv) and adamantanone (**151p**, 0.20 M, 2.50 equiv) in hexane:Et_2O (2:1) and a solution of *t*-BuLi (ca. 0.20 M in hexane, 2.85 equiv) were prepared. The solution of *t*-BuLi was pumped by pump A (flow rate A: 5.7 mL/min) into a precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The solution of the alkyl iodide was pumped by pump B (flow rate B: 5.0 mL/min) into a second precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The precooled solutions were mixed in a T-shaped mixer and passed within a residence time of (t^1 = 5.5 to 5.6 s) through a coil reactor (V_R = 1.0 mL) at the corresponding temperature (T^1 = –20 to 25 °C). The stream was subsequently upon reaching steady state injected for 4 min 42 s into a flask charged with sat. aq. NH_4Cl. The aqueous phase was extracted Et_2O (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was removed under reduced pressure and the remaining crude product was purified by flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152at** (352 mg, 1.1 mmol, 61%, 93% *ee*) as white solid.

(*R*)-1,1-Dicyclopropyl-2-(3-fluoro-4-methoxybenzyl)butan-1-ol (*R*-152au):



(*R*)-**152au**

The alcohol (*R*)-**152au** was prepared according to **TP11** from the iodide (*R*)-**142u** (30.8 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 28 µL, 27.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The

crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*R*)-**152au** (18.1 mg, 0.062 mmol, 62%, 93% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.02–6.90 (m, 2H), 6.85 (t, *J* = 8.5 Hz, 1H), 3.86 (s, 3H), 3.09 (dd, *J* = 14.1, 4.2 Hz, 1H), 2.45 (dd, *J* = 14.2, 8.4 Hz, 1H), 1.87–1.72 (m, 2H), 1.43–1.27 (m, 1H), 0.96–0.76 (m, 6H), 0.52–0.36 (m, 6H), 0.31–0.20 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 244.7 Hz), 145.5 (d, *J* = 10.8 Hz), 136.4 (d, *J* = 6.0 Hz), 124.5 (d, *J* = 3.3 Hz), 116.6 (d, *J* = 17.7 Hz), 113.3 (d, *J* = 2.1 Hz), 73.3, 56.4, 54.4, 35.9, 23.4, 17.3, 16.6, 14.1, 1.9, 1.6, -0.6, -0.8.

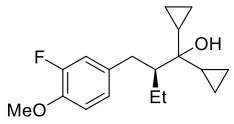
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3594 (vw), 3083 (vw), 3006 (w), 2957 (w), 2930 (m), 2873 (w), 2843 (w), 2840 (w), 1624 (vw), 1584 (w), 1515 (vs), 1463 (m), 1442 (m), 1427 (w), 1378 (w), 1270 (s), 1224 (m), 1182 (w), 1146 (w), 1126 (m), 1055 (w), 1027 (s), 986 (m), 956 (m), 926 (w), 912 (w), 876 (w), 848 (vw), 832 (w), 828 (w), 823 (w), 804 (m), 786 (w), 782 (w), 779 (w), 772 (w), 761 (m).

MS (70 eV, EI): m/z (%): 245 (4), 139 (100), 111 (30), 91 (12), 69 (24).

HRMS (EI) for $C_{18}H_{25}FO_2$: calc. $[M]^{+\bullet}$: 292.1839, found: 292.1832.

$[\alpha]_D^{20}$: +33.1 (c = 1.00, $CHCl_3$).

(*S*)-1,1-Dicyclopropyl-2-(3-fluoro-4-methoxybenzyl)butan-1-ol (*S*-152au):



(*S*)-**152au**

The alcohol (*S*)-**152au** was prepared according to **TP11** from the iodide (*S*)-**142u** (30.8 mg, 0.1 mmol, 1.0 equiv) and dicyclopropyl ketone (**151a**, 28 µL, 27.5 mg, 0.25 mmol, 2.5 equiv) at −78 °C. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**152au** (19.0 mg, 0.062 mmol, 62%, 90% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.01–6.82 (m, 3H), 3.86 (s, 3H), 3.09 (dd, *J* = 14.1, 4.3 Hz, 1H), 2.45 (dd, *J* = 14.1, 8.4 Hz, 1H), 1.82–1.73 (m, 2H), 1.40–1.30 (m, 1H), 0.93–0.78 (m, 6H), 0.50–0.36 (m, 6H), 0.26 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 152.3 (d, *J* = 244.7 Hz), 145.5 (d, *J* = 10.7 Hz), 136.4 (d, *J* = 5.9 Hz), 124.5 (d, *J* = 3.3 Hz), 116.7 (d, *J* = 17.8 Hz), 113.3 (d, *J* = 2.3 Hz), 73.3, 56.4, 54.4, 35.9, 23.4, 17.3, 16.6, 14.1, 2.0, 1.6, -0.6, -0.8.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3608 (vw), 3601 (vw), 3086 (vw), 3007 (w), 2958 (m), 2931 (m), 2874 (w), 2362 (vw), 1733 (vw), 1719 (vw), 1702 (vw), 1624 (vw), 1584 (w), 1517 (vs), 1464 (m), 1444 (m), 1428 (w),

1379 (w), 1272 (s), 1225 (m), 1183 (w), 1126 (m), 1055 (w), 1028 (m), 987 (m), 956 (w), 928 (w), 913 (w), 876 (w), 804 (w), 761 (m).

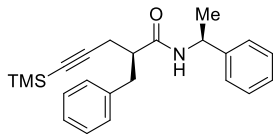
MS (70 eV, EI): m/z (%): 245 (7), 165 (7), 152 (9), 139 (98), 111 (74), 105 (11), 77 (20), 69 (100).

HRMS (EI) for $C_{18}H_{25}FO_2$: calc. $[M]^{+\bullet}$: 292.1839, found: 292.1836.

$[\alpha]_D^{20}$: −32.0 (c = 1.00, $CHCl_3$).

A solution of alkyl iodide (*S*-**142u**, 0.08 M, 1.00 equiv) and dicyclopropyl ketone (**151a**, 0.20 M, 2.50 equiv) in hexane:Et_2O (2:1) and a solution of *t*-BuLi (ca. 0.20 M in hexane, 2.85 equiv) were prepared. The solution of *t*-BuLi was pumped by pump A (flow rate A: 5.7 mL/min) into a precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The solution of the alkyl iodide was pumped by pump B (flow rate B: 5.0 mL/min) into a second precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The precooled solutions were mixed in a T-shaped mixer and passed within a residence time of (t^1 = 5.5 to 5.6 s) through a coil reactor (V_R = 1.0 mL) at the corresponding temperature (T^1 = –20 to 25 °C). The stream was subsequently upon reaching steady state injected for 4 min 42 s into a flask charged with sat. aq. NH_4Cl. The aqueous phase was extracted Et_2O (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was removed under reduced pressure and the remaining crude product was purified by flash column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (*S*)-**4ac** (293 mg, 1.0 mmol, 56%, 94% *ee*) as white solid.

(*S*)-2-Benzyl-*N*-((*S*)-1-phenylethyl)-5-(trimethylsilyl)pent-4-ynamide (2'*S*,3*S*-152av):



(2'*S*,3*S*)-**152av**

A solution of alkyl iodide (*S*-**142v**, 0.08 M, 1.00 equiv) and electrophile (*S*-**151i**, 0.20 M, 2.50 equiv) in hexane:Et_2O (2:1) and a solution of *t*-BuLi (ca. 0.20 M in hexane, 3.00 equiv) were prepared. The solution of *t*-BuLi was pumped by pump A (flow rate A: 6.0 mL/min) into a precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The solution of the alkyl iodide was pumped by pump B (flow rate B: 5.0 mL/min) into a second precooling loop (V_{pre} = 2.0 mL) at T^1 = –20 to 25 °C. The precooled solutions were mixed in a T-shaped mixer and passed within a residence time of (t^1 = 5.5 to 5.6 s) through a coil reactor (V_R = 1.0 mL) at the corresponding temperature (T^1 = –20 to 25 °C). The stream was subsequently upon reaching steady state injected for 120 s into a flask charged with sat. aq. NH_4Cl. The aqueous phase was extracted Et_2O (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$. The crude product was purified by column chromatography on silica gel with diethyl ether/pentane = 1:4 to afford (2'*S*,3*S*)-**152av** (194 mg, 0.53 mmol, 67%, dr = 96:4, 96% *ee*) as white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.25–7.19 (m, 6H), 7.12 (dd, *J* = 7.4, 2.0 Hz, 2H), 7.03–6.98 (m, 2H), 5.70 (d, *J* = 8.0 Hz, 1H), 5.08 (p, *J* = 7.1 Hz, 1H), 2.95 (dd, *J* = 13.4, 8.3 Hz, 1H), 2.83 (dd, *J* = 13.4, 5.3 Hz, 1H), 2.63–2.39 (m, 3H), 1.44 (d, *J* = 6.9 Hz, 3H), 0.15 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 172.3, 142.9, 139.2, 129.2, 128.7, 128.6, 127.3, 126.6, 126.2, 104.7, 87.1, 49.4, 48.6, 38.2, 23.2, 21.8, 0.2.

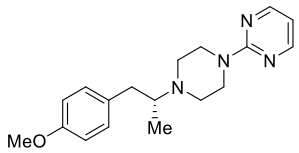
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3262 (w), 3067 (vw), 3030 (vw), 2964 (w), 2928 (w), 2899 (vw), 2180 (w), 1638 (m), 1546 (m), 1506 (w), 1494 (w), 1452 (w), 1420 (w), 1381 (w), 1341 (vw), 1318 (w), 1247 (m), 1207 (w), 1194 (vw), 1180 (vw), 1132 (w), 1122 (w), 1054 (w), 1033 (w), 1022 (w), 1012 (w), 997 (w), 890 (vw), 840 (vs), 782 (w), 759 (m), 740 (m), 696 (vs).

MS (70 eV, EI): m/z (%): 363 (32), 272 (19), 252 (91), 168 (20), 148 (40), 105 (100), 91 (25), 73 (21).

HRMS (EI) for $C_{23}H_{29}NOSi$: calc. $[M]^{+\bullet}$: 363.2018, found: 363.2011

$[\alpha]_D^{20}$: +25.9 (c = 1.51, $CHCl_3$).

(*R*)-2-(4-(1-(4-Methoxyphenyl)propan-2-yl)piperazin-1-yl)pyrimidine (*R*-155a):



(*R*)-**155a**

The tertiary amine (*R*)-**155a** was prepared according to **TP9** from the iodide (*R*)-**142f** (27.6 mg, 0.1 mmol, 1.0 equiv) and 4-(pyrimidin-2-yl)piperazin-1-yl benzoate (**154a**, 56.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/ethyl acetate (1:1) to afford (*R*)-**155a** (22.8 mg, 0.073 mmol, 73%, 91% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.31 (d, *J* = 4.7 Hz, 2H), 7.11–7.08 (m, 2H), 6.84–6.81 (m, 2H), 6.47 (t, *J* = 4.7 Hz, 1H), 3.84 (t, *J* = 5.1 Hz, 4H), 3.79 (s, 3H), 2.96 (dd, *J* = 13.3, 4.2 Hz, 1H), 2.83 (s, 1H), 2.67 (t, *J* = 5.2 Hz, 4H), 2.39 (dd, *J* = 13.2, 9.6 Hz, 1H), 0.96 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 161.9, 158.0, 157.9 132.7, 130.3, 113.8, 110.2, 109.9, 61.9, 55.4, 48.6, 44.3, 38.7, 14.4.

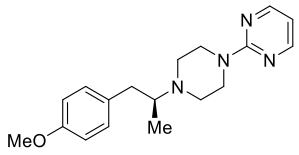
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2961 (w), 2950 (w), 2942 (w), 2930 (w), 2929 (w), 2925 (w), 2906 (w), 2855 (w), 2851 (w), 2358 (w), 1610 (w), 1585 (vs), 1570 (w), 1558 (w), 1546 (m), 1533 (w), 1511 (s), 1499 (m), 1496 (m), 1477 (m), 1474 (m), 1468 (m), 1465 (m), 1463 (m), 1457 (m), 1448 (m), 1437 (m), 1430 (w), 1419 (w), 1392 (w), 1358 (m), 1306 (w), 1260 (m), 1247 (m), 1230 (w), 1222 (w), 1220 (w), 1178 (w), 1092 (w), 1087 (w), 1083 (w), 1036 (m), 1018 (w), 1014 (w), 982 (m), 976 (w), 816 (w), 812 (w), 797 (m), 668 (w).

MS (70 eV, EI): m/z (%): 191 (100), 148 (45), 122 (81).

HRMS (EI) for $C_{18}H_{25}N_4O$: calc. $[M+H]^{+\bullet}$: 313.2028, found: 313.2025.

$[\alpha]_D^{20}$: −21.4 (c = 0.84, $CHCl_3$).

(*S*)-2-(4-(1-(4-Methoxyphenyl)propan-2-yl)piperazin-1-yl)pyrimidine (*S*-155a):



(*S*)-**155a**

The tertiary amine (*S*)-**155a** was prepared according to **TP9** from the iodide (*S*)-**142f** (27.6 mg, 0.1 mmol, 1.0 equiv) and 4-(pyrimidin-2-yl)piperazin-1-yl benzoate (**154a**, 56.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/ethyl acetate (1:1) to afford (*S*)-**155a** (22.9 mg, 0.073 mmol, 73%, 88% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.31 (d, *J* = 4.7 Hz, 2H), 7.12–7.08 (m, 2H), 6.85–6.81 (m, 2H), 6.48 (t, *J* = 4.7 Hz, 1H), 3.84 (t, *J* = 5.1 Hz, 4H), 3.79 (s, 3H), 3.00–2.92 (m, 1H), 2.83 (s, 1H), 2.67 (t, *J* = 5.1 Hz, 4H), 2.39 (dd, *J* = 13.1, 9.6 Hz, 1H), 0.96 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 161.8, 158.0, 157.9, 132.6, 130.3, 113.8, 110.2, 109.9, 61.9, 55.4, 48.6, 44.3, 38.7, 14.3.

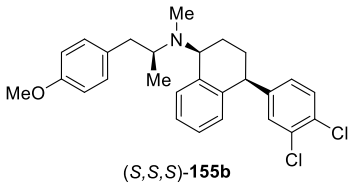
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2992 (w), 2958 (w), 2955 (w), 2928 (m), 2926 (m), 2924 (m), 2882 (w), 2878 (w), 2854 (w), 2852 (w), 2838 (w), 2832 (w), 2813 (w), 2810 (w), 2362 (w), 2360 (w), 2358 (w), 2357 (w), 1611 (w), 1585 (vs), 1546 (m), 1533 (w), 1511 (vs), 1447 (m), 1392 (w), 1377 (w), 1375 (w), 1358 (m), 1306 (w), 1261 (m), 1247 (s), 1226 (w), 1220 (w), 1179 (w), 1159 (w), 1139 (w), 1117 (w), 1037 (w), 982 (m), 803 (w), 800 (w), 797 (w), 778 (w), 668 (w).

MS (70 eV, EI): m/z (%): 191 (82), 148 (49), 122 (100).

HRMS (EI) for $C_{18}H_{25}N_4O$: calc. $[M+H]^{+\bullet}$: 313.2028, found: 313.2022.

$[\alpha]_D^{20}$: +19.4 (c = 0.92, $CHCl_3$).

(1*S*,4*S*)-4-(3,4-Dichlorophenyl)-*N*-((*S*)-1-(4-methoxyphenyl)propan-2-yl)-N-methyl-1,2,3,4-tetrahydronaphthalen-1-amine (*S*,*S*,*S*-155b):



(*S*,*S*,*S*)-**155b**

The tertiary amine (*S*,*S*,*S*)-**155b** was prepared according to **TP9** from the iodide (*R*)-**142f** (27.6 mg, 0.1 mmol, 1.0 equiv) and *O*-benzoyl-*N*-((1*S*,4*S*)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydronaphthalen-1-yl)-*N*-methylhydroxylamine (**154b**, 85.3 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (4:1) to afford (*S*,*S*,*S*)-**155b** (23.6 mg, 0.052 mmol, 52%, dr = 91:9) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.56–7.51 (m, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 7.19–7.15 (m, 1H), 7.14 (d, *J* = 2.1 Hz, 1H), 7.11 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.07–7.03 (m, 2H), 6.85–6.82 (m, 2H), 6.81–6.77 (m, 2H), 4.07 (t, *J* = 5.6 Hz, 1H), 3.94 (dd, *J* = 8.8, 4.9 Hz, 1H), 3.77 (s, 3H), 3.09–3.00 (m, 1H), 2.92 (dd, *J* = 13.3, 5.4 Hz, 1H), 2.54 (dd, *J* = 13.4, 8.6 Hz, 1H), 2.26 (s, 3H), 2.09–2.04 (m, 2H), 1.98–1.91 (m, 1H), 1.83–1.75 (m, 1H), 1.70–1.62 (m, 1H), 1.01 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.9, 148.1, 140.1, 138.6, 132.9, 132.2, 130.9, 130.3, 130.1, 129.8, 129.5, 128.3, 126.9, 126.8, 126.6, 113.7, 77.5, 77.2, 76.8, 59.9, 57.8, 55.4, 44.1, 41.1, 33.0, 29.8, 21.1, 16.6.

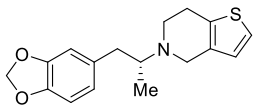
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3344 (w), 3188 (vw), 3061 (w), 2925 (vs), 2854 (s), 1734 (w), 1716 (w), 1669 (m), 1612 (m), 1585 (w), 1560 (w), 1541 (vw), 1512 (s), 1466 (s), 1419 (w), 1394 (m), 1378 (m), 1301 (m), 1286 (w), 1247 (vs), 1201 (w), 1177 (m), 1131 (m), 1114 (w), 1069 (w), 1031 (m), 881 (vw), 847 (w), 820 (w), 764 (w), 741 (w), 721 (w), 711 (w), 677 (vw).

MS (70 eV, EI): m/z (%): 332 (17), 275 (25), 161 (21), 159 (34).

HRMS (EI) for $C_{27}H_{29}Cl_2NO$: calc. $[M-C_8H_9O]^{+\bullet}$: 332.0973, found: 332.0944.

$[\alpha]_D^{20}$: −45.8 (c = 0.48, $CHCl_3$).

(*R*)-5-(1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine (*R*-155c):



(*R*)-**155c**

The tertiary amine (*R*)-**155c** was prepared according to **TP9** from the iodide (*R*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and 6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl benzoate (**154c**, 51.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/ethyl acetate (4:1) to afford (*R*)-**155c** (25.6 mg, 0.085 mmol, 85%, 87% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.07 (d, *J* = 5.1 Hz, 1H), 6.76–6.69 (m, 3H), 6.64 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.93 (s, 2H), 3.74 (s, 2H), 3.06–2.94 (m, 2H), 2.90 (t, *J* = 1.0 Hz, 4H), 2.50–2.40 (m, 1H), 1.04 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.6, 145.8, 134.5, 134.4, 133.7, 125.5, 122.8, 122.2, 109.7, 108.3, 100.9, 61.4, 48.8, 46.4, 39.5, 26.5, 14.5.

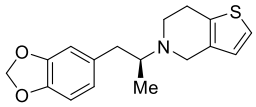
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2961 (m), 2956 (m), 2946 (m), 2942 (m), 2926 (s), 2924 (s), 2921 (s), 2908 (m), 2901 (m), 2898 (m), 2893 (m), 2882 (m), 2880 (m), 2874 (m), 2854 (m), 1502 (s), 1489 (vs), 1457 (m), 1440 (m), 1437 (m), 1249 (vs), 1122 (m), 1117 (m), 1114 (m), 1112 (m),), 1091 (m), 1087 (m), 1084 (m), 1080 (m), 1079 (m), 1075 (m), 1073 (m), 1070 (m), 1067 (m), 1065 (m), 1064 (m), 1062 (m), 1060 (m), 1038 (vs), 1023 (s), 1020 (m), 928 (m), 814 (m), 808 (s), 803 (s), 800 (s), 797 (s), 668 (m).

MS (70 eV, EI): m/z (%): 166 (100), 123 (6), 56 (12).

HRMS (EI) for $C_{17}H_{19}NO_2S$: calc. $[M+H]^{+\bullet}$: 302.1215, found: 302.1208.

$[\alpha]_D^{20}$: −15.5 (c = 0.51, $CHCl_3$).

(*S*)-5-(1-(Benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine (*S*-155c):



(*S*)-**155c**

The tertiary amine (*S*)-**155c** was prepared according to **TP9** from the iodide (*S*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and 6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl benzoate (**154c**, 51.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/ethyl acetate (4:1) to afford (*S*)-**155c** (22.0 mg, 0.073 mmol, 73%, 88% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.08 (d, *J* = 5.1 Hz, 1H), 6.78–6.69 (m, 3H), 6.64 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.93 (s, 2H), 3.74 (d, *J* = 1.8 Hz, 2H), 3.06–2.93 (m, 2H), 2.90 (d, *J* = 1.3 Hz, 4H), 2.50–2.40 (m, 1H), 1.04 (d, *J* = 6.4 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.6, 145.8, 134.5, 134.4, 133.7, 125.5, 122.8, 122.2, 109.7, 108.3, 100.9, 61.4, 48.8, 46.4, 39.5, 26.5, 14.4.

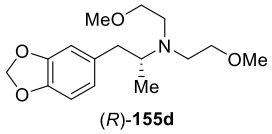
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2958 (w), 2955 (w), 2922 (m), 2901 (m), 2895 (m), 2885 (w), 2882 (w), 2874 (w), 2863 (w), 2853 (w), 1739 (w), 1734 (w), 1652 (w), 1646 (w), 1501 (s), 1488 (vs), 1456 (m), 1440 (s), 1380 (w), 1370 (w), 1358 (w), 1334 (w), 1317 (w), 1247 (vs), 1208 (m), 1188 (m), 1174 (m), 1167 (w), 1122 (w), 1120 (w), 1098 (m), 1079 (w), 1038 (s), 940 (m), 928 (m), 832 (w), 807 (m), 781 (w), 772 (w), 705 (m), 702 (m), 668 (w).

MS (70 eV, EI): m/z (%): 166 (100), 135 (10), 56 (25).

HRMS (EI) for $C_{17}H_{19}NO_2S$: calc. $[M+H]^{+\bullet}$: 302.1215, found: 302.1213.

$[\alpha]_D^{20}$: +18.8 (c = 0.70, $CHCl_3$).

(*R*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-*N*,*N*-bis(2-methoxyethyl)propan-2-amine (*R*-155d):



(*R*)-**155d**

The tertiary amine (*R*)-**155d** was prepared according to **TP9** from the iodide (*R*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and *O*-benzoyl-*N*,*N*-bis(2-methoxyethyl)hydroxylamine (**154d**, 50.7 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate to afford (*R*)-**155d** (23.0 mg, 0.078 mmol, 78%, 93% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.74–6.66 (m, 2H), 6.60 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.91 (s, 2H), 3.39 (t, *J* = 6.5 Hz, 4H), 3.34 (s, 6H), 2.99–2.86 (m, 1H), 2.82 (dd, *J* = 13.1, 5.0 Hz, 1H), 2.71 (td, *J* = 6.6, 2.8 Hz, 4H), 2.31 (dd, *J* = 13.1, 9.1 Hz, 1H), 0.93 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.5, 145.7, 134.7, 122.1, 109.7, 108.1, 100.9, 72.7, 59.6, 59.0, 50.7, 39.6, 15.0.

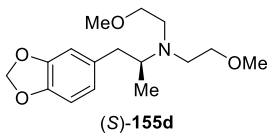
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2958 (m), 2923 (s), 2872 (s), 2854 (s), 1503 (m), 1489 (vs), 1455 (m), 1441 (m), 1370 (w), 1247 (vs), 1190 (m), 1152 (w), 1119 (vs), 1039 (s), 962 (w), 941 (m), 928 (m), 808 (m).

MS (70 eV, EI): m/z (%): 160 (100), 158 (50), 135 (18), 126 (14), 102 (11), 94 (18), 59 (10).

HRMS (EI) for $C_{16}H_{25}NO_4$: calc. $[M-H_2]^{+\bullet}$: 293.1627, found: 293.1623.

$[\alpha]_D^{20}$: −8.3 (c = 0.59, $CHCl_3$).

(*S*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-*N*,*N*-bis(2-methoxyethyl)propan-2-amine (*S*-155d):



(*S*)-**155d**

The tertiary amine (*S*)-**155d** was prepared according to **TP9** from the iodide (*S*)-**142k** (29.0 mg, 0.1 mmol, 1.0 equiv) and *O*-benzoyl-*N*,*N*-bis(2-methoxyethyl)hydroxylamine (**154d**, 50.7 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate to afford (*S*)-**155d** (20.7 mg, 0.070 mmol, 70%, 84% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 6.74–6.66 (m, 2H), 6.60 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.92 (s, 2H), 3.39 (t, *J* = 6.5 Hz, 4H), 3.34 (s, 6H), 2.97–2.88 (m, 1H), 2.82 (dd, *J* = 13.1, 4.9 Hz, 1H), 2.75–2.67 (m, 4H), 2.32 (dd, *J* = 13.2, 9.1 Hz, 1H), 0.93 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 147.5, 145.7, 134.7, 122.2, 109.7, 108.1, 100.9, 72.7, 59.6, 59.0, 50.7, 39.6, 15.0.

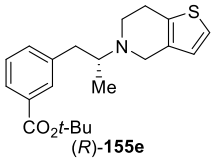
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2958 (m), 2924 (m), 2873 (m), 2853 (m), 2815 (w), 1743 (m), 1503 (m), 1489 (s), 1450 (m), 1442 (m), 1365 (w), 1246 (vs), 1197 (m), 1119 (vs), 1080 (m), 1059 (m), 1039 (s), 1024 (m), 962 (w), 940 (w), 928 (m), 808 (w), 710 (m).

MS (70 eV, EI): m/z (%): 160 (100), 135 (14), 102 (20), 96 (9), 70 (18), 59 (25).

HRMS (EI) for $C_{16}H_{25}NO_4$: calc. $[M-H]^{+\bullet}$: 294.1705, found: 294.1696.

$[\alpha]_D^{20}$: +9.2 (c = 0.61, $CHCl_3$).

***tert*-Butyl (*R*)-3-(2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl)propyl)benzoate (*R*-155e):**



(*R*)-**155e**

The tertiary amine (*R*)-**155e** was prepared according to **TP9** from the iodide (*R*)-**142i** (34.6 mg, 0.1 mmol, 1.0 equiv) and 6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl benzoate (**154c**, 51.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate to afford (*R*)-**155e** (24.3 mg, 0.068 mmol, 68%, 83% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.82 (dd, *J* = 6.8, 1.6 Hz, 2H), 7.40–7.28 (m, 2H), 7.08 (d, *J* = 5.1 Hz, 1H), 6.75 (d, *J* = 5.1 Hz, 1H), 3.76 (d, *J* = 1.9 Hz, 2H), 3.16–3.01 (m, 2H), 2.99–2.87 (m, 4H), 2.64–2.54 (m, 1H), 1.59 (s, 9H), 1.04 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.1, 140.7, 134.4, 133.7, 133.5, 132.2, 130.3, 128.3, 127.3, 125.5, 122.8, 81.1, 61.1, 48.7, 46.4, 39.5, 28.3, 26.5, 14.5.

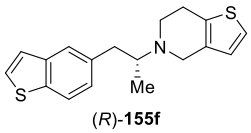
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2961 (w), 2927 (m), 2856 (w), 1741 (m), 1711 (s), 1606 (vw), 1587 (w), 1477 (w), 1456 (w), 1404 (w), 1392 (w), 1367 (m), 1336 (w), 1292 (s), 1256 (m), 1219 (m), 1209 (m), 1160 (vs), 1110 (s), 1088 (m), 1053 (w), 1043 (w), 1001 (w), 978 (w), 934 (w), 903 (w), 850 (w), 832 (w), 747 (s), 697 (s), 675 (w), 666 (w).

MS (70 eV, EI): m/z (%):284 (4), 166 (100), 110 (3), 56 (12).

HRMS (EI) for $C_{21}H_{27}SNO_2$: calc. $[M]^{+\bullet}$: 357.1762, found: 357.1762.

$[\alpha]_D^{20}$: −18.8 (c = 0.51, $CHCl_3$).

(*R*)-5-(1-(Benzo[*b*]thiophen-5-yl)propan-2-yl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine (*R*-155f):



(*R*)-**155f**

The tertiary amine (*R*)-**155f** was prepared according to **TP9** from the iodide (*R*)-**142l** (30.2 mg, 0.1 mmol, 1.0 equiv) and 6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl benzoate (**154c**, 51.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *i*-hexanes/dichloro methane/ethyl acetate (1:1:1) to afford (*R*)-**155f** (26.3 mg, 0.084 mmol, 84%, 88% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.80 (dt, *J* = 8.2, 0.8 Hz, 1H), 7.65 (d, *J* = 1.7 Hz, 1H), 7.43 (d, *J* = 5.5 Hz, 1H), 7.29 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.21 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.09 (d, *J* = 5.1 Hz, 1H), 6.76 (d, *J* = 5.1 Hz, 1H), 3.80 (s, 2H), 3.22 (dd, *J* = 12.9, 4.0 Hz, 1H), 3.12 (m, 1H), 2.98–2.91 (m, 4H), 2.65 (dd, *J* = 12.9, 9.8 Hz, 1H), 1.07 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 137.6, 136.7, 134.5, 133.7, 126.7, 126.1, 125.5, 124.1, 123.7, 122.9, 122.4, 61.6, 48.8, 46.6, 39.7, 26.5, 14.6.

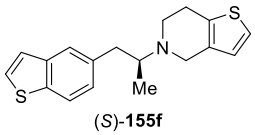
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2965 (m), 2959 (m), 2954 (m), 2935 (m), 2930 (m), 2928 (m), 2924 (m), 2921 (m), 2919 (m), 2911 (m), 2908 (m), 2360 (w), 2336 (w), 1584 (w), 1517 (vs), 1453 (m), 1445 (m), 1443 (m), 1275 (s), 1224 (m), 1127 (m), 1029 (m), 760 (m), 702 (m), 668 (m).

MS (70 eV, EI): m/z (%): 207 (5), 166 (100), 147 (16), 110 (10), 56 (27).

HRMS (EI) for $C_{18}H_{19}NS_2$: calc. $[M-H]^{+\bullet}$: 312.0875, found: 312.0870.

$[\alpha]_D^{20}$: −5.0 (c = 0.60, $CHCl_3$).

(*S*)-5-(1-(Benzo[*b*]thiophen-5-yl)propan-2-yl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine (*S*-155f):



(*S*)-**155f**

The tertiary amine (*S*)-**155f** was prepared according to **TP9** from the iodide (*S*)-**142l** (30.2 mg, 0.1 mmol, 1.0 equiv) and 6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl benzoate (**154c**, 51.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with i-hexanes/dichloro methane/ethyl acetate (1:1:1) to afford (*S*)-**155f** (26.3 mg, 0.085 mmol, 85%, 97% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.80 (d, *J* = 8.2 Hz, 1H), 7.66–7.63 (m, 1H), 7.43 (d, *J* = 5.4 Hz, 1H), 7.29 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.21 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.09 (d, *J* = 5.1 Hz, 1H), 6.76 (d, *J* = 5.1 Hz, 1H), 3.79 (d, *J* = 1.6 Hz, 2H), 3.22 (dd, *J* = 12.9, 4.0 Hz, 1H), 3.18–3.05 (m, 1H), 2.98–2.90 (m, 4H), 2.65 (dd, *J* = 12.9, 9.9 Hz, 1H), 1.07 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 137.6, 136.7, 134.5, 133.7, 126.7, 126.1, 125.5, 124.1, 123.7, 122.8, 122.4, 61.6, 48.8, 46.5, 39.7, 26.5, 14.6.

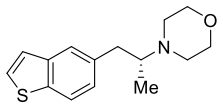
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2965 (m), 2962 (m), 2932 (m), 2929 (m), 2922 (m), 2910 (w), 2908 (w), 2903 (w), 2838 (w), 2167 (m), 1624 (w), 1517 (vs), 1460 (m), 1456 (m), 1444 (m), 1442 (m), 1434 (m), 1313 (m), 1273 (vs), 1225 (m), 1135 (m), 1125 (s), 1029 (m), 955 (w), 809 (w), 807 (w), 805 (w), 761 (m).

MS (70 eV, EI): m/z (%): 166 (100), 147 (23), 110 (8), 56 (34).

HRMS (EI) for $C_{18}H_{19}NS_2$: calc. $[M-H_2]^{+\bullet}$: 311.0797, found: 311.0804.

$[\alpha]_D^{20}$: +6.7 (c = 0.58, $CHCl_3$).

(*R*)-4-(1-(Benzo[*b*]thiophen-5-yl)propan-2-yl)morpholine (*R*-155g):



(*R*)-**155g**

The tertiary amine (*R*)-**155g** was prepared according to **TP9** from the iodide (*R*)-**142l** (30.2 mg, 0.1 mmol, 1.0 equiv) and morpholino benzoate (**154e**, 41.5 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate to afford (*R*)-**155g** (18.8 mg, 0.072 mmol, 78%, 89% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.79 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 1.6 Hz, 1H), 7.42 (d, *J* = 5.5 Hz, 1H), 7.29–7.27 (m, 1H), 7.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.76 (t, *J* = 4.7 Hz, 4H), 3.14 (dd, *J* = 13.0, 4.3 Hz, 1H), 2.88–2.78 (m, 1H), 2.66 (t, *J* = 4.6 Hz, 4H), 2.53 (dd, *J* = 13.2, 9.7 Hz, 1H), 0.98 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 137.6, 127.2, 126.7, 126.1, 124.1, 123.7, 122.3, 67.5, 62.1, 49.3, 39.3, 14.5.

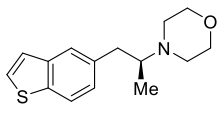
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2968 (m), 2964 (m) 2930 (s), 2928 (s), 2925 (s), 2922 (s), 2912 (m), 2906 (m), 2903 (m), 2900 (m), 2866 (m), 2853 (m), 2851 (m), 1739 (w), 1683 (w), 1674 (w), 1662 (w), 1456 (m), 1454 (m), 1448 (m), 1436 (m), 1255 (m), 1145 (m), 1116 (vs), 1104 (m), 1091 (m), 969 (m), 708 (m), 706 (m), 689 (m).

MS (70 eV, EI): m/z (%): 147 (15), 114 (100),

HRMS (EI) for $C_{15}H_{19}NOS$: calc. $[M]^{+\bullet}$: 260.1104, found: 260.1104.

$[\alpha]_D^{20}$: −5.3 (c = 0.95, $CHCl_3$).

(*S*)-4-(1-(Benzo[*b*]thiophen-5-yl)propan-2-yl)morpholine (*S*-155g):



(*S*)-**155g**

The tertiary amine (*S*)-**155g** was prepared according to **TP9** from the iodide (*S*)-**142l** (30.2 mg, 0.1 mmol, 1.0 equiv) and morpholino benzoate (**154e**, 41.5 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with ethyl acetate to afford (*S*)-**155g** (19.1 mg, 0.073 mmol, 73%, 94% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.79 (d, *J* = 8.3 Hz, 1H), 7.62 (d, *J* = 1.6 Hz, 1H), 7.42 (d, *J* = 5.4 Hz, 1H), 7.28 (dd, *J* = 5.5, 0.8 Hz, 1H), 7.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.79–3.73 (m, 4H), 3.14 (dd, *J* = 13.1, 4.3 Hz, 1H), 2.88–2.80 (m, 1H), 2.69–2.63 (m, 4H), 2.53 (dd, *J* = 13.1, 9.7 Hz, 1H), 0.98 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 140.0, 137.6, 136.6, 126.7, 126.1, 124.1, 123.7, 122.3, 67.5, 62.0, 49.3, 39.2, 14.4.

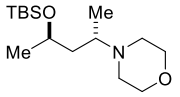
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2964 (m), 2962 (m), 2958 (m), 2950 (m), 2924 (m), 2922 (m), 2856 (m), 2362 (w), 2336 (w), 1739 (vs), 1719 (w), 1702 (w), 1644 (w), 1456 (m), 1451 (m), 1257 (vs), 1255 (vs), 1250 (vs), 1116 (s), 1103 (vs), 1085 (s), 1065 (s), 1049 (s), 1025 (m), 1009 (m), 709 (vs).

MS (70 eV, EI): m/z (%): 147 (51), 114 (100), 105 (28), 57 (21).

HRMS (EI) for $C_{15}H_{19}NOS$: calc. $[M-H]^{+\bullet}$: 260.1109, found: 260.1104.

$[\alpha]_D^{20}$: +5.8 (c = 1.08, $CHCl_3$).

4-(*anti*-4-((*tert*-Butyldimethylsilyl)oxy)pentan-2-yl)morpholine (*anti*-155h):



anti-**155h**

The amine *anti*-**155h** was prepared according to **TP9** from the iodide *anti*-**142b** (32.8 mg, 0.1 mmol, 1.0 equiv) and morpholino benzoate (**154e**, 41.4 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether and 2% triethylamine to afford *anti*-**155h** (17.9 mg, 0.063 mmol, 63%, dr = 14:86) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 3.91–3.84 (m, 1H), 3.71–3.68 (m, 4H), 2.73–2.64 (m, 1H), 2.52–2.48 (m, 4H), 1.74 (m, 1H), 1.25–1.19 (m, 1H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H).

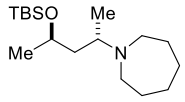
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 67.6, 66.3, 56.1, 48.9, 42.9, 26.0, 24.3, 18.2, 14.7, -4.0, -4.7.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2957 (s), 2928 (s), 2891 (m), 2889 (m), 2854 (m), 2814 (w), 1472 (m), 1462 (m), 1374 (m), 1361 (m), 1255 (m), 1157 (m), 1137 (m), 1118 (vs), 1079 (m), 1046 (m), 1031 (m), 1005 (m), 987 (m), 919 (m), 913 (m), 852 (w), 835 (s), 826 (m), 807 (m), 774 (s).

MS (70 eV, EI): m/z (%): 230 (4), 144 (6), 114 (100), 103 (7), 75 (10).

HRMS (EI) for $C_{15}H_{33}NO_2Si$: calc. $[M]^{+\bullet}$: 287.2281, found: 287.2275.

1-(*anti*-4-((*tert*-Butyldimethylsilyl)oxy)pentan-2-yl)azepane (*anti*-155i):



anti-**155i**

The amine *anti*-**155i** was prepared according to **TP9** from the iodide *anti*-**142b** (32.8 mg, 0.1 mmol, 1.0 equiv) and azepan-1-yl benzoate (**154f**, 43.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with diethyl ether to afford *anti*-**155i** (16.8 mg, 0.056 mmol, 56%, dr = 3:97) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 3.95–3.83 (m, 1H), 2.77 (m, 1H), 2.63–2.45 (m, 4H), 1.70 (dt, *J* = 13.7, 7.0 Hz, 2H), 1.62–1.55 (m, 7H), 1.33–1.21 (m, 1H), 1.21–1.15 (m, 1H), 1.13 (d, *J* = 6.0 Hz, 3H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H).

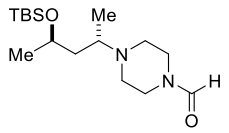
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 66.7, 57.2, 51.3, 43.8, 29.8, 27.0, 26.1, 23.9, 18.3, 15.0, -4.1, -4.6.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2955 (s), 2926 (vs), 2890 (m), 2884 (m), 2854 (s), 1472 (m), 1462 (m), 1445 (m), 1373 (m), 1361 (m), 1255 (s), 1177 (m), 1151 (m), 1135 (m), 1099 (m), 1060 (s), 1039 (s), 1005 (m), 834 (vs), 826 (s), 807 (m), 773 (vs), 722 (m).

MS (70 eV, EI): m/z (%): 284 (3), 127 (9), 126 (100), 103 (5), 75 (5).

HRMS (EI) for $C_{17}H_{37}NOSi$: calc. $[M]^{+\bullet}$: 299.2644, found: 299.2637.

4-(*anti*-4-((*tert*-Butyldimethylsilyl)oxy)pentan-2-yl)piperazine-1-carbaldehyde (*anti*-155j):



anti-**155j**

The amine *anti*-**155j** was prepared according to **TP9** from the iodide *anti*-**142b** (32.8 mg, 0.1 mmol, 1.0 equiv) and 4-formylpiperazin-1-yl benzoate (**154g**, 46.9 mg, 0.2 mmol, 2.0 equiv). The crude product was purified *via* flash column chromatography on silica gel with *n*-pentane/diethyl ether (10:1) and 2% triethylamine to afford *anti*-**155j** (19.5 mg, 0.062 mmol, 62%, dr = 8:92) as a colorless oil.

^{1}H-NMR (CD_2Cl_2, 400 MHz): δ [ppm] = 7.95 (s, 1H), 3.89 (dp, *J* = 7.6, 6.0 Hz, 1H), 3.50–3.41 (m, 2H), 3.31 (h, *J* = 4.3 Hz, 2H), 2.77 (q, *J* = 6.7 Hz, 1H), 2.55–2.37 (m, 4H), 1.68 (dt, *J* = 13.6, 6.8 Hz, 1H), 1.26–1.19 (m, 1H), 1.13 (d, *J* = 6.1 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H).

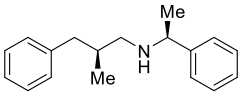
^{13}C-NMR (CD_2Cl_2, 100 MHz): δ [ppm] = 161.0, 66.7, 60.7, 56.5, 49.4, 48.1, 46.7, 43.8, 40.9, 26.2, 24.3, 18.5, 14.3, -4.0, -4.6.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3388 (m), 3386 (m), 3220 (w), 3217 (w), 3214 (w), 3212 (w), 3199 (w), 3196 (m), 3194 (m), 3192 (m), 3188 (m), 3186 (w), 3182 (w), 3180 (w), 3177 (w), 2362 (w), 2358 (w), 2357 (w), 2354 (w), 1645 (vs), 1628 (m), 1624 (m), 1617 (m), 1577 (m), 1513 (vw), 1448 (w), 1405 (w), 1300 (w), 1269 (vw), 1115 (w), 930 (vw), 773 (vw), 699 (w), 694 (w), 668 (w).

MS (70 eV, EI): m/z (%): 141 (100), 113 (18), 75 (13).

HRMS (EI) for $C_{16}H_{34}N_2O_2Si$: calc. $[M]^{+\bullet}$: 312.2390, found: 314.2381.

(*S*)-2-Methyl-3-phenyl-*N*-((*S*)-1-phenylethyl)propan-1-amine (2'*S*,3*S*-159):



(2'*S*,3*S*)-**159**

The secondary amine (2'*S*,3*S*)-**159** was prepared from the amide (2'*S*,3*S*)-**152ad** according to a modified literature procedure.[129] Thus, (2'*S*,3*S*)-**152ad** (133 mg, 0.5 mmol, 1.0 equiv) was dissolved in THF (2.5 mL). The mixture was cooled to 0 °C and $LiAlH_4$ (1.0 M in THF, 1.5 mL, 3.0 equiv) was added dropwise. The mixture was heated at 50 °C overnight and after completion, diluted with Et_2O (15 mL). The reaction was carefully quenched with sat. aq. $NaHCO_3$ (5 mL) and extracted with EtOAc (3 x 30 mL). The crude product was washed with Brine and concentrated under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:2 to afford (2'*S*,3*S*)-**159** (102.6 mg, 0.405 mmol, 81%, dr = 98:2, 96% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.36–7.28 (m, 4H), 7.28–7.21 (m, 3H), 7.20–7.10 (m, 3H), 3.73 (q, *J* = 6.6 Hz, 1H), 2.80 (dd, *J* = 13.4, 5.5 Hz, 1H), 2.45–2.34 (m, 2H), 2.30 (dd, *J* = 13.4, 8.6 Hz, 1H), 1.97–1.81 (m, 1H), 1.50 (d, *J* = 7.5 Hz, 1H), 1.33 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 146.1, 141.2, 129.3, 128.5, 128.3, 126.9, 126.8, 125.8, 58.5, 54.1, 41.5, 35.7, 24.5, 18.2.

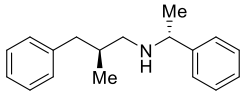
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3568 (vw), 3064 (vw), 3027 (vw), 2963 (w), 2925 (w), 1748 (w), 1711 (vs), 1654 (vw), 1636 (vw), 1603 (vw), 1495 (w), 1452 (w), 1438 (w), 1419 (w), 1360 (s), 1220 (s), 1128 (w), 1091 (w), 1030 (vw), 911 (vw), 763 (w), 742 (m), 701 (s).

MS (70 eV, EI): 238 (14), 134 (35), 105 (100), 91 (22).

HRMS (EI) for $C_{18}H_{23}N$: calc. $[M]^{+\bullet}$: 253.1830, found: 253.1826.

$[\alpha]_D^{20}$: −33 (c = 1.01, $CHCl_3$).

(*S*)-2-Methyl-3-phenyl-*N*-((*R*)-1-phenylethyl)propan-1-amine (2'*S*,3*R*-159):



(2'*S*,3*R*)-**159**

The secondary amine (2'*S*,3*R*)-**159** was prepared from the amide (2'*S*,3*R*)-**152ad** according to a modified literature procedure.[129] Thus, (2'*S*,3*S*)-**152ad** (53.5 mg, 0.2 mmol, 1.0 equiv) was dissolved in THF (1.0 mL). The mixture was cooled to 0 °C and $LiAlH_4$ (1.0 M in THF, 0.6 mL, 3.0 equiv) was added dropwise. The mixture was heated at 50 °C overnight and after completion, diluted with Et_2O (5 mL). The reaction was carefully quenched with sat. aq. $NaHCO_3$ (5 mL) and extracted with EtOAc (3 x 10 mL). The crude product was washed with Brine and concentrated under reduced pressure. The crude product was purified *via* flash column chromatography on silica gel with diethyl ether/pentane = 1:2 to afford (2'*S*,3*R*)-**159** (39 mg, 0.154 mmol, 77%, dr = 2:98, 96% *ee*) as a colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 7.35–7.26 (m, 4H), 7.26–7.20 (m, 3H), 7.18–7.13 (m, 1H), 7.12–7.08 (m, 2H), 3.69 (q, *J* = 6.6 Hz, 1H), 2.64 (dd, *J* = 13.4, 6.1 Hz, 1H), 2.48 (dd, *J* = 11.6, 5.5 Hz, 1H), 2.35 (dd, *J* = 13.4, 8.2 Hz, 1H), 2.24 (dd, *J* = 11.5, 7.4 Hz, 1H), 1.96–1.79 (m, 1H), 1.31 (d, *J* = 6.6 Hz, 3H), 1.26–1.17 (m, 1H), 0.86 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 146.2, 141.2, 129.3, 128.5, 128.3, 126.9, 126.7, 125.8, 58.6, 54.1, 41.8, 35.7, 24.7, 18.2.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3367 (w), 3062 (vw), 3026 (w), 2959 (w), 2924 (w), 1713 (m), 1684 (w), 1654 (vw), 1636 (vw), 1603 (w), 1494 (w), 1452 (m), 1362 (w), 1304 (vw), 1220 (w), 1127 (w), 1089 (w), 1074 (vw), 1029 (w), 911 (vw), 761 (m), 741 (m), 698 (vs).

MS (70 eV, EI): 238 (15), 134 (46), 105 (100), 91 (23).

HRMS (EI) for $C_{18}H_{23}N$: calc. $[M]^{+\bullet}$: 253.1830, found: 253.1825.

$[\alpha]_D^{20}$: +30.9 (c = 0.95, $CHCl_3$).

2-Iodopyrimidine (165a):

165a

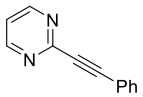
According to **TP13**, **165a** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h and a solution of I_2 (228 mg, 1.0 M in THF, 0.9 mmol) was added dropwise. The crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 to afford 2-iodopyrimidine (**165a**, 98.9 mg, 0.48 mmol, 96%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.47 (d, *J* = 4.8 Hz, 2H), 7.32 (t, *J* = 4.8 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 158.7, 129.7, 120.7.

The analytical data was in accordance with literature values.[145]

2-(Phenylethynyl)pyrimidine (165b):



165b

According to **TP13**, **165b** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h and a solution of I_2 (228 mg, 1.0 M in THF, 0.9 mmol) was added dropwise. The reaction mixture was further stirred at room temperature for 30 min before a mixture of NEt_3 (2 mL), CuI (4 mg, 4 mol%), $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol 6 mol%) and phenylacetylene (66.4 mg, 0.65 mmol, 1.3 equiv) in THF (1 mL) was added dropwise to the solution.[184] The reaction mixture was stirred for 2 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*.

[184] M. Mosrin, T. Bresser, P. Knochel, *Org. Lett.* **2009**, *11*, 3406–3409.

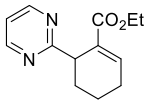
The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:1 to afford 2-(phenylethynyl)pyrimidine (**165b,** 70.3 mg, 0.39 mmol, 78%) as a light brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.75 (d, *J* = 4.9 Hz, 2H), 7.68–7.65 (m, 2H), 7.41–7.35 (m, 3H), 7.24 (t, *J* = 4.9 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.5, 153.4, 132.7, 129.8, 128.6, 121.4, 119.8, 88.1, 88.0.

The analytical data was in accordance with literature values.[185]

Ethyl 6-(pyrimidin-2-yl)cyclohex-1-ene-1-carboxylate (165c):



165c

According to **TP13**, **165c** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h and then cooled to 0 °C. CuCN·2LiCl (1 M in THF, 1.0 mL, 1.0 mmol, 1.0 equiv) as well as ethyl 6-bromocyclohex-1-ene-1-carboxylate[146] (170 mg, 0.75 mmol, 1.5 equiv) were added. The reaction mixture was stirred for 14 h at 25 °C. The crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 2:3 containing 1% triethylamine to afford ethyl 6-(pyrimidin-2-yl)cyclohex-1-ene-1-carboxylate (**165c**, 79.0 mg, 0.34 mmol, 68%) as a brown liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.67 (d, *J* = 4.9 Hz, 2H), 7.29 (td, *J* = 4.0, 1.6 Hz, 1H), 7.11 (t, *J* = 4.9 Hz, 1H), 4.28–3.92 (m, 3H), 2.50–2.23 (m, 2H), 2.20–2.07 (m, 1H), 2.01–1.89 (m, 1H), 1.73–1.54 (m, 2H), 1.09 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 173.7, 167.2, 157.2, 141.4, 131.3, 118.4, 60.2, 44.2, 29.9, 26.0, 19.2, 14.2.

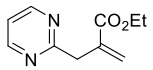
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2980 (w), 2937 (w), 2869 (w), 1707 (s), 1650 (w), 1563 (s), 1446 (w), 1420 (s), 1392 (w), 1371 (m), 1330 (w), 1241 (vs), 1203 (m), 1172 (m), 1145 (m), 1096 (m), 1062 (m), 1046 (m), 1011 (m), 967 (w), 939 (w), 918 (w), 808 (m), 752 (m), 711 (w).

MS (70 eV, EI): m/z (%): 186 (11), 175 (10), 159 (100), 157 (63), 131 (29).

HRMS (EI) for $C_{13}H_{16}N_2O_2$: calc. [M^+]: 232.1212, found: 232.1205.

[185] B. E. Moulton, A. C. Whitwood, A. K. Duhme-Klair, J. M. Lynam, I. J. S. Fairlamb, *J. Org. Chem.* **2011**, *76*, 5320–5334.

Ethyl 2-(pyrimidin-2-ylmethyl)acrylate (165d):



165d

According to **TP13**, **165d** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h and then cooled to 0 °C. CuCN·2LiCl (1 M in THF, 1.0 mL, 1.0 mmol, 1.0 equiv) as well as ethyl 2-(bromomethyl)acrylate (103 µL, 0.75 mmol, 1.5 equiv) were added. The reaction mixture was stirred for 14 h at 25 °C. The crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:2 containing 1% triethylamine to afford ethyl 2-(pyrimidin-2-ylmethyl)acrylate (**165d**, 60.5 mg, 0.315 mmol, 63%) as a slightly brown liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.66 (d, *J* = 4.9 Hz, 2H), 7.12 (t, *J* = 4.9 Hz, 1H), 6.36 (d, *J* = 1.2 Hz, 1H), 5.66 (q, *J* = 1.3 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.02 (d, *J* = 1.2 Hz, 2H), 1.19 (t, *J* = 7.1 Hz, 3H).

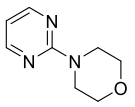
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 169.0, 166.8, 157.3, 137.5, 127.3, 118.8, 60.9, 42.3, 14.2.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 1651 (w), 1602 (w), 1566 (m), 1553 (s), 1495 (w), 1453 (w), 1417 (vs), 1287 (w), 1178 (vw), 1075 (w), 1030 (w), 978 (m), 931 (w), 877 (vw), 838 (w), 800 (w), 749 (m), 698 (s).

MS (70 eV, EI): m/z (%): 195 (100), 181 (22), 119 (14), 115 (18).

HRMS (EI) for $C_{13}H_{12}N_2$: calc. [M^+]: 196.1000, found: 196.0992.

4-(Pyrimidin-2-yl)morpholine (165e):



165e

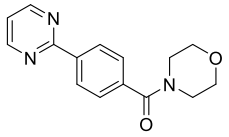
According to **TP13**, **165e** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h and a mixture of $CuCl_2$ (2.7 mg, 0.02 mmol, 5 mol%) and morpholino benzoate (83 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise to the reaction mixture. The reaction mixture was stirred for 14 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:1 to afford 4-(pyrimidin-2-yl)morpholine (**165e**, 36.3 mg, 0.22 mmol, 55%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.33 (d, J = 4.7 Hz, 2H), 6.53 (t, J = 4.8 Hz, 1H), 3.82–3.75 (m, 8H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.8, 110.4, 66.9, 44.4.

The analytical data was in accordance with literature values.[186]

Morpholino(4-(pyrimidin-2-yl)phenyl)methanone (165f):



165f

According to **TP13**, **165f** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h and a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as (4-iodophenyl)(morpholino)methanone (126.9 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise into the reaction mixture. The reaction mixture was stirred for 24 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc containing 1% triethylamine to afford morpholino(4-(pyrimidin-2-yl)phenyl)methanone (**165f**, 90.5 mg, 0.336 mmol, 84%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.79 (d, J = 4.8 Hz, 2H), 8.51–8.42 (m, 2H), 7.54–7.46 (m, 2H), 7.20 (t, J = 4.8 Hz, 1H), 3.92–3.35 (m, 8H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 170.1, 163.8, 157.4, 139.0, 137.3, 128.4, 127.5, 119.6, 66.9.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2985 (w), 1737 (vs), 1465 (w), 1447 (w), 1418 (w), 1394 (w), 1373 (m), 1301 (w), 1234 (vs), 1115 (w), 1098 (w), 1044 (s), 938 (w), 918 (vw), 847 (w), 786 (w).

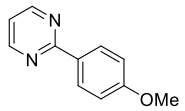
MS (70 eV, EI): m/z (%): 268 (13), 183 (100), 155 (50), 129 (14).

HRMS (EI) for $C_{15}H_{15}N_3O_2$: calc. [M^+]: 269.1164, found: 227.1157.

M.p. (°C): 158-162.

2-(4-Methoxyphenyl)pyrimidine (165g):

[186] X. Wei, C. Zhang, Y. Wang, Q. Zhan, G. Qiu, L. Fan, G. Yin, *Eur. J. Org. Chem.* **2019**, 7142–7150.



165g

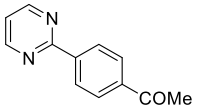
According to **TP13**, **165g** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h and a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-iodo-4-methoxybenzene (93.6 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise into the reaction mixture. The reaction mixture was stirred for 16 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 to afford 2-(4-methoxyphenyl)pyrimidine (**165g**, 66.3 mg, 0.356 mmol, 89%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.79 (d, J = 4.8 Hz, 2H), 8.51–8.46 (m, 2H), 8.16–8.10 (m, 2H), 7.19 (t, J = 4.8 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.4, 163.8, 157.4, 141.5, 132.3, 129.8, 128.1, 119.7, 61.2, 14.4.

The analytical data was in accordance with literature values.[187]

1-(4-(Pyrimidin-2-yl)phenyl)ethan-1-one (165h):



165h

According to **TP13**, **165h** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h and a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-(4-iodophenyl)ethan-1-one (98.4 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise into the reaction mixture. The reaction mixture was stirred for 16 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 to afford 1-(4-(pyrimidin-2-yl)phenyl)ethan-1-one (**165h**, 69.8 mg, 0.352 mmol, 88%) as a brown solid.

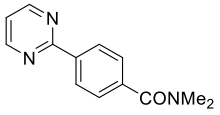
[187] X. Zheng, B. Song, B. Xu, *Eur. J. Org. Chem.* **2010**, 4376–4380.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.87 (d, J = 4.8 Hz, 2H), 8.59–8.54 (m, 2H), 8.12–8.07 (m, 2H), 7.29–7.27 (m, 1H), 2.68 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 198.1, 163.8, 157.5, 141.8, 138.7, 128.7, 128.4, 119.8, 27.0.

The analytical data was in accordance with literature values.[188]

***N*,*N*-Dimethyl-4-(pyrimidin-2-yl)benzamide (165i):**



165i

According to **TP13**, **165i** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h and a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 4-iodo-*N*,*N*-dimethylbenzamide (110.0 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise into the reaction mixture. The reaction mixture was stirred for 30 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc containing 1% triethylamine to afford *N*,*N*-dimethyl-4-(pyrimidin-2-yl)benzamide (**165i**, 81.8 mg, 0.36 mmol, 90%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.79 (d, J = 4.9 Hz, 2H), 8.51–8.42 (m, 2H), 7.58–7.47 (m, 2H), 7.19 (t, J = 4.8 Hz, 1H), 3.10 (s, 3H), 2.97 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 171.3, 164.0, 157.4, 138.7, 138.5, 128.2, 127.4, 119.5, 39.6, 35.4.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 1614 (s), 1570 (s), 1557 (m), 1551 (m), 1516 (m), 1489 (m), 1454 (w), 1416 (s), 1397 (s), 1317 (w), 1294 (w), 1263 (m), 1250 (m), 1216 (m), 1179 (w), 1096 (w), 1081 (m), 1052 (m), 1018 (m), 918 (w), 865 (m), 805 (vs), 775 (m), 757 (s), 726 (w), 701 (w).

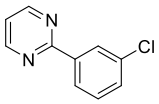
MS (70 eV, EI): m/z (%): 227 (11), 226 (56), 183 (100), 155 (59), 129 (12), 128 (12).

HRMS (EI) for $C_{13}H_{13}N_3O$: calc. [M^+]: 227.1059, found: 227.1051.

M.p. (°C): 112-115.

2-(3-Chlorophenyl)pyrimidine (165j):

[188] J-M. Bégouin, C. Gosmini, *J. Org. Chem.* **2009**, *74*, 3221–3224.



165j

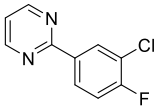
According to **TP13**, **165j** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for before $ZnCl_2$ (1.0 M in THF, 0.5 mL, 0.5 mmol) was added. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-chloro-3-iodobenzene (95.4 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise to the reaction mixture. The reaction mixture was stirred for 12 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 containing 1% triethylamine to afford 2-(3-chlorophenyl)pyrimidine (**165j**, 66.3 mg, 0.348 mmol, 87%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.80 (d, J = 4.8 Hz, 2H), 8.45 (t, J = 1.9 Hz, 1H), 8.33 (dt, J = 7.3, 1.6 Hz, 1H), 7.52–7.38 (m, 2H), 7.21 (t, J = 4.8 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 163.6, 157.4, 139.5, 134.9, 130.9, 123.0, 128.4, 126.3, 119.7.

The analytical data was in accordance with literature values.[188]

2-(3-Chloro-4-fluorophenyl)pyrimidine (165k):



165k

According to **TP13**, **165k** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h before $ZnCl_2$ (1.0 M in THF, 0.5 mL, 0.5 mmol) was added. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 2-chloro-1-fluoro-4-iodobenzene (102.6 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise into the reaction mixture. The reaction mixture was stirred for 12 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 containing 1% triethylamine to afford 2-(3-chloro-4-fluorophenyl)pyrimidine (**165k**, 70.1 mg, 0.336 mmol, 84%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.78 (d, J = 4.8 Hz, 2H), 8.53 (dd, J = 7.3, 2.2 Hz, 1H), 8.37–8.29 (m, 1H), 7.26–7.18 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 162.8 (d, *J* = 1.3 Hz), 160.0 (d, *J* = 253.0 Hz), 157.4, 134.9 (d, *J* = 3.5 Hz), 130.8, 128.3 (d, *J* = 7.8 Hz), 121.6 (d, *J* = 18.0 Hz), 119.5, 116.8 (d, *J* = 21.4 Hz).

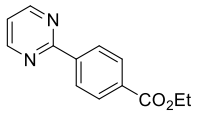
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3350 (s), 1634 (m), 1597 (m), 1566 (s), 1558 (s), 1505 (m), 1493 (m), 1411 (vs), 1389 (s), 1316 (m), 1299 (m), 1261 (w), 1243 (s), 1216 (w), 1120 (w), 1100 (w), 1089 (w), 1066 (w), 1041 (m), 902 (w), 862 (m), 808 (s), 796 (s), 749 (m), 695 (s).

MS (70 eV, EI): m/z (%): 210 (31), 208 (100), 157 (28), 155 (83).

HRMS (EI) for $C_{10}H_6N_2ClF$: calc. [M^+]: 208.0204, found: 208.0197.

M.p. (°C): 97-99.

Ethyl 4-(pyrimidin-2-yl)benzoate (165l):



165l

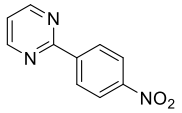
According to **TP13**, **165l** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h before $ZnCl_2$ (1.0 M in THF, 0.5 mL, 0.5 mmol) was added. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as ethyl 4-iodobenzoate (110.5 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise into the reaction mixture. The reaction mixture was stirred for 12 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 to afford ethyl 4-(pyrimidin-2-yl)benzoate (**165l**, 74.9 mg, 0.328 mmol, 82%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.79 (d, *J* = 4.8 Hz, 2H), 8.51–8.46 (m, 2H), 8.16–8.10 (m, 2H), 7.19 (t, *J* = 4.8 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.4, 163.8, 157.4, 141.5, 132.3, 129.8, 128.1, 119.7, 61.2, 14.4.

The analytical data was in accordance with literature values.[187]

2-(4-Nitrophenyl)pyrimidine (165m):



165m

According to **TP13**, **165m** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h before $ZnCl_2$ (1.0 M in THF, 0.5 mL, 0.5 mmol) was added. Next, a solution of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-iodo-4-nitrobenzene (99.6 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise into the reaction mixture. The reaction mixture was stirred for 12 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 and to afford 2-(4-nitrophenyl)pyrimidine (**165m**, 74.8 mg, 0.372 mmol, 93%) as a brown solid.

On **5 mmol** scale the reaction was performed as follows:

Pyrimidine (**160a**, 390 µL, 5.0 mmol) dissolved in THF (25 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 24 mL, 8.75 mmol). After the metalation was complete, $ZnCl_2$ (1.0 M in THF, 5.0 mL, 5.0 mmol) was added. Next, a solution of $Pd(dba)_2$ (69 mg, 0.12 mmol, 3 mol%), tri(2-furyl)phosphine (56 mg, 0.24 mmol, 6 mol%) as well as 1-iodo-4-nitrobenzene (996 mg, 4.0 mmol, 0.8 equiv) in THF (10 mL) was added dropwise. The reaction mixture was worked up and purified as mentioned above. Yield: (708.2 mg, 3.52 mmol, 88%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.87 (d, J = 4.8 Hz, 2H), 8.67–8.61 (m, 2H), 8.37–8.31 (m, 2H), 7.30 (t, J = 4.8 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 162.8, 157.6, 149.5, 143.4, 129.2, 123.9, 120.3.

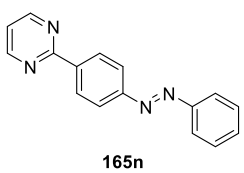
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2922 (w), 2853 (w), 1600 (m), 1561 (s), 1517 (m), 1505 (s), 1443 (w), 1419 (s), 1404 (m), 1380 (w), 1362 (w), 1347 (s), 1331 (s), 1322 (s), 1295 (m), 1250 (m), 1220 (w), 1179 (w), 1172 (m), 1116 (w), 1105 (s), 1090 (m), 1009 (m), 992 (w), 974 (w), 865 (m), 855 (m), 806 (vs), 797 (s), 769 (m), 738 (vs), 703 (w), 688 (m).

MS (70 eV, EI): m/z (%): 201 (100), 171 (87), 155 (64), 143 (39), 130 (17), 128 (43).

HRMS (EI) for $C_{10}H_7N_3O_2$: calc. [M^+]: 201.0538, found: 201.0532.

M.p. (°C): 195-197.

(*E*)-2-(4-(Phenyldiazenyl)phenyl)pyrimidine (165n):



165n

According to **TP13**, **165n** was prepared from pyrimidine (**160a**, 39 µL, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 25 °C for 6 h before $ZnCl_2$ (1.0 M in THF, 0.5 mL, 0.5 mmol) was added. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as (*E*)-1-(4-iodophenyl)-2-phenyldiazene (123.3 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 12 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 to afford (*E*)-2-(4-(phenyldiazenyl)phenyl)pyrimidine (**165n**, 95.8 mg, 0.368 mmol, 92%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.88 (d, J = 4.8 Hz, 2H), 8.69–8.63 (m, 2H), 8.11–8.05 (m, 2H), 8.02–7.96 (m, 2H), 7.61–7.50 (m, 3H), 7.31–7.23 (m, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 164.2, 157.5, 154.1, 152.8, 139.8, 131.4, 129.3, 129.2, 123.2, 123.2, 119.5.

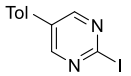
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 1582 (w), 1565 (m), 1550 (m), 1435 (w), 1410 (vs), 1312 (w), 1299 (w), 1241 (w), 1224 (w), 1183 (w), 1157 (w), 1145 (w), 1095 (w), 1072 (w), 1012 (w), 1000 (w), 923 (w), 866 (m), 814 (m), 800 (s), 770 (s), 722 (s), 684 (s), 673 (m).

MS (70 eV, EI): m/z (%): 260 (19), 183 (31), 155 (100), 128 (15), 77 (16).

HRMS (EI) for $C_{16}H_{12}N_4$: calc. [M^+]: 260.1062, found: 260.1056.

M.p. (°C): 152.

2-Iodo-5-(*p*-tolyl)pyrimidine (166a):



166a

According to **TP14**, **166a** was prepared from 5-(*p*-tolyl)pyrimidine (**160b**, 85.1 mg, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred at 50 °C for 3 h and then quenched at room temperature with I_2 (228 mg, 1.0 M in THF, 0.9 mmol). The crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:9 containing 1% triethylamine to afford 2-iodo-5-(*p*-tolyl)pyrimidine (**166a**, 81.0 mg, 0.395 mmol, 79%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.63 (s, 2H), 7.46–7.40 (m, 2H), 7.31 (d, J = 7.9 Hz, 2H), 2.41 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 156.5, 139.7, 133.8, 130.4, 130.1, 127.0, 126.7, 21.4.

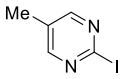
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3056 (w), 3030 (w), 2923 (w), 2865 (w), 2364 (w), 1917 (w), 1617 (w), 1598 (s), 1582 (m), 1576 (m), 1558 (w), 1531 (w), 1520 (w), 1506 (m), 1433 (m), 1383 (m), 1328 (m), 1316 (w), 1303 (w), 1290 (w), 1280 (w), 1240 (w), 1219 (m), 1203 (m), 1189 (m), 1176 (w), 1149 (m), 1116 (w), 1090 (m), 1078 (w), 1041 (w), 1022 (w), 1010 (m), 1000 (w), 984 (w), 974 (w), 960 (w), 948 (w), 940 (w), 855 (m), 843 (w), 820 (s), 796 (vs), 762 (m), 718 (m), 655 (m).

MS (70 eV, EI): m/z (%): 296 (53), 169 (57), 152 (21), 142 (28), 127 (47), 115 (100).

HRMS (EI) for $C_{11}H_9IN_2$: calc. [M^+]: 295.9810, found: 295.9804.

M.p. (°C): 66.

2-Iodo-5-methylpyrimidine (166b):



166b

According to **TP14**, **166b** was prepared from 5-methylpyrimidine (**160c**, 47.1 mg, 0.5 mmol), dissolved in THF (2.5 ml) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv). The reaction mixture was stirred at room temperature for 6 h and then quenched with I_2 (228 mg, 1.0 M in THF, 0.9 mmol). The crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:9 containing 1% triethylamine to afford 2-iodo-5-methylpyrimidine (**166b**, 102.3 mg, 0.465 mmol, 93%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.33–8.27 (m, 2H), 2.27 (d, J = 0.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 159.1, 130.5, 125.8, 15.3.

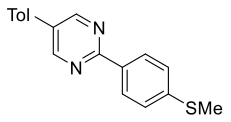
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3022 (w), 2914 (w), 2680 (w), 1568 (m), 1538 (s), 1490 (w), 1458 (w), 1383 (vs), 1359 (s), 1238 (vs), 1191 (m), 1167 (m), 1108 (vs), 1088 (s), 1076 (s), 1055 (s), 1041 (m), 994 (m), 937 (m), 911 (m), 825 (s), 806 (m), 776 (w), 750 (vs).

MS (70 eV, EI): m/z (%): 220 (100), 154 (12), 127 (13), 111 (16), 93 (44).

HRMS (EI) for $C_5H_5N_2I$: calc. [M^+]: 219.9497, found: 219.9492.

M.p. (°C): 199.

2-(4-(Methylthio)phenyl)-5-(*p*-tolyl)pyrimidine (166c):



166c

According to **TP14**, **166c** was prepared from 5-(*p*-tolyl)pyrimidine (**160b**, 85.1 mg, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv). The reaction mixture was stirred at 50 °C for 3 h before cooling to room temperature and a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as (4-iodophenyl)(methyl)sulfane (100.0 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred at 25 °C for 14 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. After prep-HPLC purification (MeCN/H_2O) 2-(4-(methylthio)phenyl)-5-(*p*-tolyl)pyrimidine (**166c**, 94.7 mg, 0.324 mmol, 81%) was obtained as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.97 (s, 2H), 8.42–8.36 (m, 2H), 7.54–7.50 (m, 2H), 7.38–7.30 (m, 4H), 2.55 (s, 3H), 2.43 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 162.9, 155.1, 142.3, 138.9, 134.0, 131.7, 131.5, 130.3, 128.5, 126.7, 125.9, 21.4, 15.3.

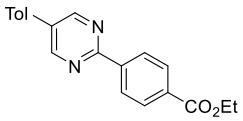
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2916 (w), 1593 (w), 1572 (m), 1546 (w), 1536 (w), 1523 (w), 1488 (w), 1437 (m), 1421 (s), 1397 (m), 1372 (m), 1354 (m), 1333 (m), 1313 (w), 1275 (w), 1237 (w), 1189 (w), 1176 (m), 1099 (m), 1085 (m), 1042 (w), 1011 (m), 999 (w), 962 (w), 941 (w), 819 (s), 789 (vs), 751 (w), 718 (w), 655 (m).

MS (70 eV, EI): m/z (%): 292 (100), 277 (14), 115 (16).

HRMS (EI) for $C_{18}H_{16}N_2S$: calc. [M^+]: 292.1034, found: 292.1026.

M.p. (°C): 59.

Ethyl 4-(5-(*p*-tolyl)pyrimidin-2-yl)benzoate (166d):



166d

According to **TP14**, **166d** was prepared from 5-(*p*-tolyl)pyrimidine (**160b**, 85.1 mg, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv). The reaction mixture was stirred at 50 °C for 3 h before cooling to room temperature and addition of $ZnCl_2$ (1.0 M, 0.5 mL. 0.5 mmol, 1.0 equiv). Next, a mixture of of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%),

tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as ethyl 4-iodobenzoate (110.5 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred at 25 °C for 14 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. After prep-HPLC purification ($MeCN/H_2O$) ethyl 4-(5-(*p*-tolyl)pyrimidin-2-yl)benzoate (**166d**, 96.8 mg, 0.304 mmol, 76%) was obtained as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.04 (s, 2H), 8.58–8.51 (m, 2H), 8.21–8.15 (m, 2H), 7.58–7.51 (m, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.6, 162.4, 155.2, 141.5, 139.3, 132.3, 132.3, 131.5, 130.3, 130.0, 128.1, 126.8, 61.3, 21.4, 14.5.

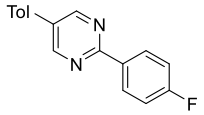
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2989 (w), 1716 (s), 1610 (w), 1579 (w), 1564 (vw), 1532 (w), 1523 (w), 1479 (w), 1435 (m), 1425 (m), 1402 (w), 1377 (w), 1370 (w), 1360 (m), 1301 (w), 1274 (s), 1246 (m), 1217 (w), 1181 (w), 1169 (m), 1126 (m), 1106 (s), 1096 (s), 1023 (m), 1016 (m), 987 (w), 944 (w), 873 (m), 854 (w), 822 (s), 806 (w), 758 (vs), 732 (w), 724 (w), 718 (w), 696 (m), 657 (w).

MS (70 eV, EI): m/z (%): 318 (98), 290 (19), 273 (100), 245 (19), 137 (11), 115 (26).

HRMS (EI) for $C_{20}H_{18}N_2O_2$: calc. [M^+]: 318.1368, found: 318.1368.

M.p. (°C): 64.

4-Fluorophenyl-5-(*p*-tolyl)pyrimidine (166e):



166e

According to **TP14**, **166e** was prepared from 5-(*p*-tolyl)pyrimidine (**160b**, 85.1 mg, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv). The reaction mixture was stirred at 50 °C for 3 h before cooling to room temperature and addition of $ZnCl_2$ (1.0 M, 0.5 mL. 0.5 mmol, 1.0 equiv). Next, a mixture of of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-fluoro-4-iodobenzene (88.8 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred overnight at 40 °C, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:9 containing 1% triethylamine to afford 4-fluorophenyl-5-(*p*-tolyl)pyrimidine (**166e**, 83.5 mg, 0.316 mmol, 79%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = δ 8.98 (s, 2H), 8.52–8.44 (m, 2H), 7.56–7.49 (m, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 7.21–7.15 (m, 2H), 2.44 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 164.8 (d, J = 250.5 Hz), 162.4, 155.1, 139.0, 133.7 (d, J = 2.9 Hz), 131.7, 131.6, 130.3, 130.3 (t, J = 8.7 Hz), 126.7, 115.7 (d, J = 21.7 Hz), 21.4.

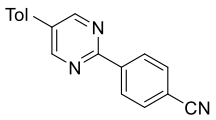
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3056 (w), 3030 (w), 2923 (w), 2865 (w), 2364 (w), 1917 (w), 1617 (w), 1598 (s), 1582 (m), 1576 (m), 1558 (w), 1531 (w), 1520 (w), 1506 (m), 1433 (m), 1383 (m), 1328 (m), 1316 (w), 1303 (w), 1290 (w), 1280 (w), 1240 (w), 1219 (m), 1203 (m), 1189 (m), 1176 (w), 1149 (m), 1116 (w), 1090 (m), 1078 (w), 1041 (w), 1022 (w), 1010 (m), 1000 (w), 984 (w), 974 (w), 960 (w), 948 (w), 940 (w), 855 (m), 843 (w), 820 (s), 796 (vs), 762 (m), 718 (m), 655 (m).

MS (70 eV, EI): m/z (%): 264 (100), 116 (41), 115 (53).

HRMS (EI) for $C_{17}H_{13}N_2F$: calc. [M^+]: 264.1063, found: 264.1061.

M.p. (°C): 82.

4-(5-(*p*-Tolyl)pyrimidin-2-yl)benzonitrile (166f):



166f

According to **TP14**, **166f** was prepared from 5-(*p*-tolyl)pyrimidine (**160b**, 85.1 mg, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv). The reaction mixture was stirred at 50 °C for 3 h before cooling to room temperature. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 4-iodobenzonitrile (91.6 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred overnight at 40 °C, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:9 to afford 4-(5-(*p*-tolyl)pyrimidin-2-yl)benzonitrile (**166f**, 78.1 mg, 0.288 mmol, 72%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.04 (s, 2H), 8.61 (d, J = 8.0 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 7.7 Hz, 2H), 7.36 (d, J = 7.7 Hz, 2H), 2.45 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 161.3, 155.2, 141.4, 139.4, 132.7, 132.5, 131.1, 130.3, 128.5, 126.7, 118.9, 113.9, 21.3.

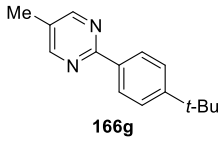
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2922 (w), 2229 (m), 1605 (w), 1573 (w), 1536 (w), 1523 (w), 1430 (s), 1402 (w), 1377 (m), 1328 (w), 1317 (w), 1289 (w), 1175 (w), 1103 (w), 1078 (w), 1015 (m), 940 (w), 858 (m), 815 (vs), 794 (vs), 719 (w), 654 (m).

MS (70 eV, EI): m/z (%): 271 (100), 116 (26).

HRMS (EI) for $C_{18}H_{13}N_3$: calc. [M^+]: 271.1109, found: 271.1102.

M.p. (°C): 185.

2-(4-(*tert*-Butyl)phenyl)-5-methylpyrimidine (166g):



166g

According to **TP14**, **166g** was prepared from 5-methylpyrimidine (**160c**, 47.1 mg, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred for 6 h at 25 °C and a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-(*tert*-butyl)-4-iodobenzene (104.5 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 16 h at 25 °C. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:9 to afford 2-(4-(*tert*-butyl)phenyl)-5-methylpyrimidine (**166g**, 63.4 mg, 0.28 mmol, 70%) as a white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.61 (s, 2H), 8.36–8.30 (m, 2H), 7.53–7.47 (m, 2H), 2.32 (s, 3H), 1.37 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 162.6, 157.5, 153.7, 135.0, 128.0, 127.7, 125.7, 34.9, 31.4, 15.6.

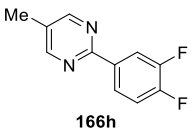
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2957 (w), 1609 (w), 1589 (m), 1552 (m), 1521 (s), 1435 (vs), 1384 (m), 1362 (m), 1334 (s), 1270 (s), 1244 (m), 1214 (m), 1184 (s), 1151 (w), 1111 (m), 1039 (m), 1013 (w), 984 (w), 913 (m), 883 (s), 848 (w), 828 (m), 789 (vs), 775 (s), 748 (w), 739 (m), 675 (m), 655 (s), 577 (m), 566 (m), 501 (m), 494 (m), 447 (m).

MS (70 eV, EI): m/z (%): 226 (13), 211 (100), 207 (38), 196 (21), 183 (18), 116 (13), 73 (16).

HRMS (EI) for $C_{15}H_{18}N_2$: calc. [M^+]: 226.1470, found: 226.1467.

M.p. (°C): 106.

2-(3,4-Difluorophenyl)-5-methylpyrimidine (166h):



166h

According to **TP14**, **166h** was prepared from 5-methylpyrimidine (**160c**, 47.1 mg, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred for 6 h at 25 °C and a solution of $ZnCl_2$ (1.0 M, 0.5 mL. 0.5 mmol, 1.0 equiv) was added. Next,

a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1,2-difluoro-4-iodobenzene (96.0 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 16 h at 25 °C. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes/trimethylamine = 1:9 containing 1% triethylamine to afford 2-(3,4-difluorophenyl)-5-methylpyrimidine (**166h**, 66.8 mg, 0.324 mmol, 81%) as a white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.69–8.63 (m, 2H), 8.30 (ddd, *J* = 11.8, 7.9, 2.1 Hz, 1H), 8.23 (ddt, *J* = 8.4, 4.5, 1.8 Hz, 1H), 7.34–7.27 (m, 1H), 2.40 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] =160.6 (t, *J* = 2.3 Hz), 157.5, 152.6 (dd, *J* = 150.7, 12.9 Hz), 150.1 (dd, *J* = 146.1, 12.9 Hz), 134.9 (dd, *J* = 6.1, 3.5 Hz), 128.9, 124.2 (dd, *J* = 6.8, 3.5 Hz), 117.4 (d, *J* = 17.5 Hz), 117.1 (d, *J* = 19.0 Hz), 15.6.

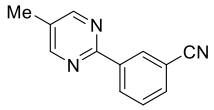
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2928 (w), 1623 (w), 1609 (w), 1589 (m), 1551 (m), 1520 (s), 1439 (s), 1422 (s), 1383 (s), 1351 (w), 1334 (s), 1305 (m), 1270 (s), 1245 (m), 1214 (m), 1183 (s), 1151 (w), 1110 (m), 1054 (w), 1039 (m), 983 (m), 950 (w), 912 (m), 883 (s), 828 (m), 788 (s), 774 (vs), 675 (m), 654 (s), 613 (w), 577 (m), 565 (s), 501 (m), 494 (m), 447 (m).

MS (70 eV, EI): m/z (%): 206 (100), 179 (27), 139 (92).

HRMS (EI) for $C_{11}H_8N_2F_2$: calc. [M^+]: 206.0656, found: 206.0650.

M.p. (°C): 101.

3-(5-Methylpyrimidin-2-yl)benzonitrile (166i):



7i

According to **TP14**, **166i** was prepared from 5-methylpyrimidine (**160c**, 47.1 mg, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred for 6 h at 25 °C and then a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 3-iodobenzonitrile (91.6 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred at 25 °C for 16 h. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 and to afford 3-(5-methylpyrimidin-2-yl)benzonitrile (**166i**, 64.8 mg, 0.332 mmol, 83%) as a white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.74 (d, *J* = 1.7 Hz, 1H), 8.64 (d, *J* = 6.3 Hz, 3H), 7.72 (dq, *J* = 7.6, 1.3 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 1H), 2.37 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 160.4, 157.7, 138.9, 133.6, 132.0, 131.8, 129.6, 129.5, 118.9, 112.9, 15.7.

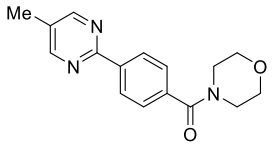
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2228 (m), 1588 (m), 1552 (s), 1441 (s), 1415 (s), 1382 (m), 1322 (m), 1177 (w), 1091 (w), 989 (w), 904 (m), 811 (w), 806 (w), 777 (vs), 677 (s), 654 (s), 608 (m), 479 (m), 432 (m), 427 (m).

MS (70 eV, EI): m/z (%): 195 (100), 168 (38), 129 (51).

HRMS (EI) for $C_{12}H_9N_3$: calc. [M^+]: 195.0796, found: 195.0791.

M.p. (°C): 92.

(4-(5-Methylpyrimidin-2-yl)phenyl)(morpholino)methanone (166j):



166j

According to **TP14**, **166j** was prepared from 5-methylpyrimidine (**160c**, 47.1 mg, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred for 6 h at 25 °C and a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as (4-iodophenyl)(morpholino)methanone (126.9 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 16 h at 25 °C. The crude product was purified by flash column chromatography on silica gel with EtOAc containing 1% triethylamine to afford (4-(5-methylpyrimidin-2-yl)phenyl)(morpholino)methanone (**166j**, 82.7 mg, 0.292 mmol, 73%) as a white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.63 (s, 2H), 8.44 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 3.83–3.41 (m, 8H), 2.33 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 170.2, 161.6, 157.6, 139.2, 136.9, 129.0, 128.1, 127.5, 67.0, 15.6.

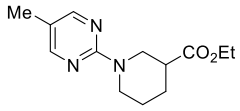
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2962 (w), 2922 (m), 2857 (m), 1741 (w), 1629 (s), 1608 (m), 1583 (w), 1574 (m), 1543 (w), 1508 (w), 1460 (w), 1422 (vs), 1381 (m), 1366 (m), 1300 (m), 1274 (s), 1256 (s), 1242 (m), 1224 (m), 1214 (m), 1200 (m), 1187 (w), 1177 (w), 1154 (m), 1112 (s), 1068 (m), 1059 (m), 1024 (s), 1008 (s), 981 (m), 937 (w), 919 (w), 897 (m), 864 (s), 844 (m), 829 (m), 802 (vs), 759 (vs), 713 (m), 654 (m).

MS (70 eV, EI): m/z (%): 283 (25), 197 (100), 169 (24).

HRMS (EI) for $C_{16}H_{17}N_3O_2$: calc. [M^+]: 283.1321, found: 283.1317.

M.p. (°C): 99.

Ethyl 1-(5-methylpyrimidin-2-yl)piperidine-3-carboxylate (166k):



166k

According to **TP14**, **166k** was prepared from 5-methylpyrimidine (**160c**, 47.1 mg, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred for 6 h at 25 °C and a mixture of $CoCl_2$ (2.6 mg, 0.02 mmol, 5 mol%), TMEDA (6 µL, 0.04 mmol, 10 mol%) as well as ethyl 1-(benzoyloxy)piperidine-3-carboxylate[108a] (110.9 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 16 h. The crude product was purified by flash column chromatography on silica gel with EtOAc containing 1% triethylamine to afford ethyl 1-(5-methylpyrimidin-2-yl)piperidine-3-carboxylate (**166k**, 60.8 mg, 0.244 mmol, 61%) as a brown oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.15 (s, 2H), 4.75 (ddt, *J* = 13.2, 3.8, 1.7 Hz, 1H), 4.55–4.46 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.14 (dd, J = 13.2, 10.5 Hz, 1H), 2.97 (ddd, *J* = 13.2, 11.5, 2.9 Hz, 1H), 2.50 (tt, *J* = 10.7, 3.9 Hz, 1H), 2.11 (s, 4H), 1.82–1.66 (m, 2H), 1.58–1.45 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

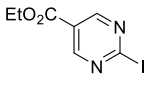
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 174.0, 160.7, 157.9, 118.1, 60.6, 46.2, 44.4, 41.5, 28.0, 24.3, 14.7, 14.4.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2958 (w), 2925 (m), 2848 (w), 1711 (s), 1580 (s), 1540 (m), 1508 (m), 1438 (s), 1421 (s), 1398 (m), 1388 (m), 1374 (m), 1365 (m), 1326 (m), 1320 (s), 1287 (vs), 1260 (s), 1249 (s), 1225 (s), 1191 (m), 1163 (w), 1139 (s), 1120 (s), 1065 (s), 1041 (m), 1033 (m), 1026 (m), 979 (w), 966 (w), 932 (w), 909 (m), 898 (s), 879 (m), 872 (m), 797 (vs), 754 (m), 746 (m).

MS (70 eV, EI): m/z (%): 249 (22), 176 (100), 148 (19), 44 (16).

HRMS (EI) for $C_{13}H_{19}N_3O_2$: calc. [M^+]: 249.1477, found: 249.1478.

Ethyl 2-iodopyrimidine-5-carboxylate (166l):



166l

According to **TP14**, **166l** was prepared from ethyl pyrimidine-5-carboxylate (**160d**, 76 mg, 0.5 mmol), dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv). The reaction mixture was stirred for 1 h at 60 °C and then quenched at room temperature with I_2 (228 mg, 1.0 M in THF, 0.9 mmol). After 30 min, the crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:9 containing 1% triethylamine to afford ethyl 2-iodopyrimidine-5-carboxylate (**166l**, 94.5 mg, 0.34 mmol, 68%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.94 (s, 2H), 4.43 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 163.5, 159.2, 134.0, 123.8, 62.4, 14.3.

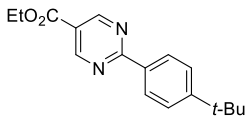
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2981 (w), 1713 (s), 1569 (s), 1537 (s), 1526 (s), 1477 (m), 1462 (m), 1445 (w), 1388 (m), 1361 (vs), 1292 (vs), 1244 (m), 1228 (s), 1178 (s), 1141 (vs), 1112 (vs), 1054 (m), 1032 (s), 1007 (s), 957 (m), 853 (s), 795 (m), 770 (s), 762 (s), 746 (m), 736 (m), 711 (w), 661 (m), 632 (s), 498 (m), 423 (w).

MS (70 eV, EI): m/z (%): 278 (69), 250 (62), 233 (65), 151 (100), 141 (36), 127 (44).

HRMS (EI) for $C_7H_7IN_2O_2$: calc. [M^+]: 277.9552, found: 277.9545.

M.p. (°C): 55.

Ethyl 2-(4-(*tert*-butyl)phenyl)pyrimidine-5-carboxylate (166m):



166m

According to **TP14**, **166m** was prepared from ethyl pyrimidine-5-carboxylate (**160d**, 76 mg, 0.5 mmol), dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv). The reaction mixture was stirred for 1 h at 60 °C before before cooling to room temperature. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-(*tert*-butyl)-4-iodobenzene (109.2 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise at room temperature. The reaction mixture was stirred at 40 °C for 12 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:9 to afford ethyl 2-(4-(*tert*-butyl)phenyl)pyrimidine-5-carboxylate (**166m**, 72.8 mg, 0.256 mmol, 64%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.30 (s, 2H), 8.47–8.43 (m, 2H), 7.56–7.52 (m, 2H), 4.45 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H), 1.37 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 167.3, 164.3, 158.6, 155.6, 134.1, 128.9, 125.9, 121.6, 61.8, 35.2, 31.3, 14.4.

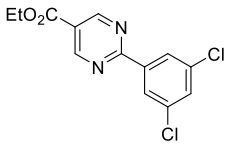
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2960 (m), 1711 (s), 1581 (s), 1552 (w), 1537 (m), 1464 (w), 1431 (s), 1406 (w), 1386 (m), 1366 (m), 1282 (vs), 1268 (s), 1236 (m), 1188 (m), 1175 (w), 1142 (m), 1126 (s), 1097 (m), 1075 (w), 1057 (m), 1034 (m), 1008 (m), 856 (m), 803 (vs), 759 (m), 737 (m).

MS (70 eV, EI): m/z (%): 284 (11), 269 (100), 241 (39).

HRMS (EI) for $C_{17}H_{20}N_2O_2$: calc. [M–Me^+]: 269.1290, found: 269.1288.

M.p. (°C): 98.

Ethyl 2-(3,5-dichlorophenyl)pyrimidine-5-carboxylate (166n):



166n

According to **TP14**, **166n** was prepared from ethyl pyrimidine-5-carboxylate (**160d**, 76 mg, 0.5 mmol), dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv). The reaction mixture was stirred for 1 h at 60 °C before cooling to room temperature and addition of $ZnCl_2$ (1.0 M, 0.5 mL, 0.5 mmol, 1.0 equiv). Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1,3-dichloro-5-iodobenzene (109.2 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred at 40 °C for 12 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:1 containing 1% triethylamine to afford ethyl 2-(3,5-dichlorophenyl)pyrimidine-5-carboxylate (**166n**, 76.1 mg, 0.256 mmol, 64%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.33 (s, 2H), 8.43 (d, J = 1.9 Hz, 2H), 7.52 (t, J = 2.0 Hz, 1H), 4.47 (q, J = 7.1 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 164.7, 163.7, 158.6, 139.5, 135.6, 131.5, 127.3, 122.7, 62.0, 14.3.

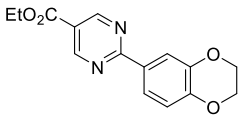
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3077 (w), 2977 (w), 1721 (s), 1592 (s), 1546 (m), 1473 (w), 1448 (m), 1428 (w), 1414 (m), 1399 (m), 1384 (m), 1366 (m), 1310 (w), 1286 (vs), 1259 (s), 1226 (m), 1146 (s), 1122 (m), 1110 (m), 1099 (m), 1081 (m), 1042 (m), 1030 (w), 1018 (m), 970 (w), 922 (w), 914 (w), 909 (w), 904 (w), 881 (w), 875 (m), 860 (w), 827 (m), 807 (s), 796 (s), 753 (s), 711 (w), 681 (w), 676 (m).

MS (70 eV, EI): m/z (%): 296 (14), 267 (25), 225 (33), 207 (100), 191 (28), 170 (58).

HRMS (EI) for $C_{13}H_{10}N_2O_2Cl_2$: calc. [M^+]: 296.0119, found: 296.0114.

M.p. (°C): 70.

Ethyl 2-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)pyrimidine-5-carboxylate (166o):



166o

According to **TP14**, **166o** was prepared from ethyl pyrimidine-5-carboxylate (**160d**, 76 mg, 0.5 mmol), dissolved in THF (5.0 m) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol, 1.75 equiv). The reaction mixture was stirred for 1 h at 60 °C before cooling to room temperature. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 6-iodo-2,3-dihydrobenzo[*b*][1,4]dioxine (104.8 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred at 40 °C for 12 h, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:19 containing 1% triethylamine to afford ethyl 2-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)pyrimidine-5-carboxylate (**166o**, 80.2 mg, 0.28 mmol, 69%) as a white solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.25 (s, 2H), 8.08–8.01 (m, 2H), 6.97 (d, J = 8.4 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 4.36–4.29 (m, 4H), 1.42 (t, J = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.8, 164.3, 158.5, 147.3, 143.8, 130.4, 122.9, 121.2, 118.4, 117.7, 64.8, 64.3, 61.7, 14.4.

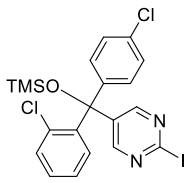
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2920 (m), 1711 (s), 1580 (s), 1540 (m), 1508 (m), 1438 (s), 1421 (s), 1398 (m), 1388 (m), 1374 (m), 1365 (m), 1326 (m), 1320 (s), 1287 (vs), 1260 (s), 1249 (s), 1225 (s), 1191 (m), 1139 (s), 1120 (s), 1065 (s), 1041 (m), 1033 (m), 1026 (m), 909 (m), 898 (s), 879 (m), 872 (m), 797 (vs), 754 (m), 746 (m).

MS (70 eV, EI): m/z (%): 286 (100), 241 (11), 202 (14), 174 (14), 57 (14), 44 (17).

HRMS (EI) for $C_{15}H_{14}N_2O_4$: calc. [M^+]: 286.0954, found: 286.0949.

M.p. (°C): 71.

5-((3-Chlorophenyl)(4-chlorophenyl)((trimethylsilyl)oxy)methyl)-2-iodopyrimidine (166p):



166p

According to **TP14**, **166p** was prepared from **160e** (201.7 mg, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.1 mL, 0.75 mmol). The reaction mixture was stirred for 12 h at 25 °C and then quenched with I_2 (228 mg, 1.0 M in THF, 0.9 mmol). The crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 containing 1% triethylamine to afford 5-((3-chlorophenyl)(4-chlorophenyl)((trimethylsilyl)oxy)methyl)-2-iodopyrimidine (**166p**, 195.8 mg, 0.37 mmol, 74%) as a yellow-brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.50 (s, 2H), 7.77–7.71 (m, 1H), 7.35–7.24 (m, 4H), 7.23–7.16 (m, 2H), -0.17 (s, 9H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 158.3, 140.7, 140.2, 138.4, 134.4, 133.2, 132.2, 130.3, 129.7, 129.6, 128.8, 127.4, 127.3, 81.3, 1.9.

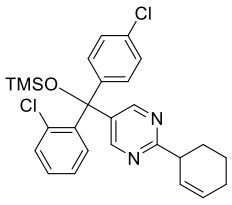
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2378 (m), 1868 (w), 1525 (s), 1505 (m), 1496 (m), 1422 (s), 1400 (s), 1341 (m), 1306 (m), 1298 (m), 1268 (m), 1227 (s), 1170 (m), 1157 (m), 1116 (s), 1085 (vs), 1028 (vs), 998 (vs), 909 (s), 879 (s), 861 (m), 846 (s), 817 (vs), 754 (w), 679 (vs), 637 (m), 601 (m), 559 (vs), 521 (s), 515 (s), 497 (m), 429 (w), 416 (m).

MS (70 eV, EI): m/z (%): 512 (11), 493 (15), 440 (22), 438 (36), 323 (13), 214 (15), 212 (16), 177 (32), 73 (100).

HRMS (EI) for $C_{20}H_{19}Cl_2IOSiN_2$: calc. [M^+]: 527.9688, found: 527.9676.

M.p. (°C): 103-106.

5-((3-Chlorophenyl)(4-chlorophenyl)((trimethylsilyl)oxy)methyl)-2-(cyclohex-2-en-1-yl)pyrimidine (166q):



166q

According to **TP14**, **166q** was prepared from **160e** (201.7 mg, 0.5 mmol) dissolved in THF (2.5 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.1 mL, 0.75 mmol). The reaction mixture was stirred for 12 h at 25 °C and then cooled to 0 °C. CuCN·2LiCl (1 M in THF, 0.5 mL, 0.5 mmol, 1.0 equiv) as well as 3-bromocyclohex-1-ene (86 µL, 120.8 mg, 0.75 mmol, 1.5 equiv) were added. The reaction mixture was warmed to room temperature and stirred for 12 h. The mixture was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 2:3 containing 1% triethylamine to afford 5-((3-chlorophenyl)(4-chlorophenyl)((trimethylsilyl)oxy)methyl)-2-(cyclohex-2-en-1-yl)pyrimidine (**166q**, 147.5 mg, 0.305 mmol, 61%) as a brown liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.80 (d, *J* = 1.7 Hz, 2H), 7.84 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.37–7.24 (m, 7H), 5.99–5.83 (m, 2H), 3.76 (qd, *J* = 5.7, 2.5 Hz, 1H), 2.20–1.99 (m, 2H), 1.90–1.59 (m, 4H), -0.14 (s, 9H).

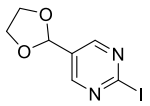
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 172.0, 156.9, 141.6, 141.6, 141.0, 141.0, 135.0, 134.0, 133.1, 133.1, 132.1, 129.9, 129.6, 129.6, 128.9, 128.5, 128.5, 127.7, 127.1, 81.4, 44.7, 29.4, 24.9, 21.5, 1.8.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2934 (w), 2861 (vw), 1579 (w), 1540 (w), 1488 (m), 1463 (w), 1433 (s), 1401 (w), 1382 (w), 1253 (s), 1218 (w), 1170 (w), 1159 (w), 1128 (w), 1089 (s), 1054 (m), 1036 (s), 1014 (m), 923 (m), 907 (m), 878 (vs), 840 (vs), 799 (m), 755 (s), 730 (vs), 691 (w).

MS (70 eV, EI): m/z (%): 484 (46), 482 (72), 455 (64), 453 (100), 447 (43), 393 (44), 371 (83), 217 (65), 189 (73), 73 (82).

HRMS (EI) for $C_{26}H_{28}Cl_2N_2OSi$: calc. [M^+]: 482.1348, found: 482.1348.

5-(1,3-Dioxolan-2-yl)-2-iodopyrimidine (166r):



166r

According to **TP14**, **166r** was prepared from **160f** (76.1 mg, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.6 mL, 0.875 mmol). The reaction mixture was stirred for 2 h at 60 °C and then quenched at room temperature with I_2 (228 mg, 1.0 M in THF, 0.9 mmol). After 30 min, the crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:1 containing 1% triethylamine to afford 5-(1,3-dioxolan-2-yl)-2-iodopyrimidine (**166r**, 89.0 mg, 0.32 mmol, 64%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.50 (s, 2H), 5.82 (s, 1H), 4.11–3.99 (m, 4H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 157.2, 131.3, 129.9, 99.9, 65.6.

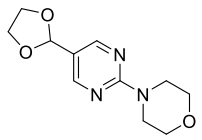
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2960 (w), 2895 (w), 2885 (w), 1710 (w), 1574 (m), 1537 (s), 1504 (w), 1473 (w), 1380 (s), 1372 (s), 1359 (s), 1308 (w), 1260 (w), 1248 (w), 1227 (w), 1163 (w), 1117 (vs), 1085 (s), 1034 (m), 1019 (s), 974 (s), 937 (s), 849 (m), 820 (w), 800 (w), 759 (m), 725 (m), 707 (w).

MS (70 eV, EI): m/z (%): 278 (85), 233 (25), 151 (62), 124 (59), 73 (100), 45 (36).

HRMS (EI) for $C_7H_7IN_2O_2$: calc. [M$^+$]: 277.9552, found: 277.958.

M.p. (°C): 59.

4-(5-(1,3-Dioxolan-2-yl)pyrimidin-2-yl)morpholine (166s):



166s

According to **TP14**, **166s** was prepared from **160f** (76.1 mg, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.6 mL, 0.875 mmol). The reaction mixture was stirred for 2 h at 60 °C and cooled to room temperature. Next, a mixture of $CoCl_2$ (2.6 mg, 0.02 mmol, 5 mol%), TMEDA (6 µL, 0.04 mmol, 10 mol%) as well as morpholino benzoate (83 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL). The reaction mixture was stirred for 16 h at 25 °C, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc containing 1% triethylamine to afford 4-(5-(1,3-dioxolan-2-yl)pyrimidin-2-yl)morpholine (**166s**, 51.2 mg, 0.216 mmol, 54%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.38 (s, 2H), 5.70 (s, 1H), 4.14–3.98 (m, 4H), 3.85–3.73 (m, 8H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 162.4, 156.9, 119.6, 101.5, 66.9, 65.4, 44.4.

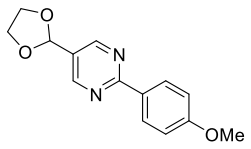
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2968 (w), 2957 (m), 2896 (m), 2858 (m), 1615 (s), 1547 (s), 1519 (m), 1498 (vs), 1463 (w), 1448 (s), 1417 (m), 1384 (s), 1355 (vs), 1304 (s), 1260 (m), 1242 (s), 1212 (m), 1195 (w), 1178 (m), 1114 (s), 1086 (vs), 1062 (m), 1042 (m), 1022 (m), 989 (m), 975 (s), 958 (vs), 952 (vs), 941 (vs), 849 (s), 795 (s), 708 (w), 654 (w).

MS (70 eV, EI): m/z (%): 237 (76), 206 (100), 192 (27), 180 (39).

HRMS (EI) for $C_{11}H_{15}N_3O_3$: calc. [M$^+$]: 237.1113, found: 237.1100.

M.p. (°C): 109.

5-(1,3-Dioxolan-2-yl)-2-(4-methoxyphenyl)pyrimidine (166t):



166t

According to **TP14**, **166t** was prepared from **160f** (76.1 mg, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.6 mL, 0.875 mmol). The reaction mixture was stirred for 2 h at 60 °C and cooled to room temperature. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-iodo-4-methoxybenzene (93.6 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 12 h at 40 °C, quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 containing 1% triethylamine to afford 5-(1,3-dioxolan-2-yl)-2-(4-methoxyphenyl)pyrimidine (**166t**, 74.4 mg, 0.288 mmol, 72%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.74 (s, 2H), 8.36–8.31 (m, 2H), 6.94–6.90 (m, 2H), 5.81 (s, 1H), 4.07–3.98 (m, 4H), 3.80 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 165.2, 162.2, 155.9, 131.5, 130.1, 128.2, 114.1, 100.8, 65.6, 55.5.

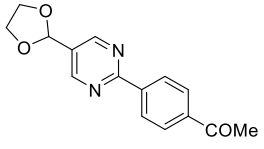
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2974 (w), 2932 (w), 2889 (w), 1607 (m), 1592 (s), 1585 (s), 1562 (w), 1547 (m), 1513 (m), 1456 (w), 1426 (vs), 1410 (m), 1381 (m), 1363 (m), 1327 (m), 1313 (w), 1301 (m), 1252 (vs), 1180 (m), 1167 (s), 1092 (s), 1061 (s), 1026 (s), 981 (m), 931 (m), 845 (s), 798 (s), 732 (m), 721 (m), 704 (w).

MS (70 eV, EI): m/z (%): 258 (100), 213 (27), 199 (14), 186 (48), 133 (16).

HRMS (EI) for $C_{14}H_{14}N_2O_3$: calc. [M^+]: 258.1004, found: 258.0995.

M.p. (°C): 78.

1-(4-(5-(1,3-Dioxolan-2-yl)pyrimidin-2-yl)phenyl)ethan-1-one (166u):



166u

According to **TP14**, **166u** was prepared from **160f** (76.1 mg, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.6 mL, 0.875 mmol). The reaction mixture was stirred for 2 h at 60 °C

and cooled to room temperature. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-(4-iodophenyl)ethan-1-one (98.4 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 12 h at 40 °C quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 1:4 containing 1% triethylamine to afford 1-(4-(5-(1,3-dioxolan-2-yl)pyrimidin-2-yl)phenyl)ethan-1-one (**166u**, 70.3 mg, 0.26 mmol, 65%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 8.90 (s, 2H), 8.55 (d, J = 8.4 Hz, 2H), 8.14–8.02 (m, 2H), 5.93 (s, 1H), 4.19–4.05 (m, 4H), 2.66 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 198.1, 164.3, 156.1, 141.5, 138.8, 129.8, 128.7, 128.6, 100.6, 65.7, 27.0.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2879 (w), 1678 (s), 1654 (w), 1606 (m), 1593 (m), 1576 (m), 1552 (m), 1522 (w), 1506 (w), 1429 (s), 1400 (m), 1377 (m), 1359 (m), 1324 (w), 1314 (w), 1302 (w), 1265 (s), 1246 (s), 1178 (w), 1136 (w), 1093 (s), 1054 (w), 1039 (m), 1025 (m), 1014 (m), 976 (m), 947 (s), 937 (s), 865 (m), 850 (m), 798 (vs), 776 (w), 728 (m), 652 (w).

MS (70 eV, EI): m/z (%): 270 (25), 255 (100), 227 (21), 211 (39), 183 (69), 155 (41).

HRMS (EI) for $C_{15}H_{14}N_2O_3$: calc. [M^+]: 270.1004, found: 270.0999.

M.p. (°C): 161.

3-Iodopyridazine (167a):

167a

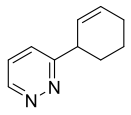
According to **TP15**, **167a** was prepared from pyridazine (**161**, 36 µL, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred in a microwave vessel at 70 °C for 2 h and then quenched with I_2 (228 mg, 1.0 M in THF, 0.9 mmol). The reaction mixture was stirred for 30 min, concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 4:1 containing 1% triethylamine to afford 3-iodopyridazine (**167a**, 72.1 mg, 0.35 mmol, 70%) as a yellow-brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = δ 9.18 (d, J = 4.7 Hz, 1H), 7.94 (d, J = 8.5 Hz, 1H), 7.22 (dd, J = 8.2, 4.9 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 150.6, 137.4, 127.3, 125.8.

The analytical data was in accordance with literature values.[152]

3-(Cyclohex-2-en-1-yl)pyridazine (167b):



167b

According to **TP15**, **167b** was prepared from pyridazine (**161**, 36 µL, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred in a microwave vessel at 70 °C for 2 h and then cooled to 0 °C. CuCN·2LiCl (1 M in THF, 1.0 mL, 0.5 mmol, 1.0 equiv) as well as 3-bromocyclohex-1-ene (120.8 mg, 0.75 mmol, 1.5 equiv) were added. The reaction mixture was warmed to room temperature and stirred for 12 h. After the reaction was completed, the crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 3:2 containing 1% triethylamine to afford 3-(cyclohex-2-en-1-yl)pyridazine (**167b**, 44.9 mg, 0.28 mmol, 56%) as a brown liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.08 (dd, J = 4.5, 2.3 Hz, 1H), 7.44 (t, J = 3.1 Hz, 2H), 6.07–5.95 (m, 1H), 5.82–5.72 (m, 1H), 3.95 (s, 1H), 2.24–2.08 (m, 3H), 1.82–1.64 (m, 3H).

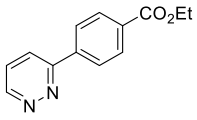
^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 167.5, 149.8, 130.6, 127.2, 127.2, 126.0, 77.5, 42.3, 30.8, 25.0, 21.0.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2945 (w), 2833 (w), 1654 (vw), 1450 (w), 1417 (w), 1114 (vw), 1021 (vs).

MS (70 eV, EI): m/z (%): 159 (16), 156 (56), 131 (100), 102 (52).

HRMS (EI) for $C_{10}H_{12}N_2$: calc. [M$^+$]:160.1000, found: 160.0994.

Ethyl 4-(pyridazin-3-yl)benzoate (167c):



167c

According to **TP15**, **167c** was prepared from pyridazine (**161**, 36 µL, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred in a microwave vessel at 70 °C for 2 h. Then, $ZnCl_2$ (1.0 M in THF, 0.5 mL, 0.5 mmol, 1.0 equiv) was added. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as ethyl 4-iodobenzoate (110.5 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise into the reaction mixture. The reaction mixture was stirred for 16 h. The crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-

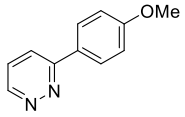
hexanes = 4:1 to afford ethyl 4-(pyridazin-3-yl)benzoate (**167c**, 67.6 mg, 0.296 mmol, 74%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = δ 9.20 (dd, *J* = 5.0, 1.5 Hz, 1H), 8.23–8.12 (m, 4H), 7.91 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.58 (dd, *J* = 8.6, 4.9 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 166.23, 158.7, 150.6, 140.4, 132.0, 130.3, 127.2, 127.0, 124.3, 61.4, 14.5.

The analytical data was in accordance with literature values.[152]

3-(4-Methoxyphenyl)pyridazine (167d):



167d

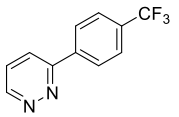
According to **TP15**, **167d** was prepared from pyridazine (**161**, 36 µL, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred in a microwave vessel at 70 °C for 2 h. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg, 0.024 mmol, 6 mol%) as well as 1-iodo-4-methoxybenzene (93.6 mg, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 16 h. The crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 4:1 to afford 3-(4-methoxyphenyl)pyridazine (**167d**, 58.1mg, 0.312 mmol, 78%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.08 (dd, *J* = 5.0, 1.5 Hz, 1H), 8.06–8.01 (m, 2H), 7.81 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.50 (dd, *J* = 8.7, 4.9 Hz, 1H), 7.06–7.00 (m, 2H) 3.86 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 161.5, 159.1, 149.4, 128.6, 127.1, 123.6, 114.6, 55.5.

The analytical data was in accordance with literature values.[152]

3-(4-(Trifluoromethyl)phenyl)pyridazine (167e):



167e

According to **TP15**, **167e** was prepared from pyridazine (**161**, 36 µL, 0.5 mmol) dissolved in THF (5.0 mL) and TMPZnCl·LiCl (**162a**, 0.36 M, 2.4 mL, 0.875 mmol). The reaction mixture was stirred in a microwave vessel at 70 °C for 2 h. Then, $ZnCl_2$ (1.0 M in THF, 0.5 mL, 0.5 mmol, 1.0 equiv) was added. Next, a mixture of $Pd(dba)_2$ (6.9 mg, 0.012 mmol, 3 mol%), tri(2-furyl)phosphine (5.6 mg,

0.024 mmol, 6 mol%) as well as 1-iodo-4-(trifluoromethyl)benzene (108.8 mg, 59 µL, 0.4 mmol, 0.8 equiv) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 16 h. The crude product was concentrated and purified by flash column chromatography on silica gel with EtOAc/*i*-hexanes = 9:1 to afford 3-(4-(trifluoromethyl)phenyl)pyridazine (**167e**, 58.3 mg, 0.26 mmol, 65%) as a brown solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 9.23 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.21 (d, *J* = 8.1 Hz, 2H), 7.92 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.62 (dd, *J* = 8.6, 4.9 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 158.4, 150.6, 139.7, 132.1 (q, *J* = 32.7 Hz), 127.6, 127.2, 126.2 (q, *J* = 3.8 Hz), 124.4, 124.0 (q, *J* = 271.2 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 1616 (w), 1582 (w), 1436 (w), 1416 (w), 1371 (w), 1360 (w), 1324 (s), 1301 (m), 1287 (m), 1229 (w), 1200 (vw), 1183 (w), 1158 (m), 1131 (m), 1109 (vs), 1068 (s), 1015 (s), 987 (m), 956 (w), 858 (m), 850 (w), 810 (s), 790 (w), 754 (w), 744 (m), 664 (m).

MS (70 eV, EI): m/z (%): 224 (68), 170 (100), 151 (17), 120 (15).

HRMS (EI) for $C_{11}H_7N_2F_3$: calc. [M^+]:224.0561, found: 224.0556.

M.p. (°C): 143-146.

7 Chiral Chromatograms

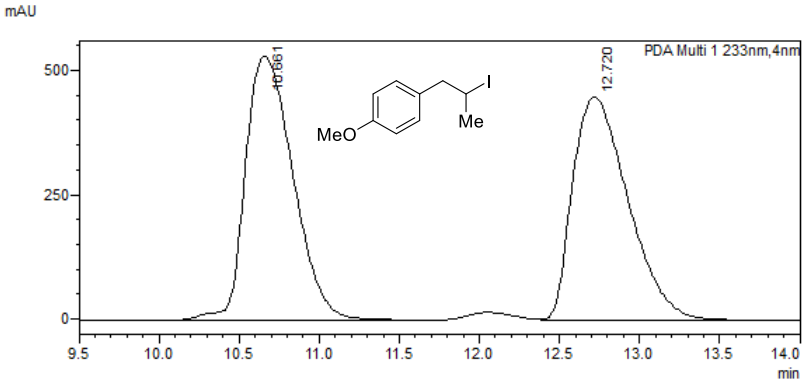
7.1 Analysis of Optically Enriched Secondary Alkyl Iodides of Type 142

(*R*)- and (*S*)-142f:

The enantiomeric excess of (*R*)- and (*S*)-**142f** was determined by chiral HPLC analysis.

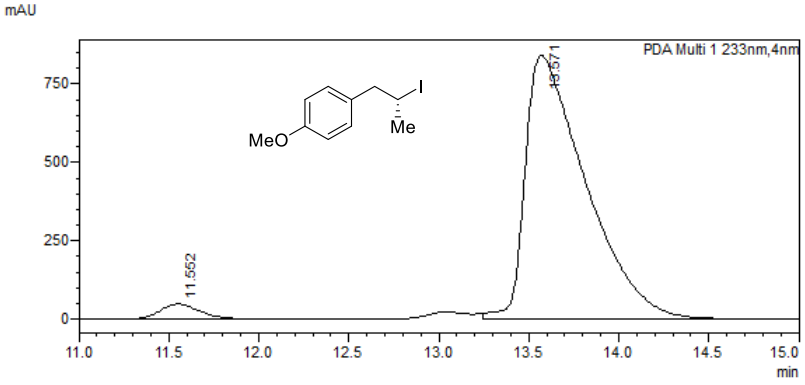
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	10.661	11065561	531348	50.458
2	12.720	10864627	449040	49.542
Total		21930188	980388	100.000

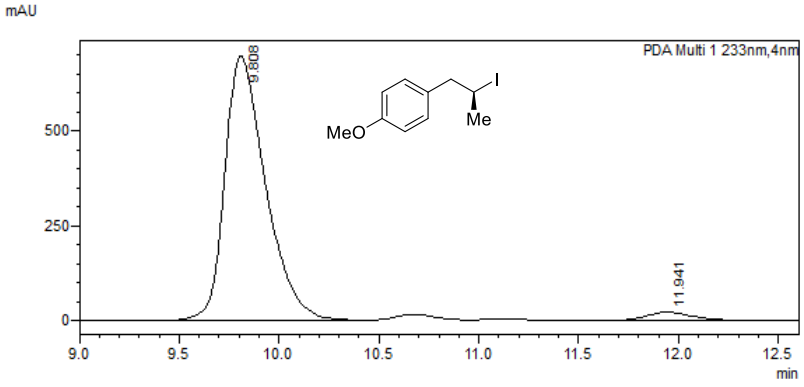
(*R*)-Enantiomer: t_R (min) = 11.6 ((*S*)-enantiomer, minor), 13.6 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	11.552	674295	46262	3.322
2	13.571	19625958	840123	96.678
Total		20300252	886385	100.000

The enantiomeric excess of (*R*)-**142f** was determined to 94%.

(*S*)-Enantiomer: t_R (min) = 9.8 ((*S*)-enantiomer, major), 11.9 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	9.808	9866016	697209	96.726
2	11.941	333951	21630	3.274
Total		10199967	718839	100.000

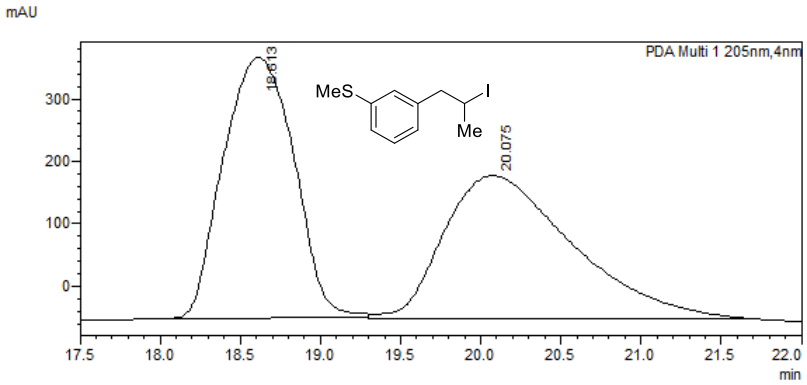
The enantiomeric excess of (*S*)-**142f** was determined 94%.

(*S*)-142g

The enantiomeric excess of (*S*)-**142g** was determined by chiral HPLC analysis.

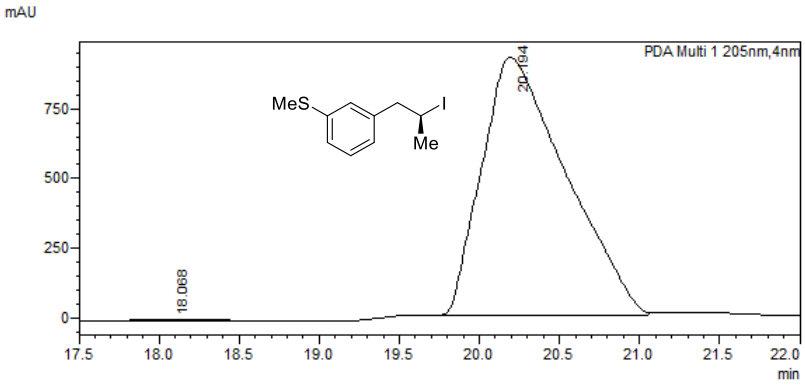
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:01, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	18.613	12815406	417724	50.188
2	20.075	12719460	228430	49.812
Total		25534866	646154	100.000

(*S*)-Enantiomer: t_R (min) = 18.1 ((*R*)-enantiomer, minor), 20.2 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	18.068	144998	4140	0.424
2	20.194	34035369	928103	99.576
Total		34180367	932243	100.000

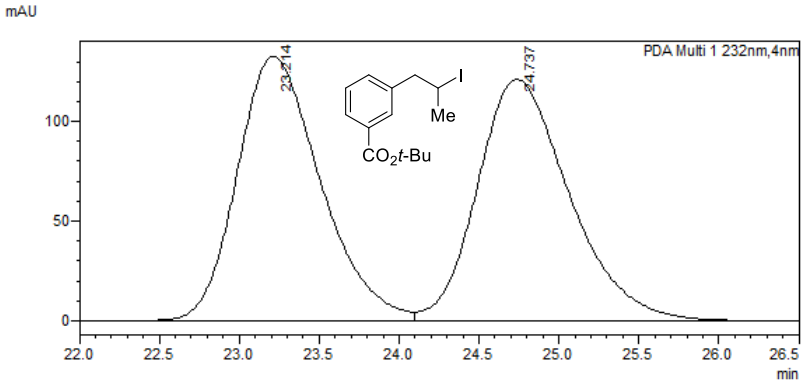
The enantiomeric excess of (*S*)-**142g** was determined to 99%.

(*R*)- and (*S*)-142i

The enantiomeric excess of (*R*)- and (*S*)-**142i** was determined by chiral HPLC analysis.

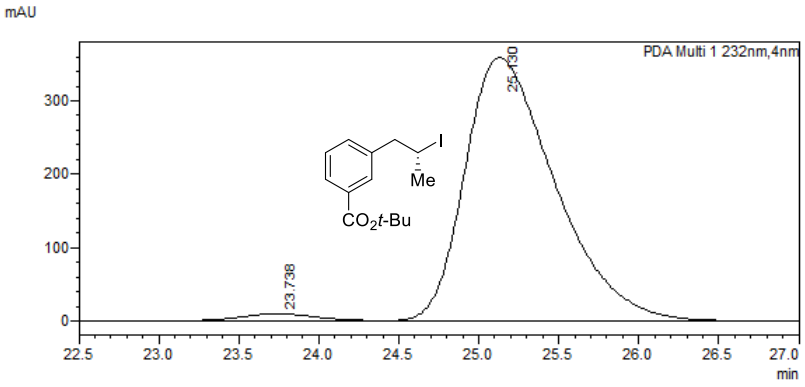
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 0.5 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	23.214	4828903	132734	49.743
2	24.737	4878869	121420	50.257
Total		9707771	254154	100.000

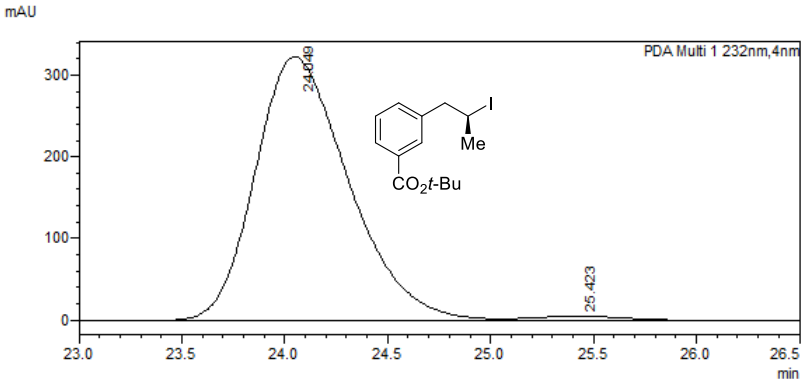
(*R*)-Enantiomer: t_R (min) = 23.7 ((*S*)-enantiomer, minor), 25.1 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	23.738	271665	8925	1.898
2	25.130	14039051	358807	98.102
Total		14310716	367731	100.000

The enantiomeric excess of (*R*)-**142i** was determined to 96%.

(*S*)-Enantiomer: t_R (min) = 24.1 ((*S*)-enantiomer, major), 25.4 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	24.049	10197771	322555	98.329
2	25.423	173315	5340	1.671
Total		10371086	327894	100.000

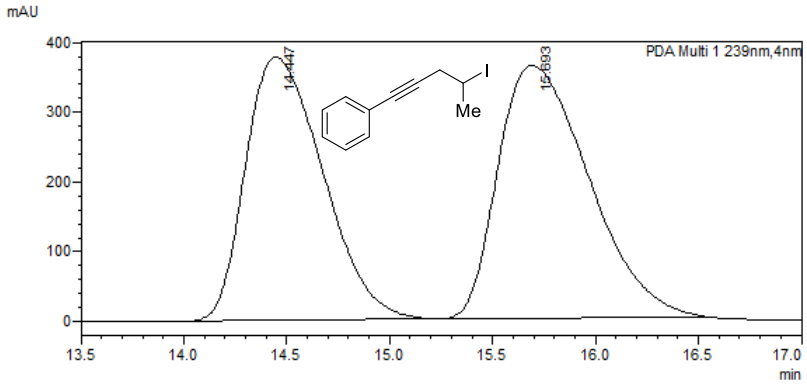
The enantiomeric excess of (*S*)-**142i** was determined to 97%.

(*R*)-142j

The enantiomeric excess of (*R*)-**142j** was determined by chiral HPLC analysis.

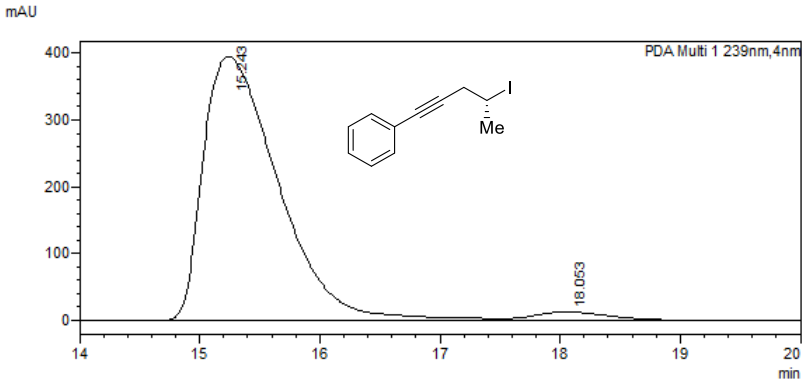
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	14.447	9864264	377571	47.019
2	15.693	11114852	361927	52.981
Total		20979117	739498	100.000

(*S*)-Enantiomer: t_R (min) = 15.2 ((*R*)-enantiomer, major), 18.1 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	15.243	17202309	394597	96.747
2	18.053	578371	13081	3.253
Total		17780680	407678	100.000

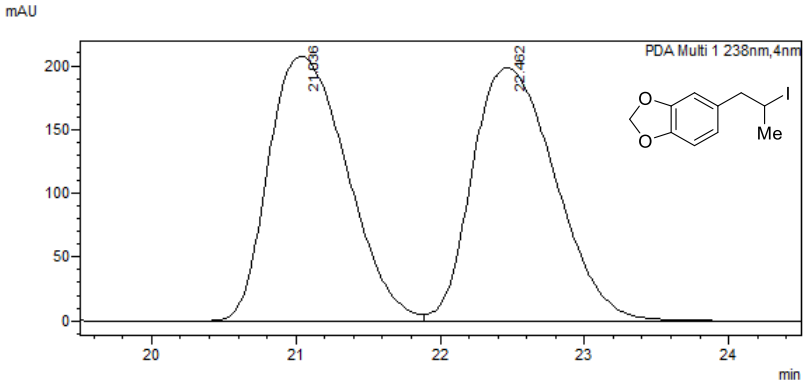
The enantiomeric excess of (*R*)-**142j** was determined to 94%.

(*R*)- and (*S*)-142k

The enantiomeric excess of (*R*)- and (*S*)-**142k** was determined by chiral HPLC analysis.

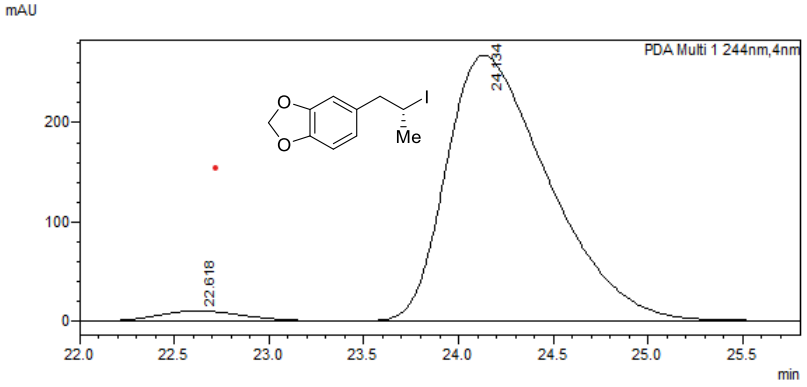
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.8:0.2, 0.5 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	21.036	7834897	207201	49.691
2	22.462	7932212	198494	50.309
Total		15767110	405695	100.000

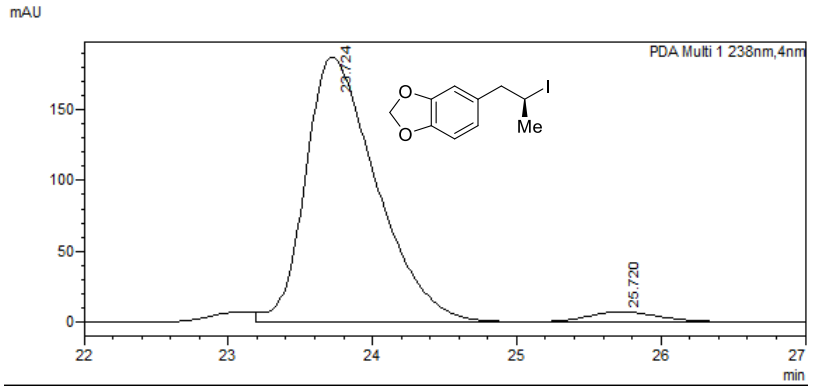
(*R*)-Enantiomer: t_R (min) = 22.6 ((*S*)-enantiomer, minor), 24.1 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	22.618	292104	9839	2.818
2	24.134	10072633	267478	97.182
Total		10364736	277316	100.000

The enantiomeric excess of (*R*)-**142k** was determined to 95%.

(*S*)-Enantiomer: t_R (min) = 23.7 ((*S*)-enantiomer, major), 25.7 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	23.724	6385689	186446	96.660
2	25.720	220628	6962	3.340
Total		6606317	193408	100.000

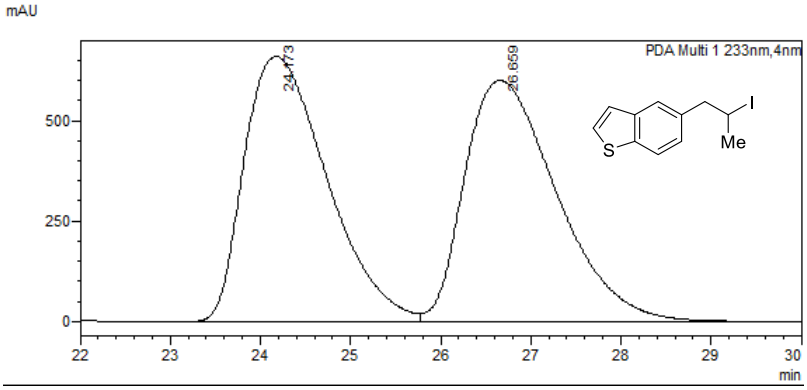
The enantiomeric excess of (*S*)-**142k** was determined to 94%.

(*R*)- and (*S*)-142l

The enantiomeric excess of (*R*)- and (*S*)-**142l** was determined by chiral HPLC analysis.

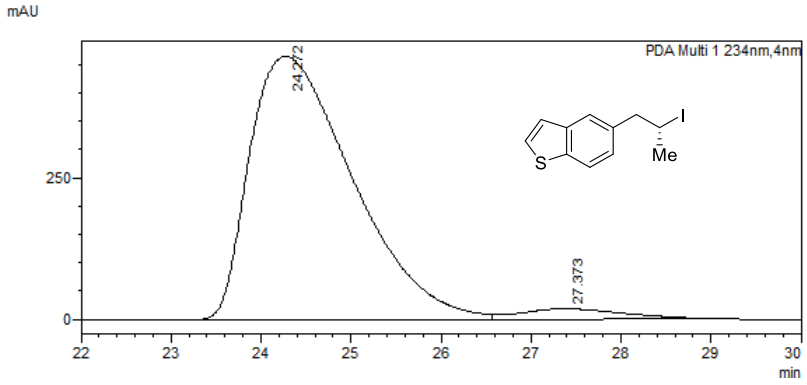
HPLC (column: OJ-H; *n*-heptane/2-propanol = 99.9:0.1, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	24.173	42209021	660675	49.815
2	26.659	42523330	600084	50.185
Total		84732352	1260760	100.000

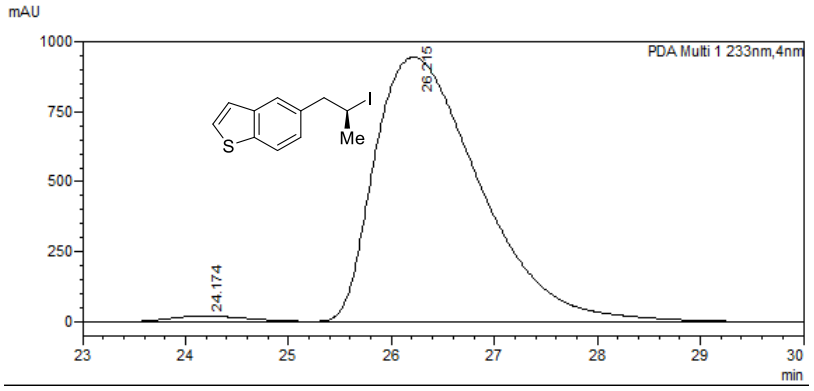
(*R*)-Enantiomer: t_R (min) = 24.3 ((*R*)-enantiomer, major), 27.4 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	24.272	37028289	465067	96.258
2	27.373	1439359	18151	3.742
Total		38467648	483218	100.000

The enantiomeric excess of (*R*)-**142l** was determined to 93%.

(*S*)-Enantiomer: t_R (min) = 24.2 ((*R*)-enantiomer, minor), 26.2 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	24.174	1203977	21662	1.758
2	26.215	67282608	943929	98.242
Total		68486585	965591	100.000

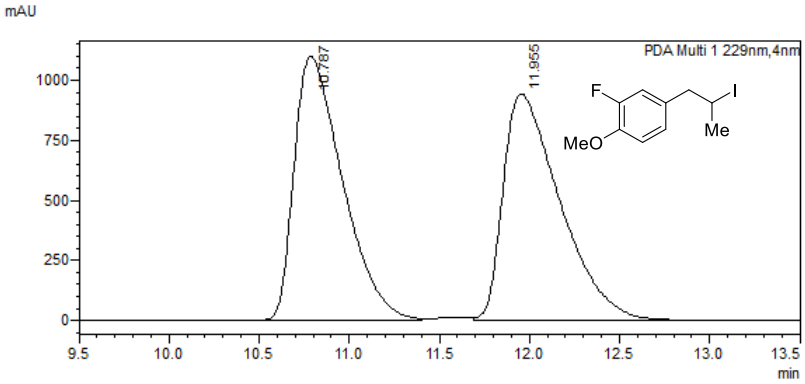
The enantiomeric excess of (*S*)-**142l** was determined to 97%.

(*R*)- and (*S*)-142n

The enantiomeric excess of (*R*)- and (*S*)-**142n** was determined by chiral HPLC analysis.

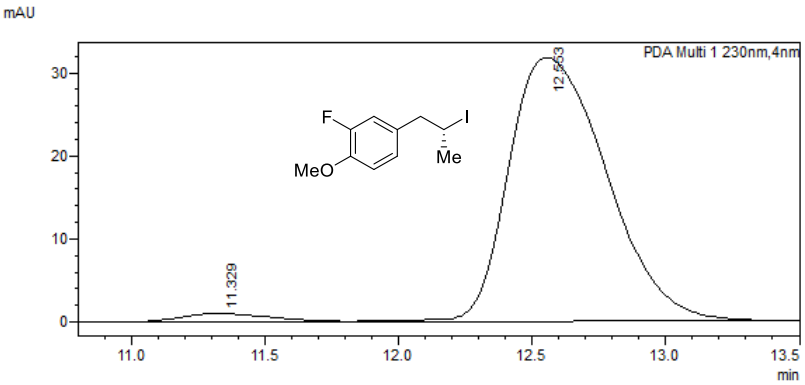
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	10.787	20456008	1096889	49.850
2	11.955	20579508	940822	50.150
Total		41035516	2037711	100.000

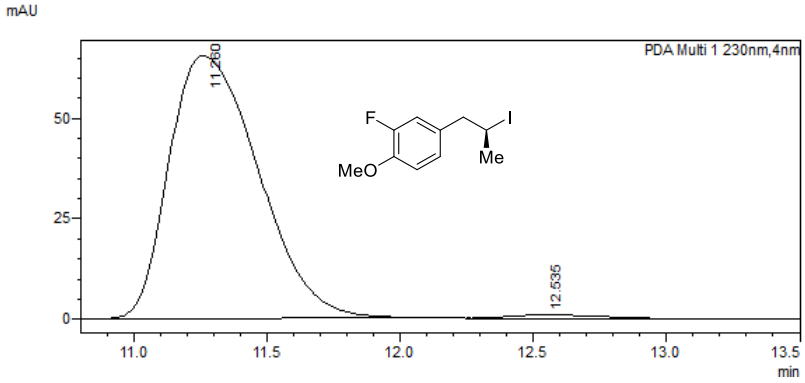
(*R*)-Enantiomer: t_R (min) = 11.3 ((*S*)-enantiomer, minor), 12.5 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	11.329	20979	957	2.532
2	12.553	807621	31696	97.468
Total		828600	32653	100.000

The enantiomeric excess of (*R*)-**142n** was determined to 95%.

(*S*)-Enantiomer: t_R (min) = 11.3 ((*S*)-enantiomer, major), 12.5 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	11.260	1527063	65399	98.742
2	12.535	19457	852	1.258
Total		1546520	66251	100.000

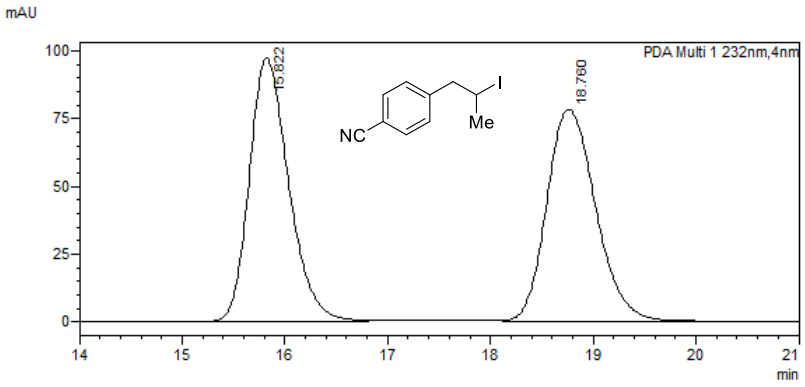
The enantiomeric excess of (*S*)-**142n** was determined to 98%

(*R*)- and (*S*)-142o

The enantiomeric excess of (*R*)- and (*S*)-**142o** was determined by chiral HPLC analysis.

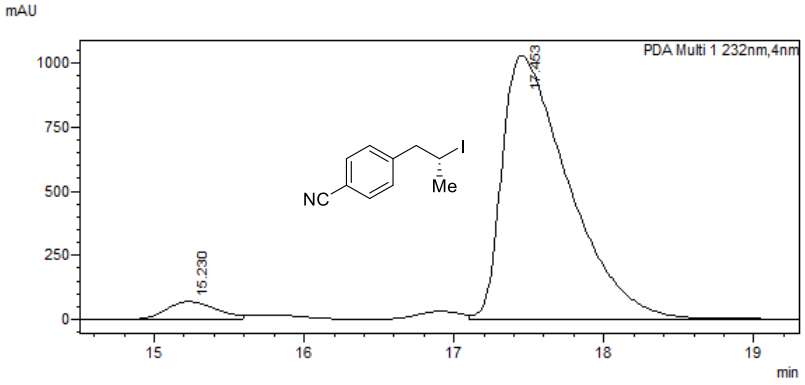
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.7:0.3, 0.5 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	15.822	2597253	97370	49.923
2	18.760	2605217	78322	50.077
Total		5202470	175693	100.000

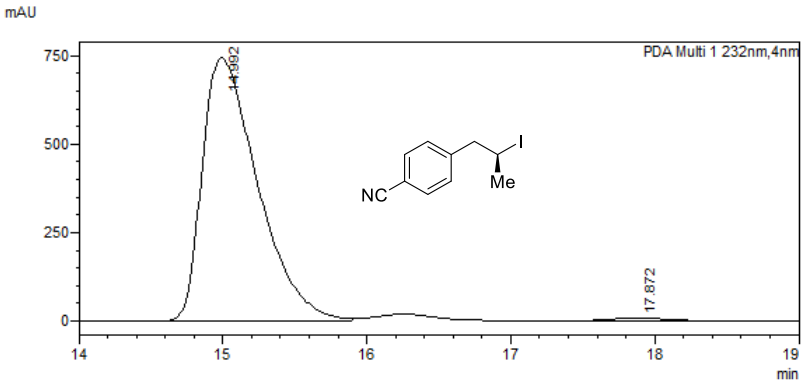
(*R*)-Enantiomer: t_R (min) = 15.2 ((*S*)-enantiomer, minor), 17.5 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	15.230	1625913	69661	4.841
2	17.453	31960916	1028500	95.159
Total		33586829	1098161	100.000

The enantiomeric excess of (*R*)-**142o** was determined to 90%.

(*S*)-Enantiomer: t_R (min) = 15.0 ((*S*)-enantiomer, major), 17.9 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	14.992	19921531	744563	98.969
2	17.872	207514	7771	1.031
Total		20129045	752334	100.000

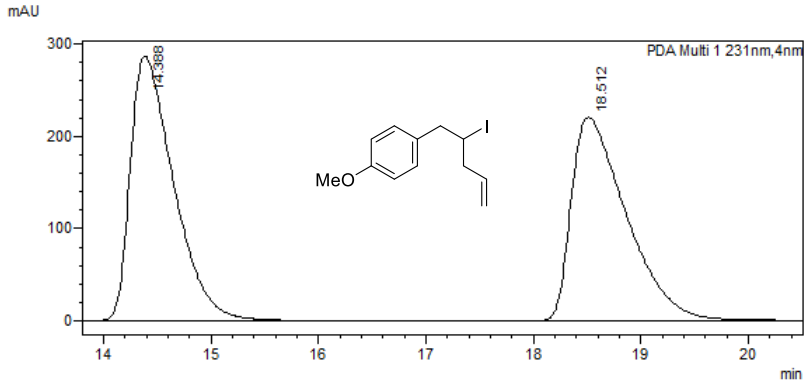
The enantiomeric excess of (*S*)-**142o** was determined to 98%.

(*S*)-142q

The enantiomeric excess of (*S*)-**142q** was determined by chiral HPLC analysis.

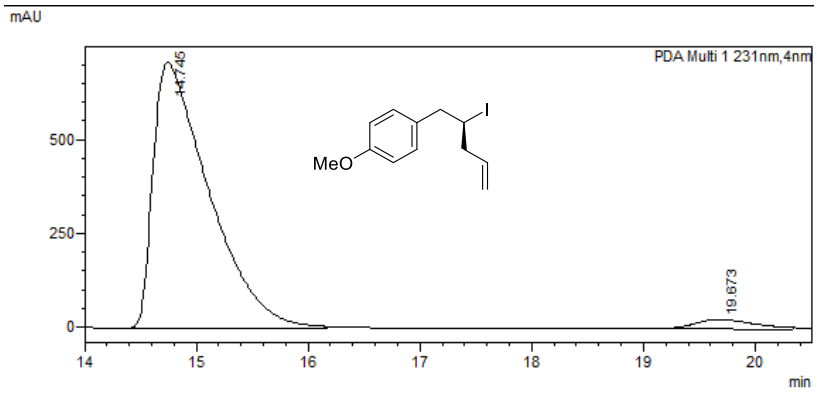
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	14.388	8039071	286566	50.501
2	18.512	7879697	220610	49.499
Total		15918768	507175	100.000

(*S*)-Enantiomer: t_R (min) = 14.8 ((*S*)-enantiomer, major), 19.6 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	14.745	24819631	710899	96.014
2	19.673	1030484	26377	3.986
Total		25850115	737276	100.000

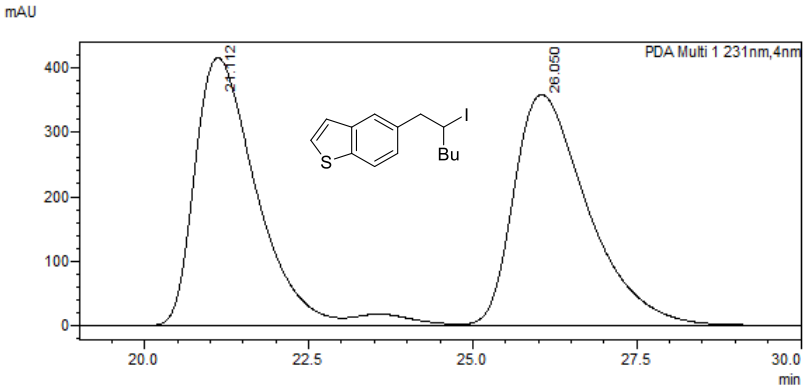
The enantiomeric excess of (*S*)-**142q** was determined to 92%

(*S*)-142r

The enantiomeric excess of (*S*)-**142r** was determined by chiral HPLC analysis.

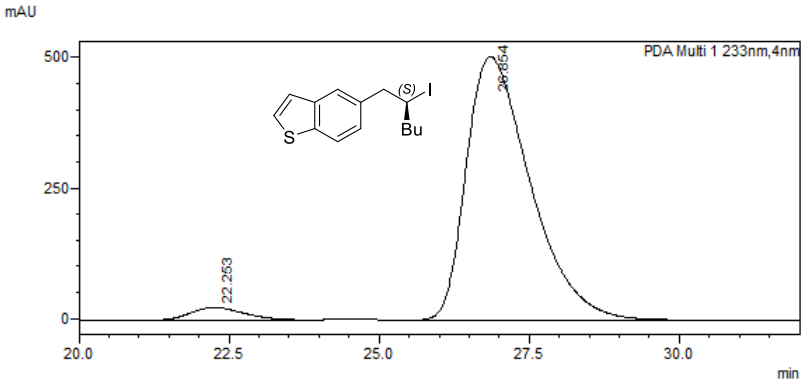
HPLC (column: OJ-H; *n*-heptane/2-propanol = 99.9:0.1, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	21.112	28045283	415285	49.927
2	26.050	28126990	358271	50.073
Total		56172273	773556	100.000

(*S*)-Enantiomer: t_R (min) = 22.3 ((*R*)-enantiomer, minor), 26.9 ((S)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	22.253	1445835	23828	3.716
2	26.854	37459734	503410	96.284
Total		38905569	527238	100.000

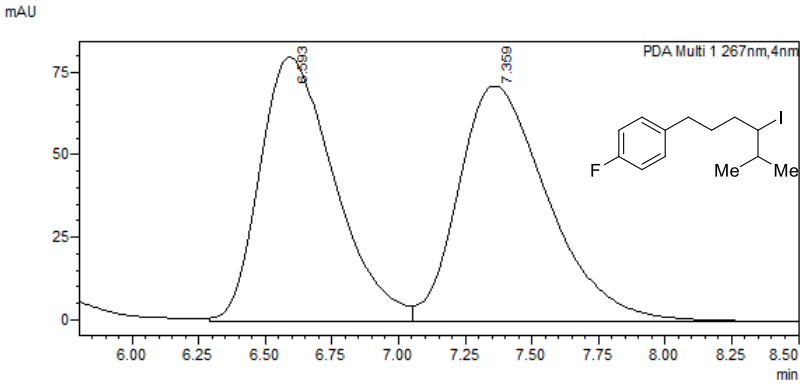
The enantiomeric excess of (*S*)-**142r** was determined to 92%

(*S*)-142t

The enantiomeric excess of (*S*)-**142t** was determined by chiral HPLC analysis.

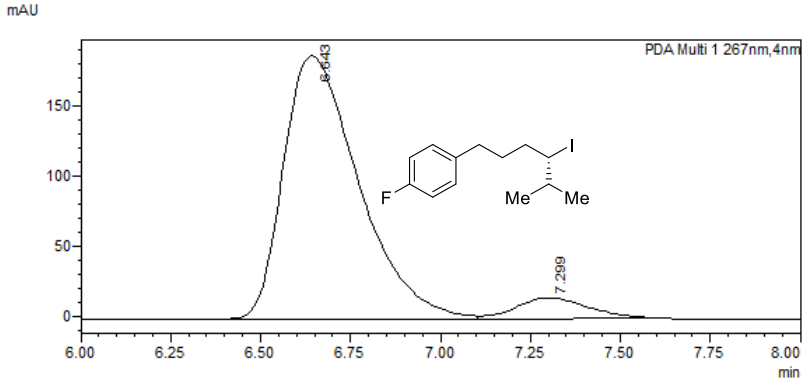
HPLC (column: OJ-H; *n*-heptane/2-propanol = 99.7:0.3, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	6.593	1570756	80297	48.279
2	7.359	1682726	71480	51.721
Total		3253482	151778	100.000

(*R*)-Enantiomer: t_R (min) = 6.6 ((*S*)-enantiomer, major), 7.3 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	6.643	2713713	187630	92.888
2	7.299	207780	14819	7.112
Total		2921493	202449	100.000

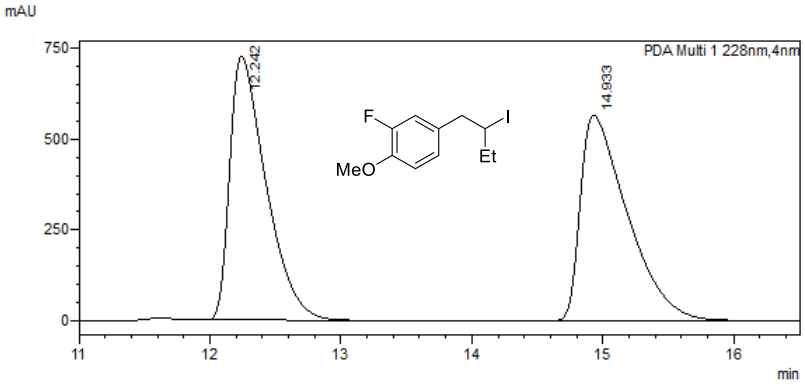
The enantiomeric excess of (*S*)-**142t** was determined 86%.

(*R*)- and (*S*)-142u

The enantiomeric excess of (*R*)- and (*S*)-**142u** was determined by chiral HPLC analysis.

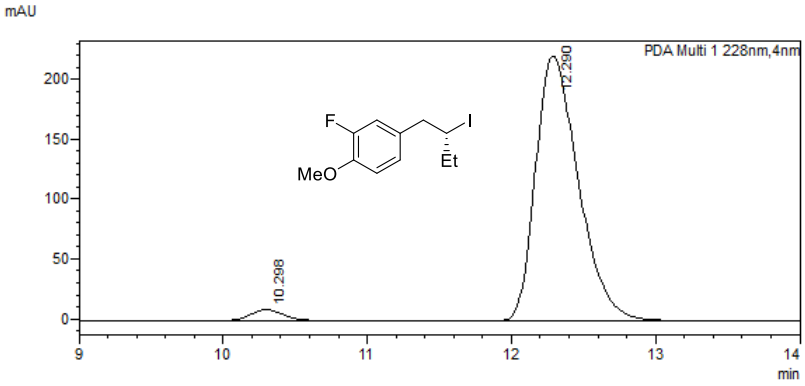
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	12.242	13912203	724032	49.718
2	14.933	14070200	565494	50.282
Total		27982403	1289526	100.000

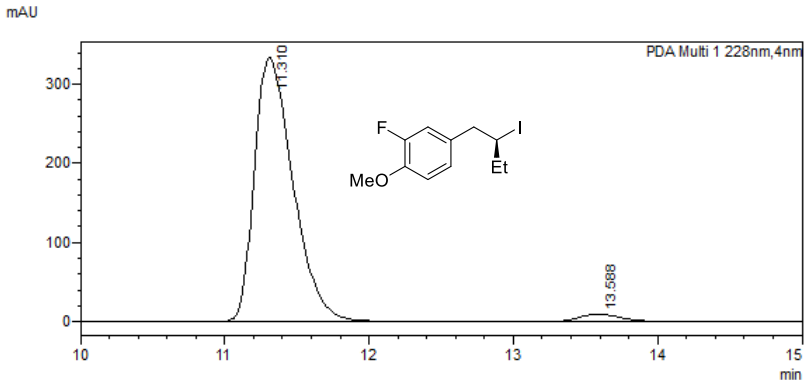
(*R*)-Enantiomer: t_R (min) = 10.3 ((*S*)-enantiomer, minor), 12.3 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	10.298	151511	9155	3.204
2	12.290	4576627	220882	96.796
Total		4728138	230036	100.000

The enantiomeric excess of (*R*)-**142u** was determined to 94%.

(*S*)-Enantiomer: t_R (min) = 11.3 ((*S*)-enantiomer, major), 13.6 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	11.310	6214971	334057	97.022
2	13.588	190773	9650	2.978
Total		6405744	343707	100.000

The enantiomeric excess of (*S*)-**142u** was determined to 94%.

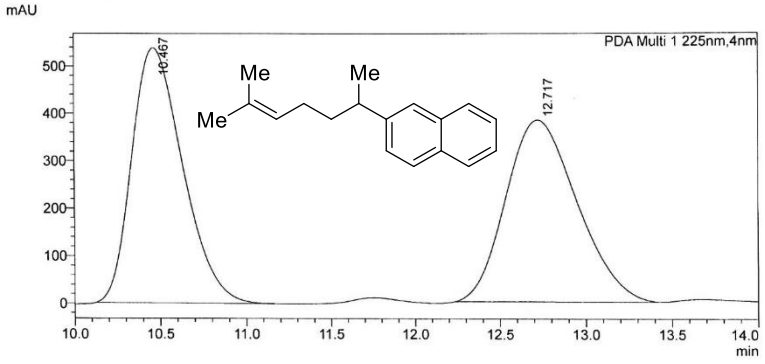
7.2 Analysis of Prepared Optically Enriched Products of Type 146, 150, 152 and 155

(*R*)- and (*S*)-146o:

The enantiomeric ratio of (*R*) and (*S*)-**146o** was determined by chiral HPLC analysis.

HPLC (column: OJ; *n*-heptane/2-propanol = 99:1, 1.0 mL/min):

Racemate:

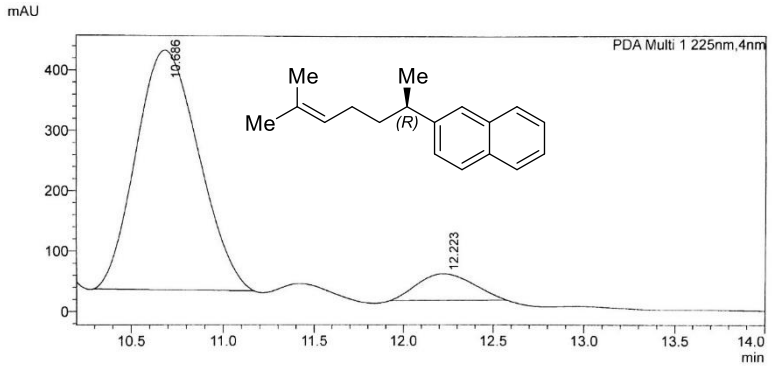


<Peak Table>

PDA Ch1 225nm

Peak#	Ret. Time	Area	Height	Area%
1	10.467	11099208	537846	50.120
2	12.717	11046146	382621	49.880

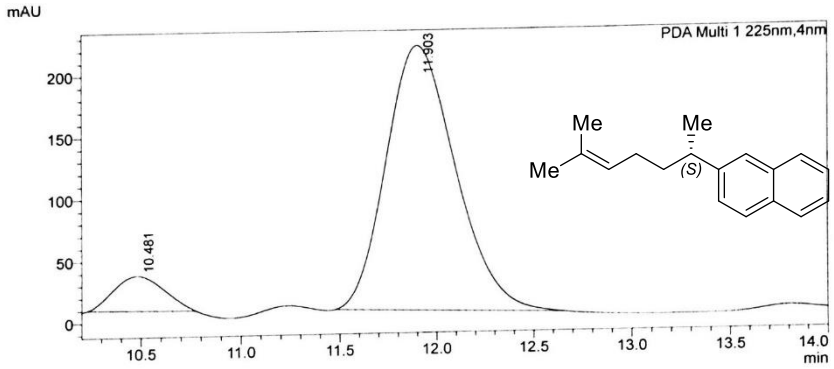
(*R*)-Enantiomer: t_R (min) = 10.7 (*R*-enantiomer; major), 12.2 (*S*-enantiomer; minor). er = 9:91.



Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	10.686	9420856	397586	90.696		M
2	12.223	966464	44377	9.304		M
Total		10387319	441964			

The enantiomeric ratio of (*R*)-**146o** was determined to 9:91.

(*S*)-Enantiomer: t_R (min) = 10.5 (*R*-enantiomer; minor), 11.9 (*S*-enantiomer; major). er = 91:9.



Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	10.481	504189	28508	8.552		M
2	11.903	5391623	215957	91.448		M
Total		5895812	244466			

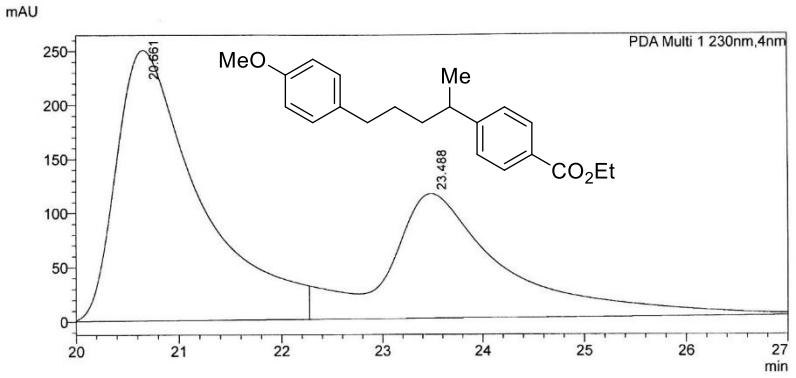
The enantiomeric ratio of (*S*)-**146o** was determined to 91:9.

(*R*)- and (*S*)-146p:

The enantiomeric ratio of (*R*)- and (*S*)-**146p** was determined by chiral HPLC analysis.

HPLC (column: AD-H; *n*-heptane/2-propanol = 98:2, 0.5 mL/min):

Racemate:

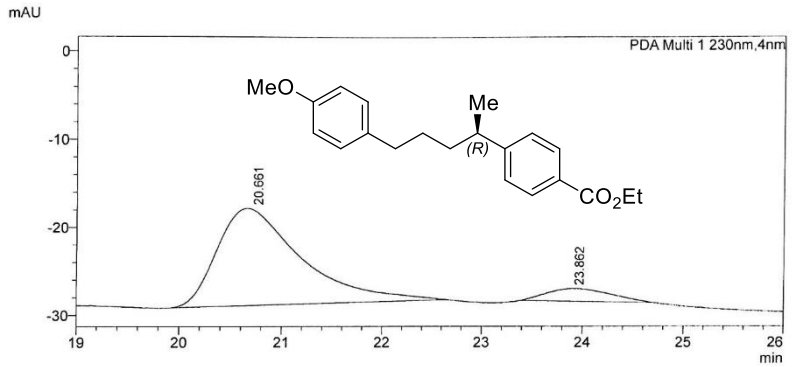


<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Height	Area%
1	20.661	14156212	249814	59.898
2	23.488	9477805	115583	40.102

(*R*)-Enantiomer: t_R (min) = 20.7 (*R*-enantiomer; major), 23.9 (*S*-enantiomer; minor).



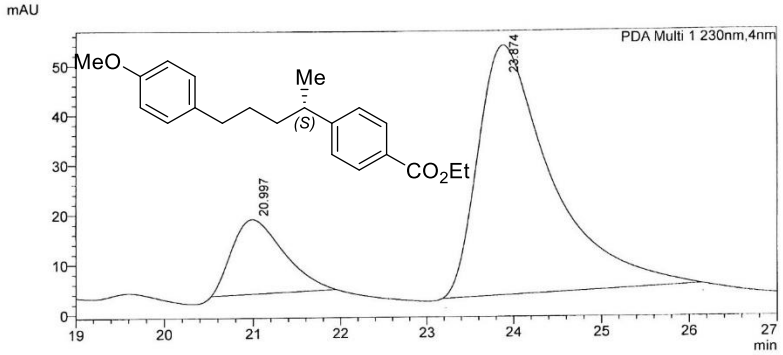
<Peak Table>

PDA Ch1 230nm

Peak#	Ret. Time	Area	Height	Area%
1	20.661	638544	11132	90.865
2	23.862	64196	1453	9.135

The enantiomeric ratio of (*R*)-**146p** was determined to 9:91.

(*S*)-Enantiomer: t_R (min) = 21.0 (*R*-enantiomer; minor), 23.9 (*S*-enantiomer; major).



<Peak Table>
PDA Ch1 230nm

Peak#	Ret. Time	Area	Height	Area%
1	20.997	616959	15033	17.305
2	23.874	2948300	50389	82.695

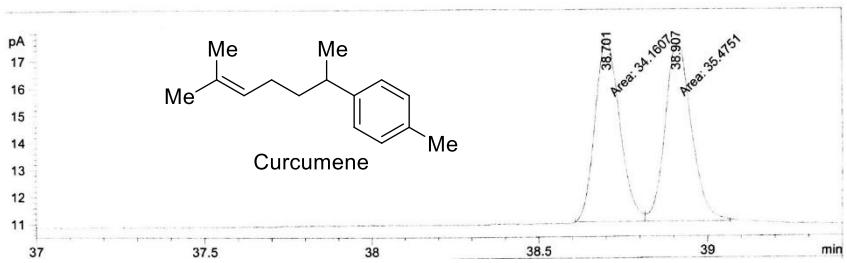
The enantiomeric ratio of (*S*)-**146p** was determined to 83:17.

***(R)*- and (*S*)-curcumene *(R)*- and (*S*)-150:**

The eantiomeric ratio of (*R*)-curcumene (*R*-**150**) was determined by chiral GC analysis.

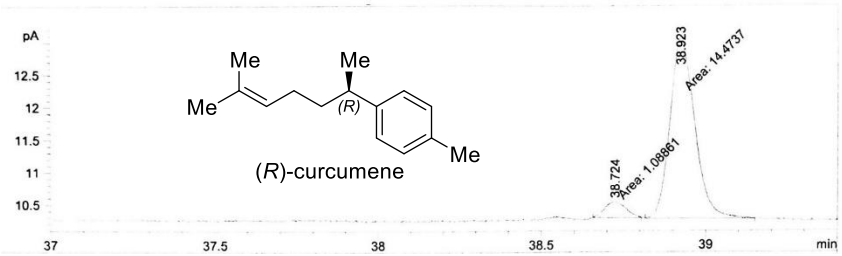
GC (Chirasil-Dex CB), 50 °C (2 min), ramp of 2 °C/ min to 145 °C;

Racemate:



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	38.701	MF	0.0856	34.16073	6.64748	49.05628
2	38.907	FM	0.0912	35.47507	6.48121	50.94372
Totals :				69.63580	13.12868	

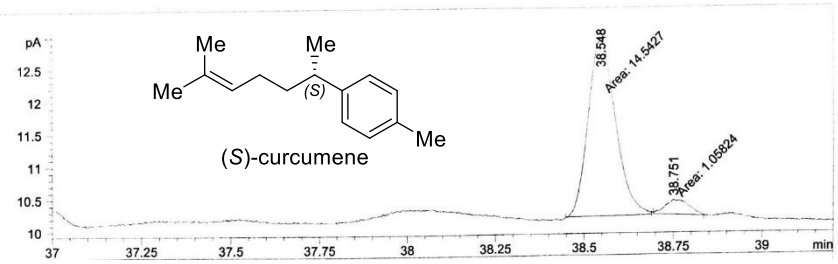
(*R*)-Enantiomer: t_R (min) = 38.7 (*S*-enantiomer; minor), 38.9 (*R*-enantiomer; major)..



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	38.724	MM	0.0735	1.08861	2.47003e-1	6.99518
2	38.923	MM	0.0855	14.47369	2.82018	93.00482
Totals :				15.56230	3.06718	

The enantiomeric ratio of (*R*)-**150** was determined to 7:93.

(*S*)-Enantiomer: t_R (min) = 38.6 (*S*-enantiomer; major), 38.8 (*R*-enantiomer; minor).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	38.548	MF	0.0885	14.54273	2.73937	93.21683
2	38.751	MM	0.0766	1.05824	2.30197e-1	6.78317
Totals :				15.60097	2.96957	

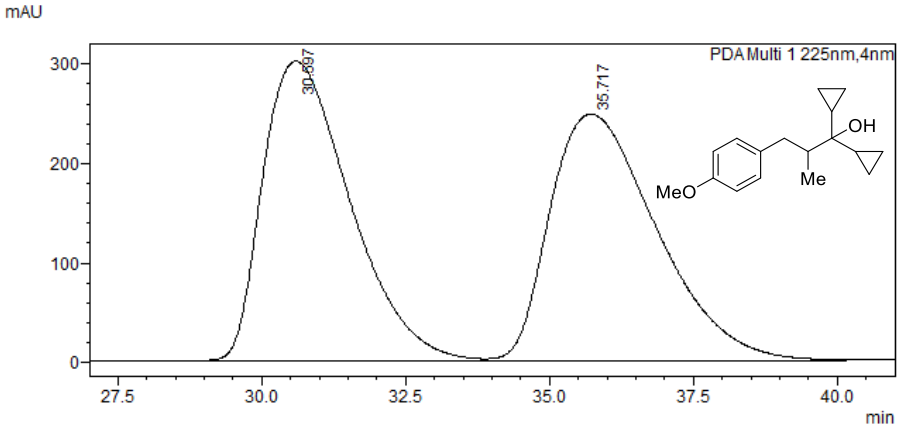
The enantiomeric ratio of (*R*)-**150** was determined to 93:7.

(*R*)- and (S)-152a

The enantiomeric excess of (*R*)- and (*S*)-**152a** was determined by chiral HPLC analysis.

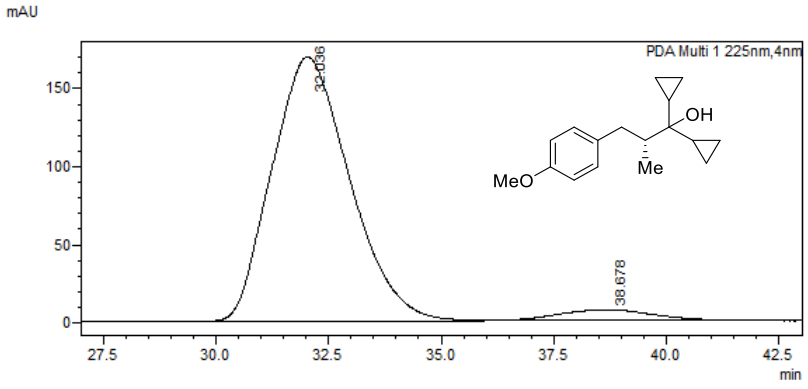
HPLC (column: OJ-H; *n*-heptane/2-propanol = 99:1, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	30.597	31717245	300745	49.856
2	35.717	31900167	247589	50.144
Total		63617412	548334	100.000

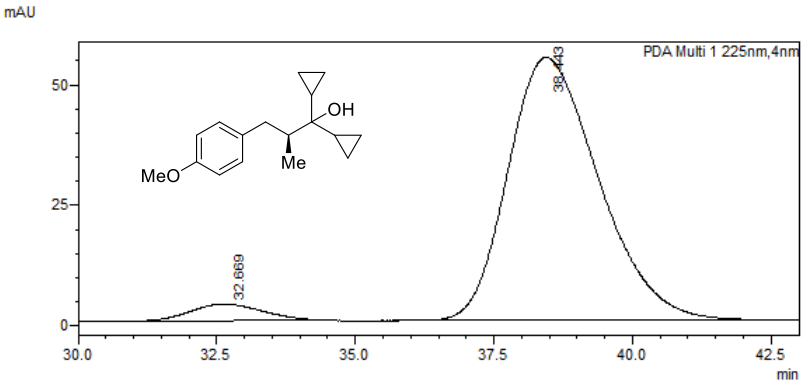
(*R*)-Enantiomer: t_R (min) = 32.0 ((*R*)-enantiomer, major), 38.7 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	32.036	20354365	169281	95.558
2	38.678	946215	6756	4.442
Total		21300581	176037	100.000

The enantiomeric excess of (*R*)-**152a** was determined to 91%.

(*S*)-Enantiomer: t_R (min) = 32.7 ((*R*)-enantiomer, minor), 38.4 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	32.669	316010	3447	4.835
2	38.443	6219453	54567	95.165
Total		6535463	58014	100.000

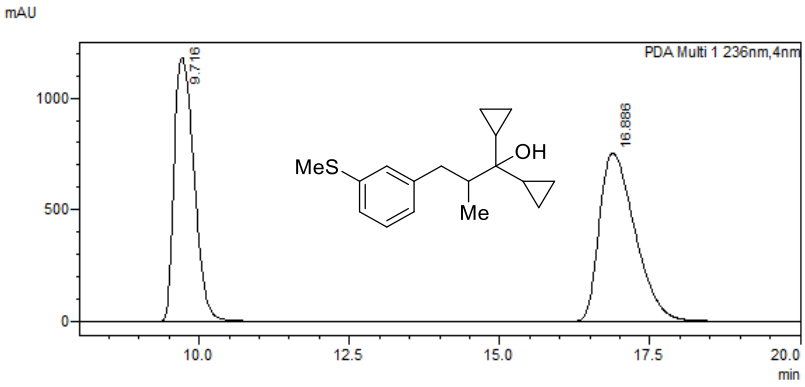
The enantiomeric excess of (*S*)-**152a** was determined to 90%.

(*R*)-152b

The enantiomeric excess of (*R*)-**152b** was determined by chiral HPLC analysis.

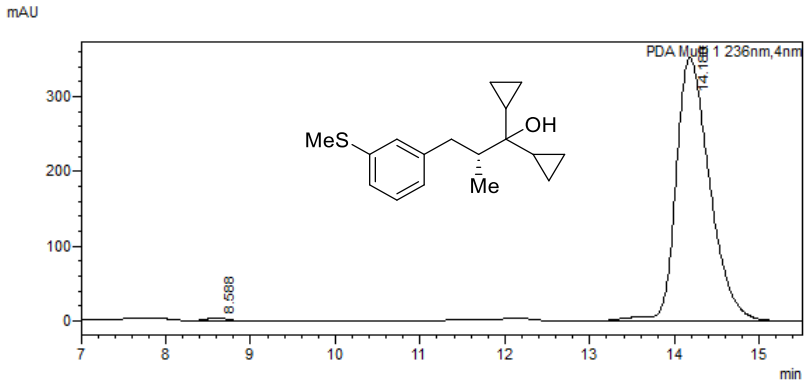
HPLC (column: OD-H; *n*-heptane/2-propanol = 98:2, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	9.716	27326583	1178811	46.684
2	16.886	31209135	752704	53.316
Total		58535718	1931516	100.000

(*R*)-Enantiomer: t_R (min) = 8.6 ((*S*)-enantiomer, minor), 14.2 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	8.588	70829	4459	0.722
2	14.180	9732780	352539	99.278
Total		9803609	356998	100.000

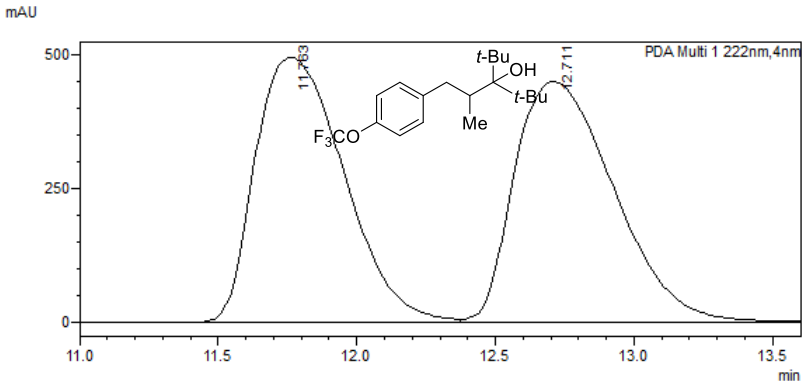
The enantiomeric excess of (*R*)-**152b** was determined to 99%.

(*S*)-152c

The enantiomeric excess of (*S*)-**152c** was determined by chiral HPLC analysis.

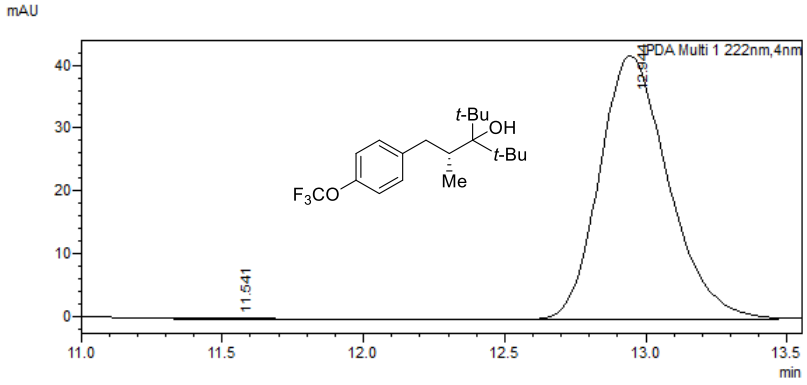
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.8:0.2, 0.5 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	11.763	11073574	495854	49.485
2	12.711	11304212	450112	50.515
Total		22377786	945966	100.000

(*S*)-Enantiomer: t_R (min) = 11.5 ((*R*)-enantiomer, minor), 12.9 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	11.541	6368	255	0.884
2	12.944	713886	41976	99.116
Total		720254	42231	100.000

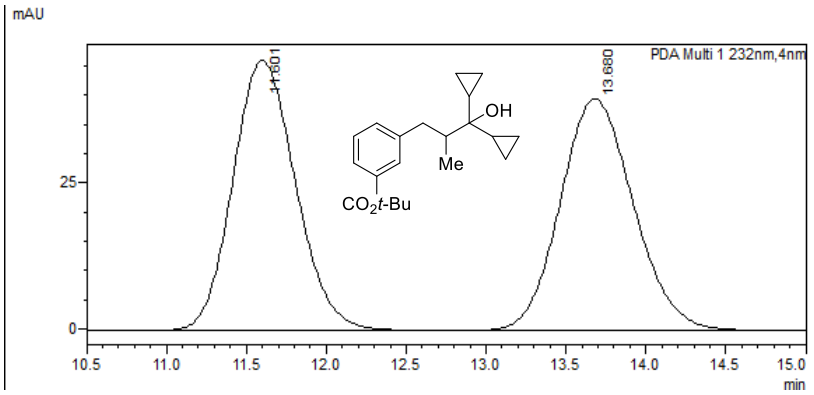
The enantiomeric excess of (*S*)-**152c** was determined to 98%.

(*R*)- and (*S*)-152e

The enantiomeric excess of (*R*)- and (*S*)-**152e** was determined by chiral HPLC analysis.

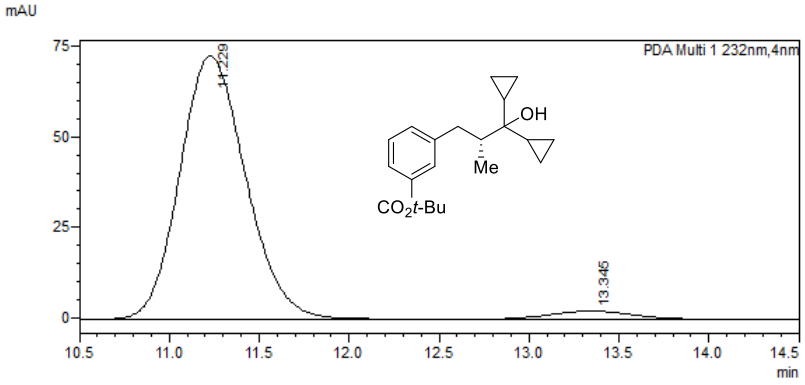
HPLC (column: OD-H; *n*-heptane/2-propanol = 99:1, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	11.601	1254758	46187	49.917
2	13.680	1258918	39559	50.083
Total		2513675	85746	100.000

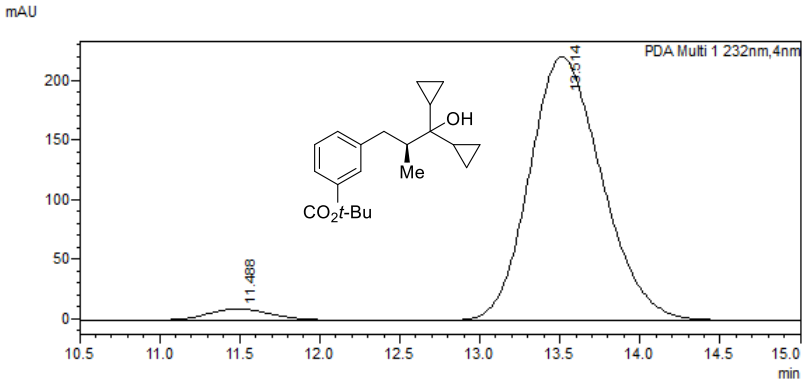
(*R*)-Enantiomer: t_R (min) = 11.3 ((*R*)-enantiomer, major), 13.5 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	11.229	1846325	72683	96.455
2	13.345	67851	2229	3.545
Total		1914176	74912	100.000

The enantiomeric excess of (*R*)-**152e** was determined to 93%.

(*S*)-Enantiomer: t_R (min) = 11.5 ((*R*)-enantiomer, minor), 13.5 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	11.488	241642	9377	3.362
2	13.514	6945710	221138	96.638
Total		7187352	230515	100.000

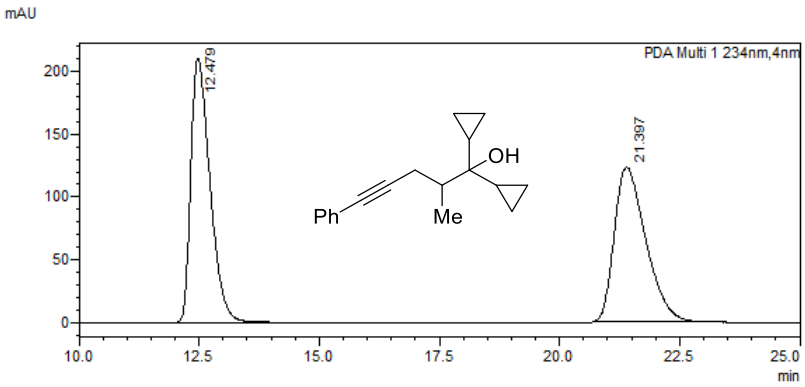
The enantiomeric excess of (*S*)-**152e** was determined to 93%.

(*R*)-152f

The enantiomeric excess of (*R*)-**152f** was determined by chiral HPLC analysis.

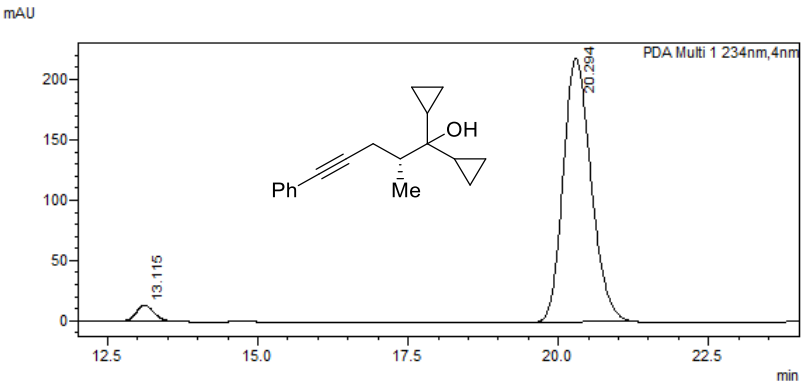
HPLC (column: OD-H; *n*-heptane/2-propanol = 98:2, 0.5 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	12.479	5828381	209942	51.048
2	21.397	5589133	122684	48.952
Total		11417514	332626	100.000

(*R*)-Enantiomer: t_R (min) = 13.1 ((*S*)-enantiomer, minor), 20.3 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	13.115	253101	12925	3.459
2	20.294	7064039	218350	96.541
Total		7317140	231275	100.000

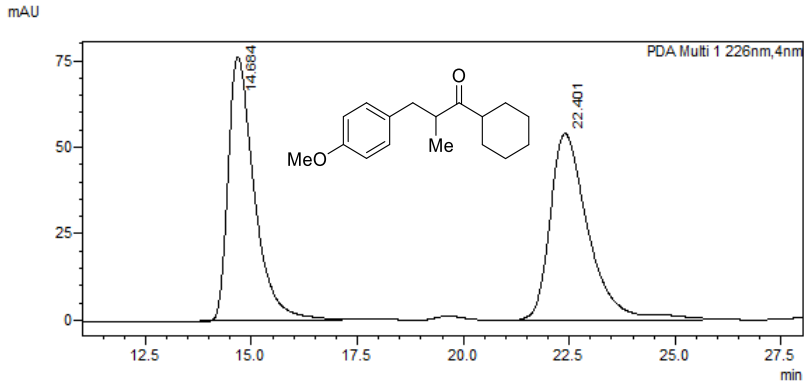
The enantiomeric excess of (*R*)-**152f** was determined to 93%.

(*R*)-152g

The enantiomeric excess of (*R*)-**152g** was determined by chiral HPLC analysis.

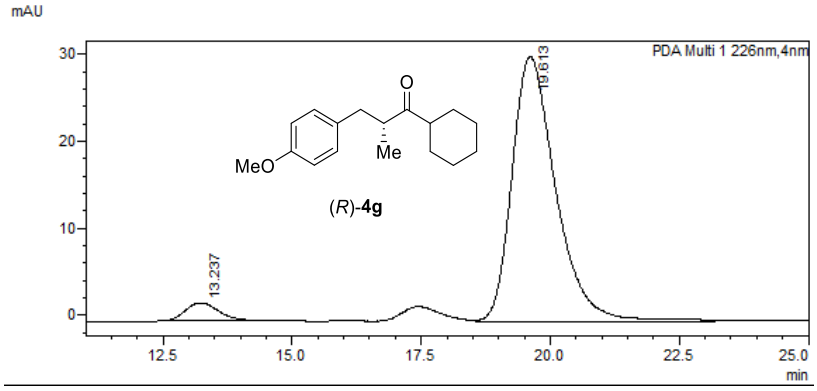
HPLC (column: OJ-H; *n*-heptane/2-propanol = 99.7:0.3, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	14.684	3282438	76146	48.896
2	22.401	3430708	54100	51.104
Total		6713146	130245	100.000

(*R*)-Enantiomer: t_R (min) = 13.2 ((*S*)-enantiomer, minor), 19.6 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	13.237	91998	2055	4.805
2	19.613	1822524	30530	95.195
Total		1914522	32586	100.000

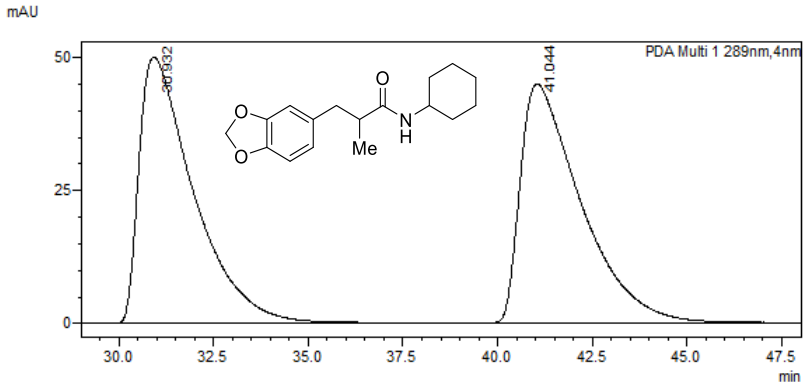
The enantiomeric excess of (*R*)-**152g** was determined to 90%.

(*R*)- and (*S*)-152l

The enantiomeric excess of (*R*)- and (*S*)-**152l** was determined by chiral HPLC analysis.

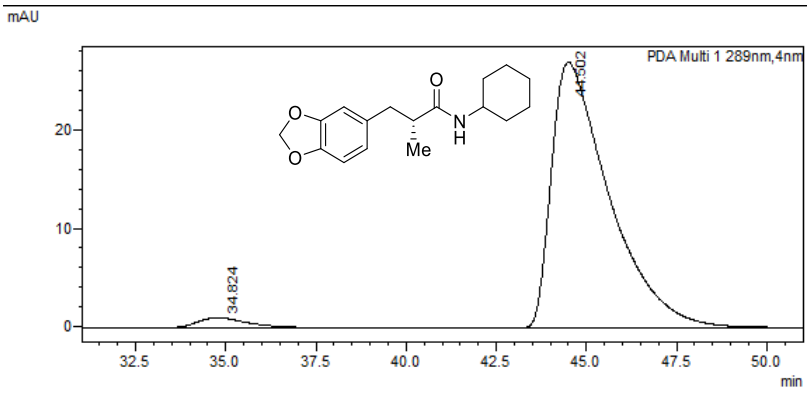
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	30.932	5017068	49987	49.872
2	41.044	5042728	44983	50.128
Total		10059796	94970	100.000

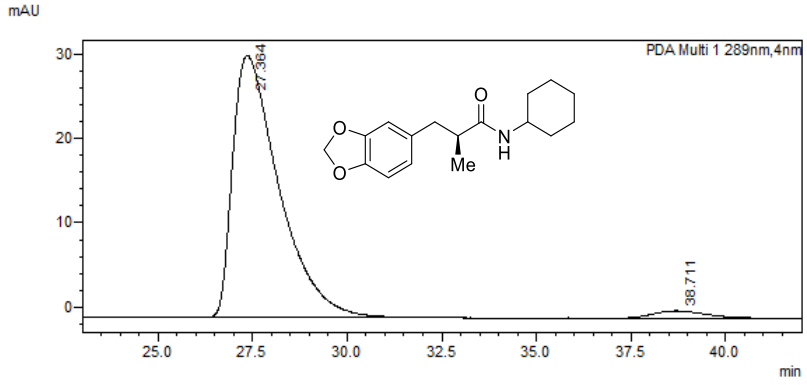
(*R*)-Enantiomer: t_R (min) = 34.8 ((*S*)-enantiomer, minor), 44.5 ((*R*)-enantiomer, major).



1	34.824	97782	1017	3.141
2	44.502	3015744	26934	96.859
Total		3113526	27951	100.000

The enantiomeric excess of (*R*)-**152l** was determined to 94%.

(*S*)-Enantiomer: t_R (min) = 27.3 ((*S*)-enantiomer, major), 38.7 ((*R*)-enantiomer, minor).

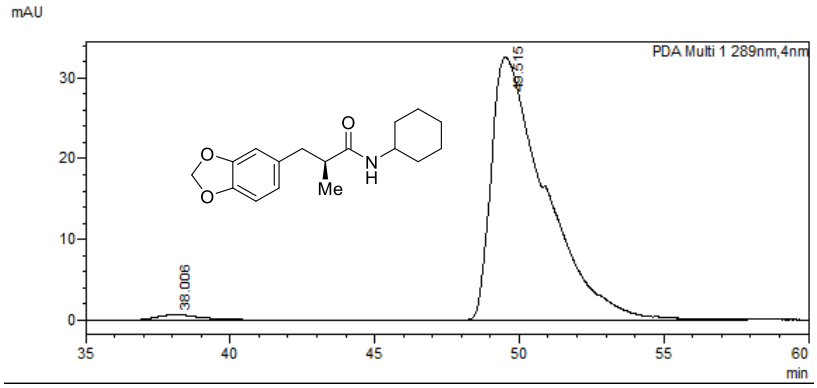


Peak#	Ret. Time	Area	Height	Area%
1	27.364	2627520	31029	96.719
2	38.711	89145	890	3.281
Total		2716666	31918	100.000

The enantiomeric excess of (*S*)-**152l** was determined to 94%.

Determination of the enantiomeric excess of (*S*)-**152l** by chiral HPLC analysis obtained after reaction in continuous flow:

(*S*)-Enantiomer: t_R (min) = 38.0 ((*R*)-enantiomer, minor), 49.5 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	38.006	90072	771	2.064
2	49.515	4273182	32599	97.936
Total		4363254	33370	100.000

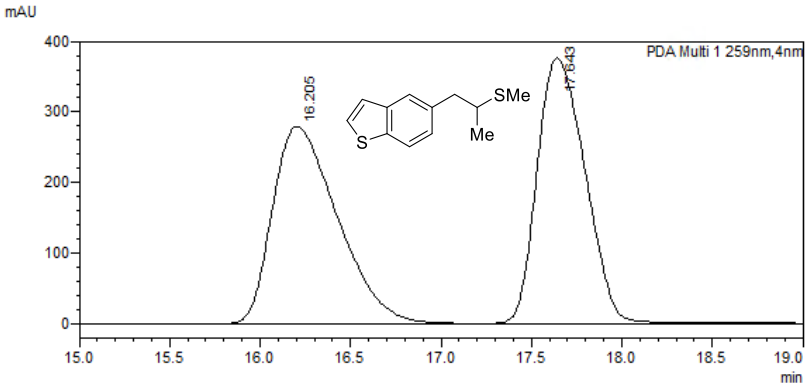
The enantiomeric excess of (*S*)-**152l** was determined to 96%

(*R*)- and (*S*)-152o

The enantiomeric excess of (*R*) and (*S*)-**152o** was determined by chiral HPLC analysis.

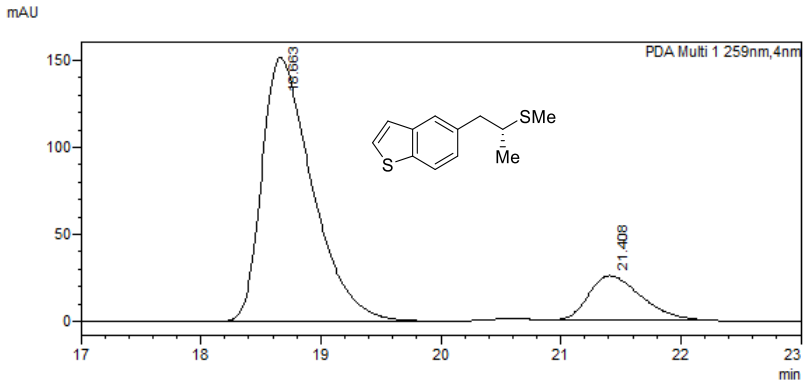
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	16.205	6992471	279140	50.083
2	17.643	6969380	376542	49.917
Total		13961851	655682	100.000

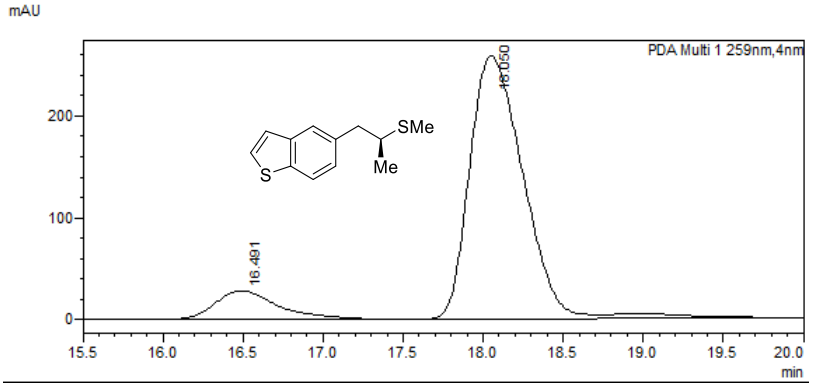
(*R*)-Enantiomer: t_R (min) = 18.6 ((*R*)-enantiomer, major), 21.4 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	18.663	4437119	151599	85.226
2	21.408	769185	25469	14.774
Total		5206304	177068	100.000

The enantiomeric excess of (*R*)-**152o** was determined to 70%

(*S*)-Enantiomer: t_R (min) = 16.5 ((*R*)-enantiomer, minor), 18.1 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	16.491	741404	27825	10.859
2	18.050	6086252	258725	89.141
Total		6827656	286550	100.000

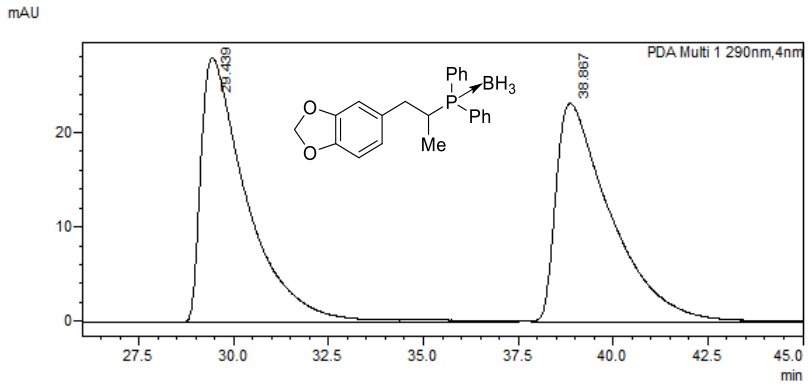
The enantiomeric excess of (*S*)-**152o** was determined to 78%

(*R*)- and (*S*)-152q

The enantiomeric excess of (*R*)- and (*S*)-**152q** was determined by chiral HPLC analysis.

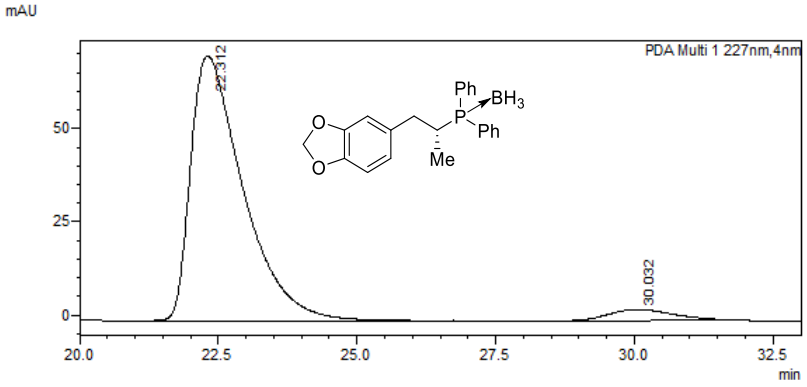
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.7:0.3, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	29.439	2408738	28058	50.330
2	38.867	2377128	23242	49.670
Total		4785867	51300	100.000

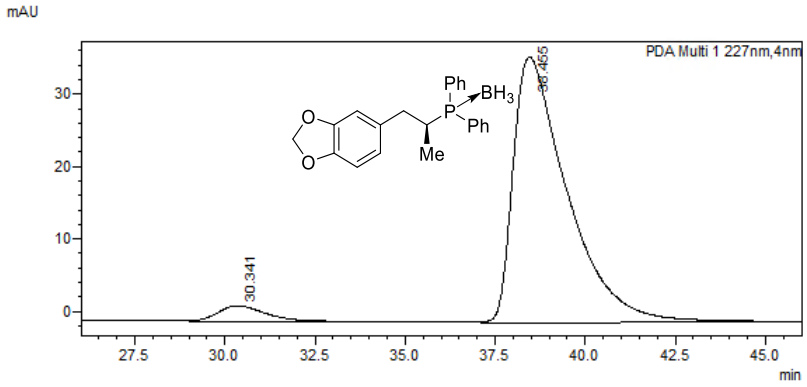
(*R*)-Enantiomer: t_R (min) = 22.3 ((*R*)-enantiomer, major), 30.0 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	22.312	4723819	71146	95.135
2	30.032	241547	2990	4.865
Total		4965367	74136	100.000

The enantiomeric excess of (*R*)-**152q** was determined to 90%.

(*S*)-Enantiomer: t_R (min) = 30.3 ((*R*)-enantiomer, minor), 38.5 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	30.341	202878	2186	5.005
2	38.455	3850935	36707	94.995
Total		4053813	38893	100.000

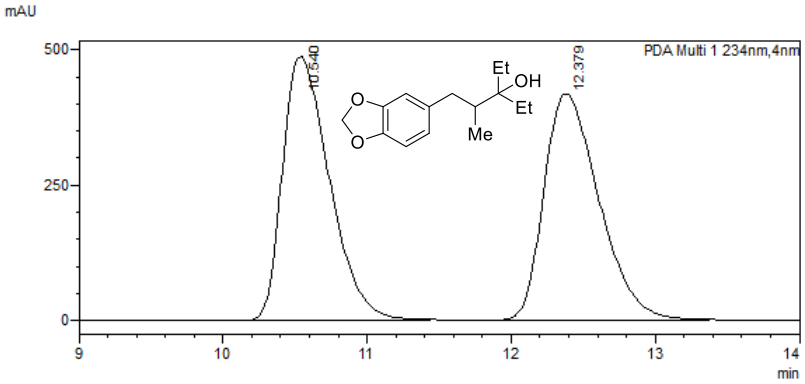
The enantiomeric excess of (*S*)-**152q** was determined to 90%.

(*R*)- and (*S*)-152s

The enantiomeric excess of (*R*)- and (*S*)-**152s** was determined by chiral HPLC analysis.

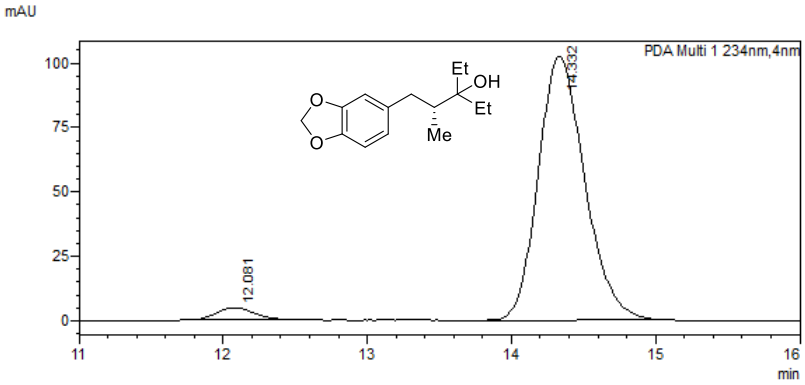
HPLC (column: OD-H; *n*-heptane/2-propanol = 98.0:2.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	10.540	11069849	488077	49.885
2	12.379	11120701	418679	50.115
Total		22190550	906756	100.000

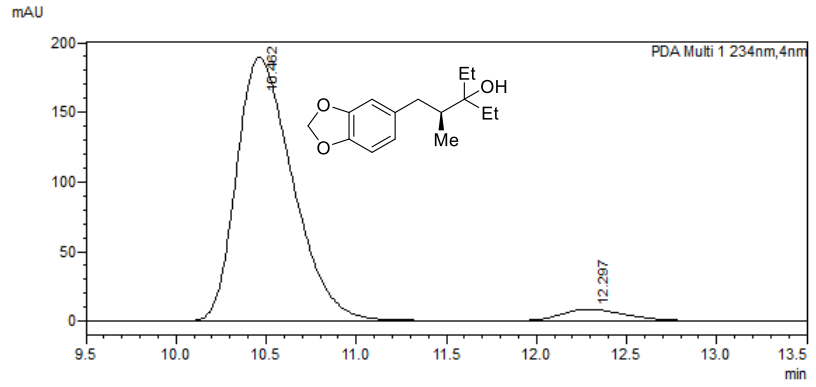
(*R*)-Enantiomer: t_R (min) = 12.1 ((*S*)-enantiomer, minor), 14.3 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	12.081	80373	4577	3.374
2	14.332	2301660	102388	96.626
Total		2382033	106965	100.000

The enantiomeric excess of (*R*)-**152s** was determined to 93%.

(*S*)-Enantiomer: t_R (min) = 10.5 ((*S*)-enantiomer, major), 12.3 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	10.462	4118091	189344	95.328
2	12.297	201805	8256	4.672
Total		4319896	197600	100.000

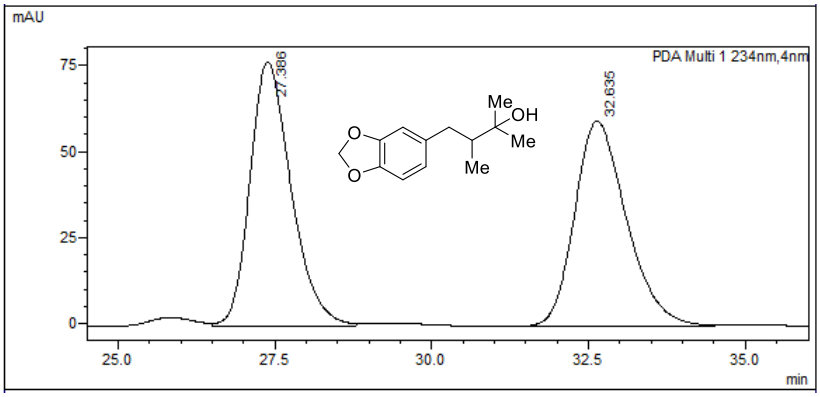
The enantiomeric excess of (*S*)-**152s** was determined to 91%.

(*S*)-152t

The enantiomeric excess of (*S*)-**152t** was determined by chiral HPLC analysis.

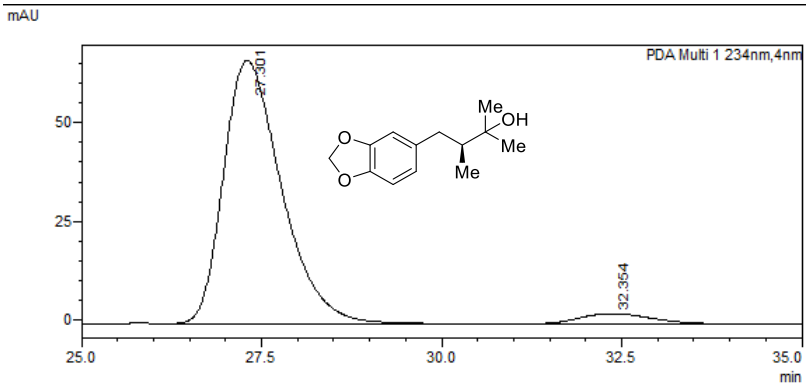
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	27.386	3522825	76752	50.645
2	32.635	3433058	59579	49.355
Total		6955883	136331	100.000

(*S*)-Enantiomer: t_R (min) = 27.3 ((*S*)-enantiomer, major), 32.4 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	27.301	3728924	66488	95.459
2	32.354	177397	2541	4.541
Total		3906322	69028	100.000

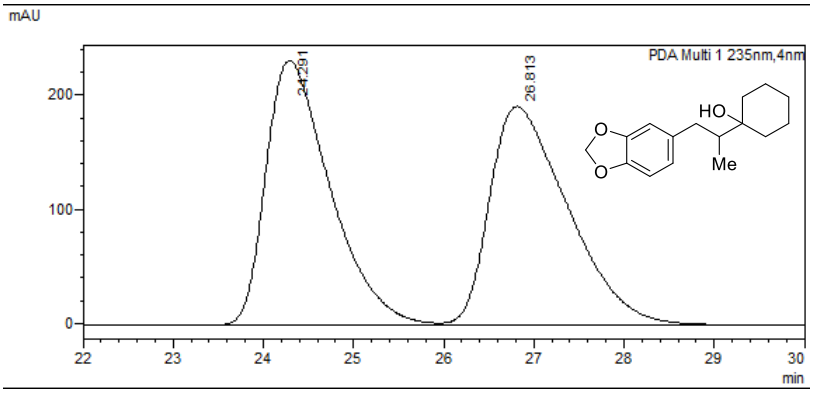
The enantiomeric excess of (*S*)-**152t** was determined to 91%.

(*S*)-152u

The enantiomeric excess of (*S*)-**152u** was determined by chiral HPLC analysis.

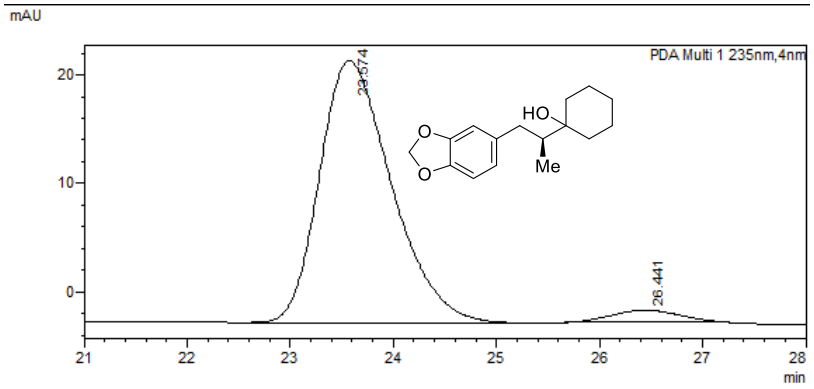
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	24.291	11471210	231145	49.897
2	26.813	11518539	191140	50.103
Total		22989750	422285	100.000

(*S*)-Enantiomer: t_R (min) = 23.6 ((*S*)-enantiomer, major), 26.4 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	23.574	1175183	24184	95.823
2	26.441	51233	1120	4.177
Total		1226416	25304	100.000

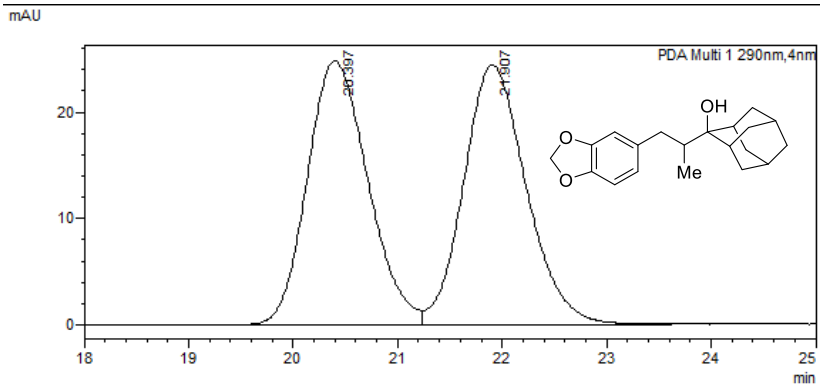
The enantiomeric excess of (*S*)-**152u** was determined to 92%.

(*R*)- and (*S*)-152v

The enantiomeric excess of (*R*)- and (*S*)-**152v** was determined by chiral HPLC analysis.

HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min).

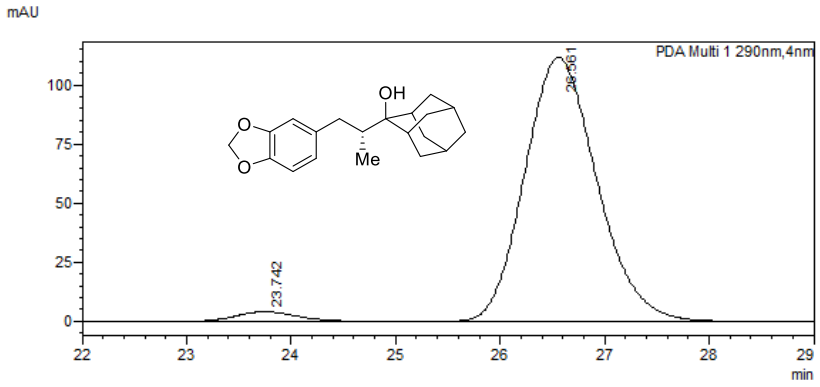
Racemate:



PDA Ch1 290nm

Peak#	Ret. Time	Area	Height	Area%
1	20.397	999979	24812	49.542
2	21.907	1018479	24434	50.458
Total		2018457	49246	100.000

(*R*)-Enantiomer: t_R (min) = 23.7 ((*S*)-enantiomer, minor), 26.6 ((*R*)-enantiomer, major):



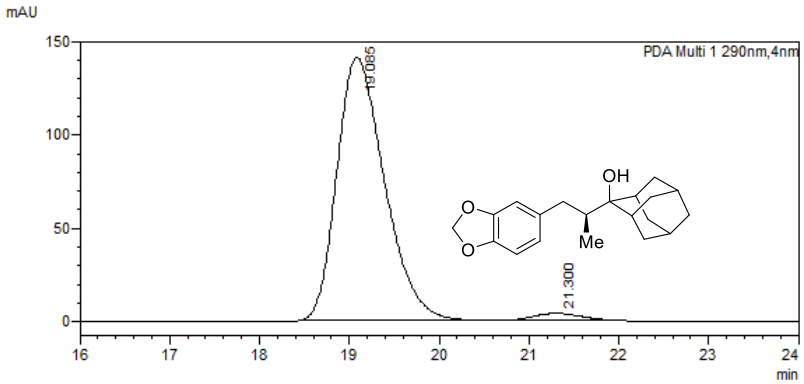
PDA Ch1 290nm

Peak#	Ret. Time	Area	Height	Area%
1	23.742	162155	4037	2.937
2	26.561	5358460	111724	97.063
Total		5520615	115761	100.000

The enantiomeric excess of (*R*)-**152v** was determined to 94%.

Determination of the enantiomeric excess of (*S*)-**152v** by chiral HPLC analysis obtained after reaction in continuous flow:

(*S*)-Enantiomer: t_R (min) = 19.1 ((*S*)-enantiomer, major), 21.3 ((*R*)-enantiomer, minor):



Peak#	Ret. Time	Area	Height	Area%
1	19.085	5207674	141017	97.353
2	21.300	141585	3832	2.647
Total		5349259	144848	100.000

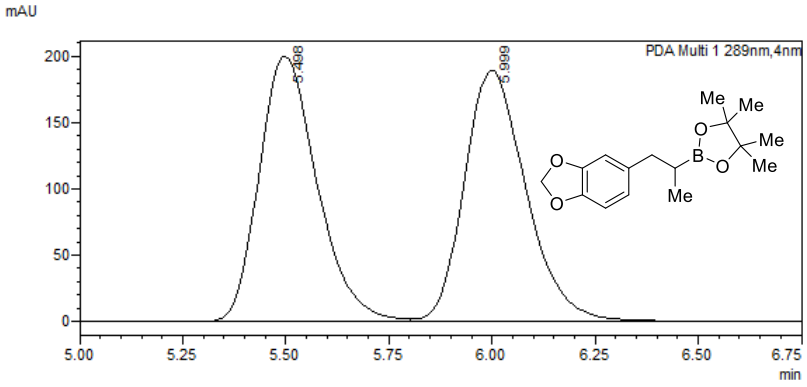
The enantiomeric excess of (*S*)-**152v** was determined to 94%.

(*R*)- and (*S*)-152w

The enantiomeric excess of (*R*)- and (*S*)-**152w** was determined by chiral HPLC analysis.

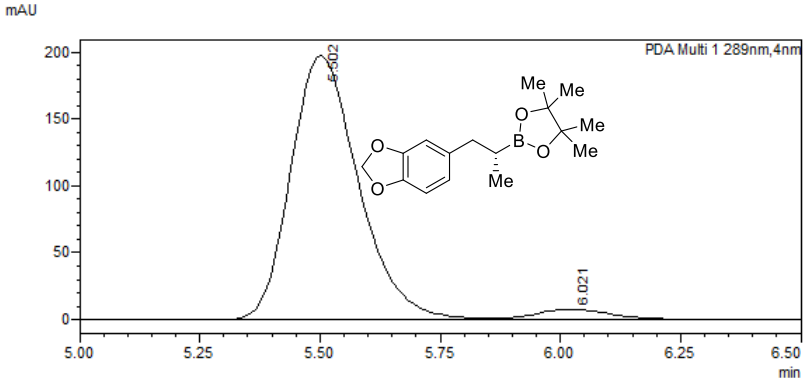
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.5:0.5, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	5.498	1955836	199893	49.768
2	5.999	1974038	189149	50.232
Total		3929874	389042	100.000

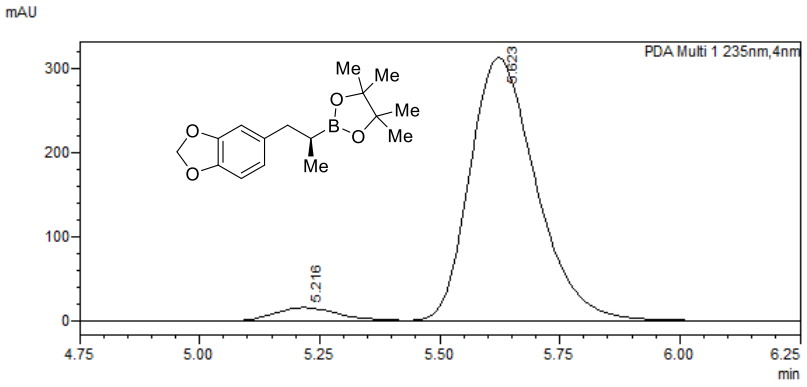
(*R*)-Enantiomer: t_R (min) = 5.5 ((*R*)-enantiomer, major), 6.0 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	5.502	1934992	197632	95.790
2	6.021	85050	7752	4.210
Total		2020042	205385	100.000

The enantiomeric excess of (*R*)-**152w** was determined to 92%.

(*S*)-Enantiomer: t_R (min) = 5.2 ((*R*)-enantiomer, minor), 5.6 ((*S*)-enantiomer, major).

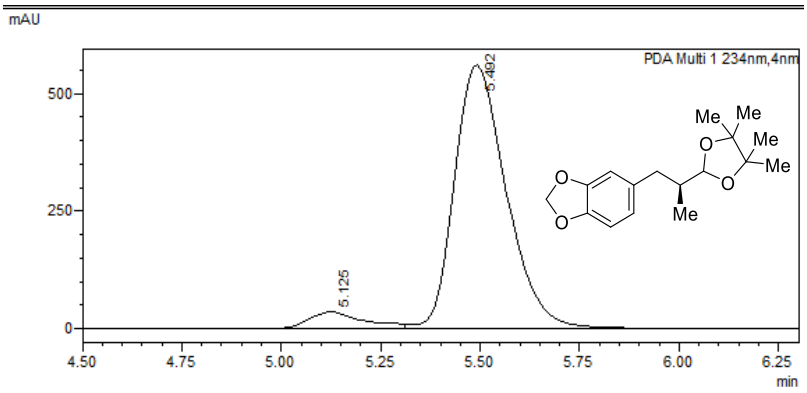


Peak#	Ret. Time	Area	Height	Area%
1	5.216	147883	16080	4.702
2	5.623	2997237	312893	95.298
Total		3145120	328973	100.000

The enantiomeric excess of (*S*)-**152w** was determined to 91%.

Determination of the enantiomeric excess of (*S*)-**152w** by chiral HPLC analysis obtained after reaction in continuous flow:

(*S*)-Enantiomer: t_R (min) = 5.1 ((*R*)-enantiomer, minor), 5.5 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	5.125	343132	34444	6.307
2	5.492	5097415	561667	93.693
Total		5440547	596111	100.000

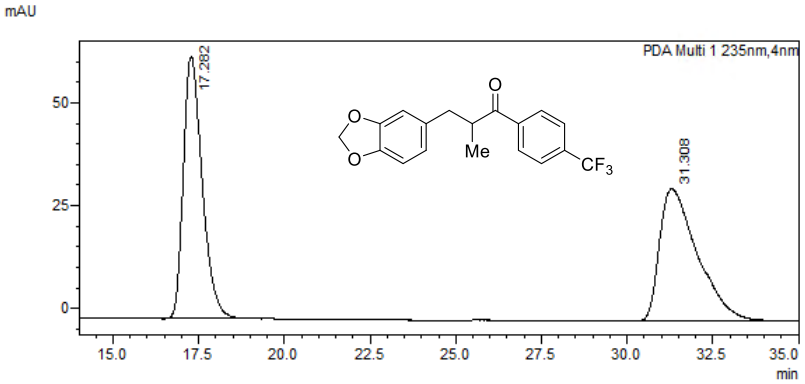
The enantiomeric excess of (*S*)-**152w** was determined to 88%.

(*R*)-152x

The enantiomeric excess of (*R*)-**152x** was determined by chiral HPLC analysis.

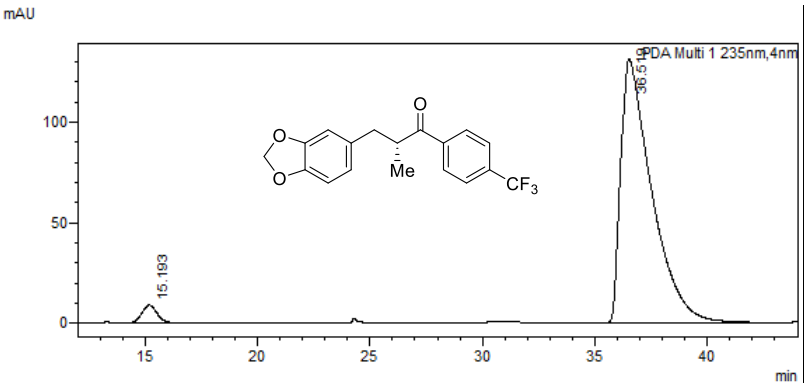
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.7:0.3, 1.0 mL/min).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	17.282	2450357	63795	49.863
2	31.308	2463780	32170	50.137
Total		4914137	95965	100.000

(*R*)-Enantiomer: t_R (min) = 15.2 ((*S*)-enantiomer, minor), 36.5 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	15.193	406314	8742	3.125
2	36.519	12595574	131309	96.875
Total		13001887	140051	100.000

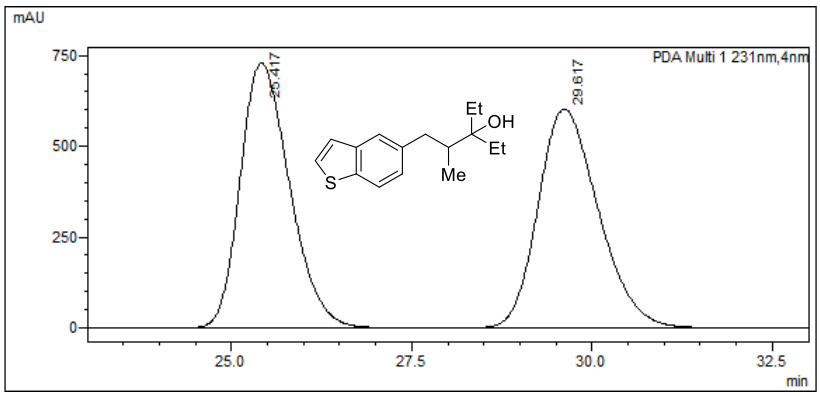
The enantiomeric excess of (*R*)-**152x** was determined to 94%.

(*R*)- and (*S*)-152y

The enantiomeric excess of (*R*)- and (*S*)-**152y** was determined by chiral HPLC analysis.

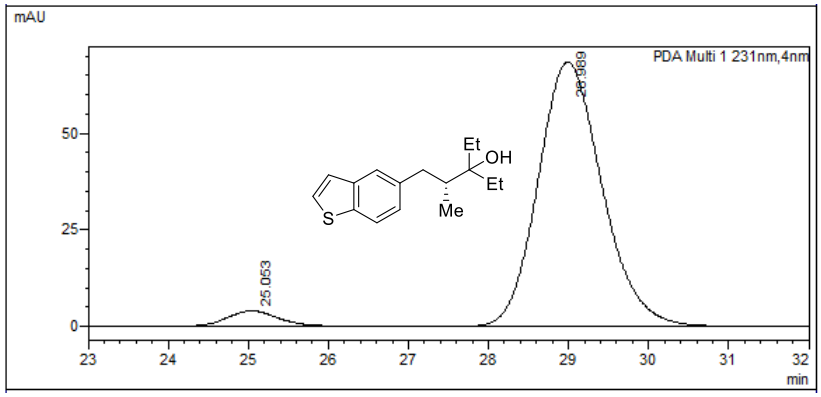
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	25.417	34549929	728255	49.722
2	29.617	34935803	601974	50.278
Total		69485732	1330228	100.000

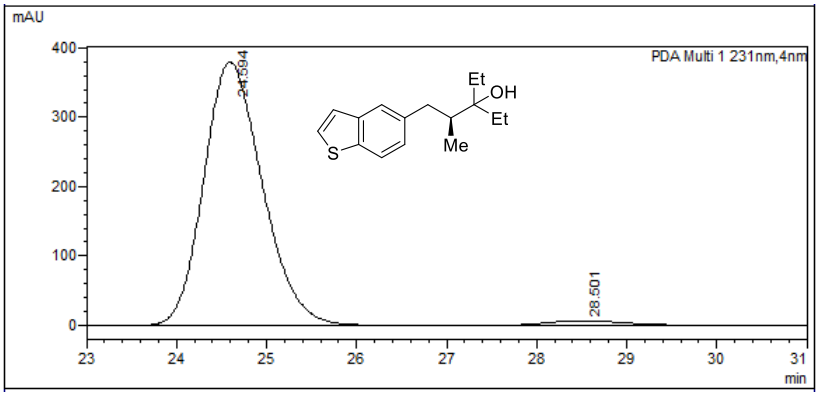
(*R*)-Enantiomer: t_R (min) = 25.1 ((*S*)-enantiomer, minor), 29.0 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	25.053	176125	3941	4.425
2	28.989	3804162	68439	95.575
Total		3980287	72379	100.000

The enantiomeric excess of (*R*)-**152y** was determined to 91%.

(*S*)-Enantiomer: t_R (min) = 24.6 ((*S*)-enantiomer, major), 28.5 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	24.594	17141542	379525	97.796
2	28.501	386320	6764	2.204
Total		17527863	386289	100.000

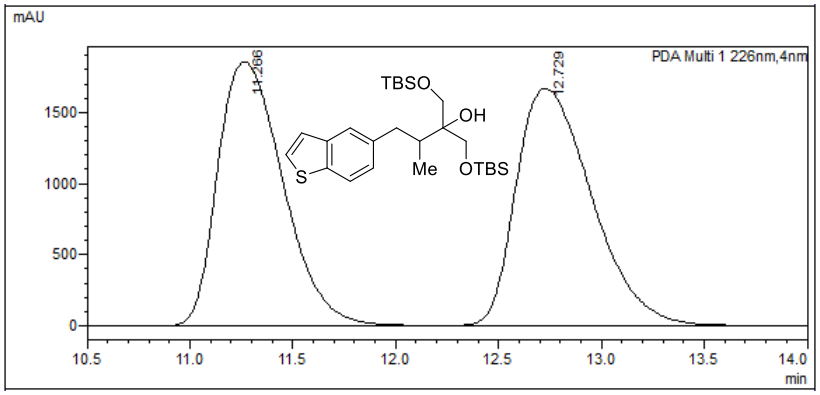
The enantiomeric excess of (*S*)-**152y** was determined to 96%.

(*S*)-152z

The enantiomeric excess of (*S*)-**152z** was determined by chiral HPLC analysis.

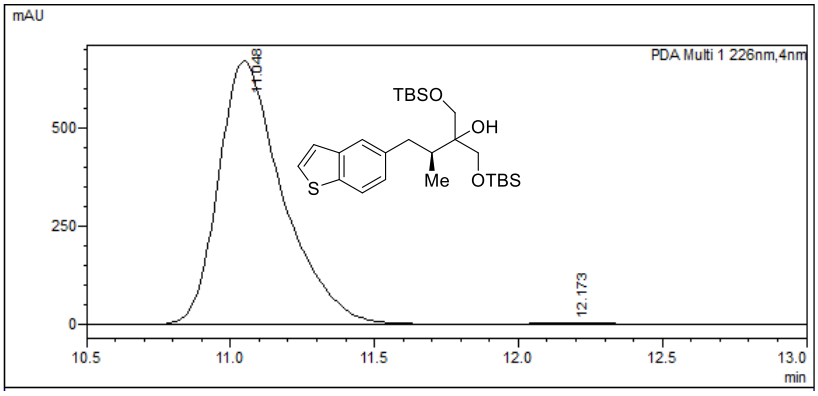
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	11.266	41021708	1852509	48.927
2	12.729	42820864	1666403	51.073
Total		83842572	3518911	100.000

(*S*)-Enantiomer: t_R (min) = 11.1 ((*S*)-enantiomer, major), 12.2 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	11.048	10414193	671241	99.298
2	12.173	73604	5116	0.702
Total		10487796	676357	100.000

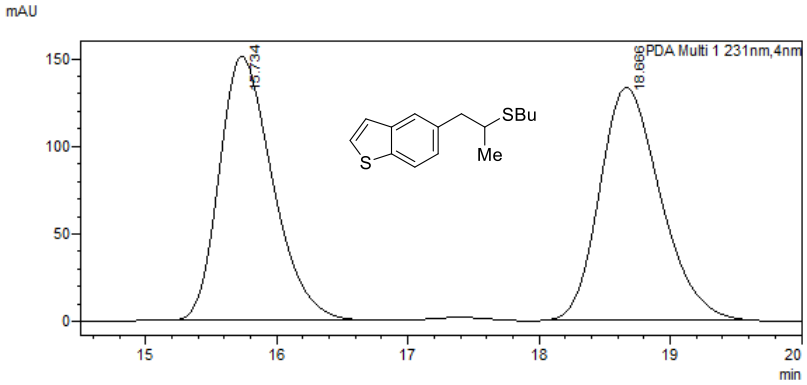
The enantiomeric excess of (*S*)-**152z** was determined to 98%.

(*S*)-152aa

The enantiomeric excess of (*S*)-**152aa** was determined by chiral HPLC analysis.

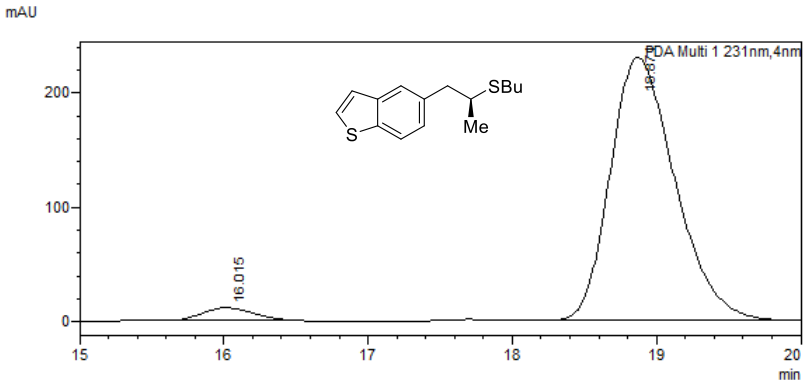
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 1.0 mL/min).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	15.734	4256077	150649	49.830
2	18.666	4285035	132999	50.170
Total		8541112	283648	100.000

(*S*)-Enantiomer: t_R (min) = 16.0 ((*R*)-enantiomer, minor), 18.9 ((*S*)-enantiomer, major).

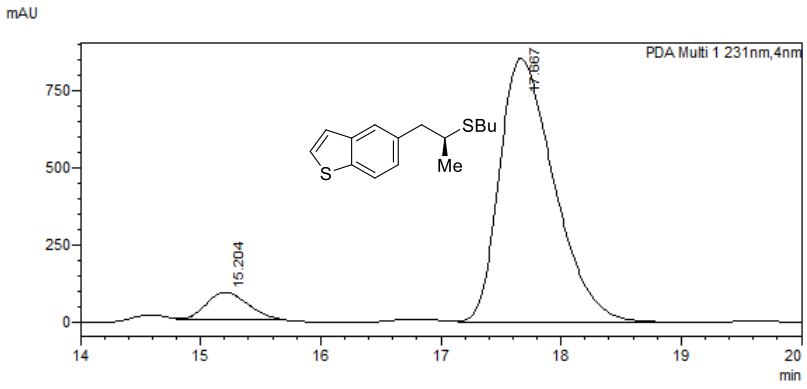


Peak#	Ret. Time	Area	Height	Area%
1	16.015	263151	10931	3.519
2	18.871	7213798	230580	96.481
Total		7476949	241511	100.000

The enantiomeric excess of (*S*)-**152aa** was determined to 93%.

Determination of the enantiomeric excess of (*S*)-**152aa** by chiral HPLC analysis obtained after reaction in continuous flow:

(*S*)-Enantiomer: t_R (min) = 15.2 ((*R*)-enantiomer, minor), 17.7 ((*S*)-enantiomer, major):



Peak#	Ret. Time	Area	Height	Area%
1	15.204	2234250	90585	7.595
2	17.667	27184989	855475	92.405
Total		29419239	946060	100.000

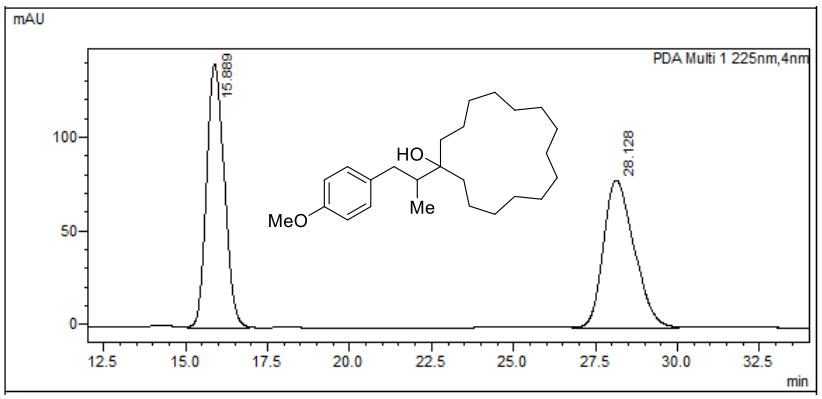
The enantiomeric excess of (*S*)-**152aa** was determined to 86%.

(*S*)-152ac

The enantiomeric excess of (*S*)-**152ac** was determined by chiral HPLC analysis.

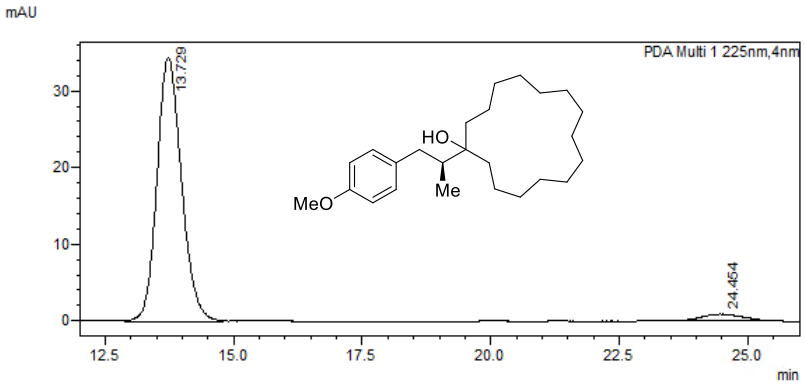
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	15.889	5298240	140806	50.853
2	28.128	5120446	78793	49.147
Total		10418687	219599	100.000

(*S*)-Enantiomer: t_R (min) = 13.8 ((*S*)-enantiomer, major), 24.5 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	13.729	1142626	34423	96.026
2	24.454	47282	873	3.974
Total		1189908	35296	100.000

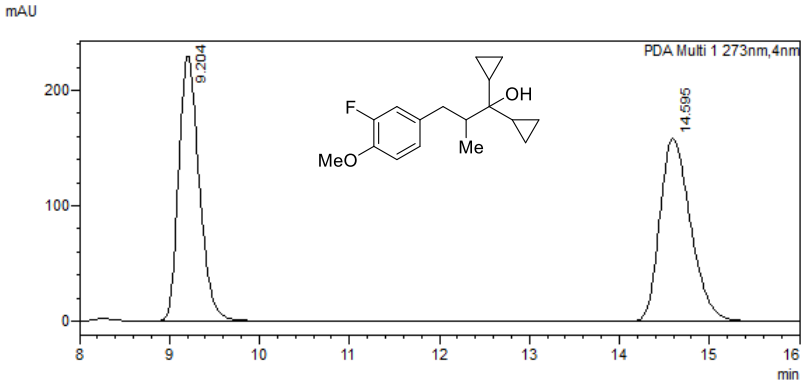
The enantiomeric excess of (*S*)-**152ac** was determined to 92%.

(*S*)-152ae

The enantiomeric excess of (*S*)-**152ae** was determined by chiral HPLC analysis.

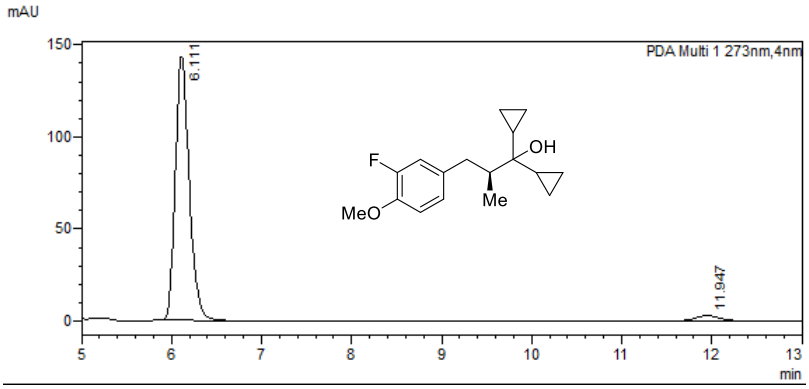
HPLC (column: OD-H; *n*-heptane/2-propanol = 95.0:5.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	9.204	3646207	229098	49.360
2	14.595	3740768	157946	50.640
Total		7386975	387044	100.000

(*S*)-Enantiomer: t_R (min) = 6.1 ((*S*)-enantiomer, major), 11.9 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	6.111	1547165	142800	96.991
2	11.947	48000	2673	3.009
Total		1595165	145472	100.000

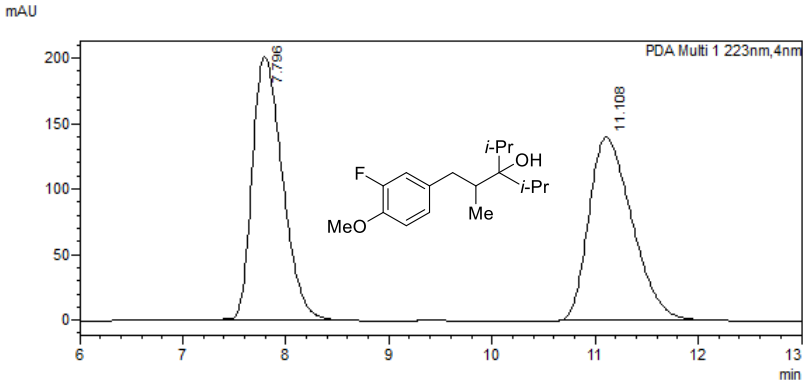
The enantiomeric excess of (*S*)-**152ae** was determined to 94%.

(*R*)- and (*S*)-152af

The enantiomeric excess of (*R*)- and (*S*)-**152af** was determined by chiral HPLC analysis.

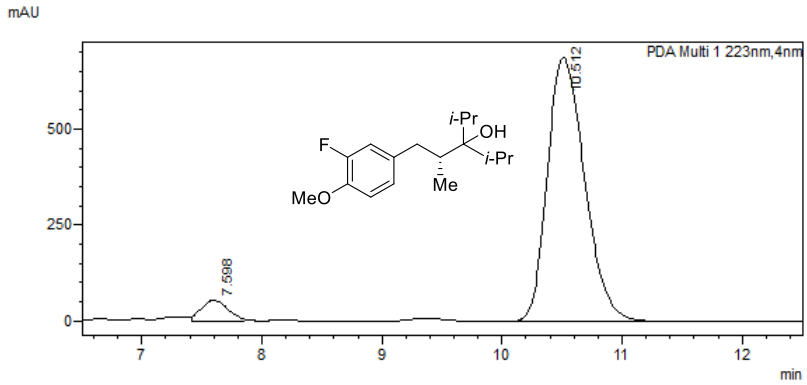
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min)

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	7.796	4096989	201070	50.322
2	11.108	4044621	139382	49.678
Total		8141610	340451	100.000

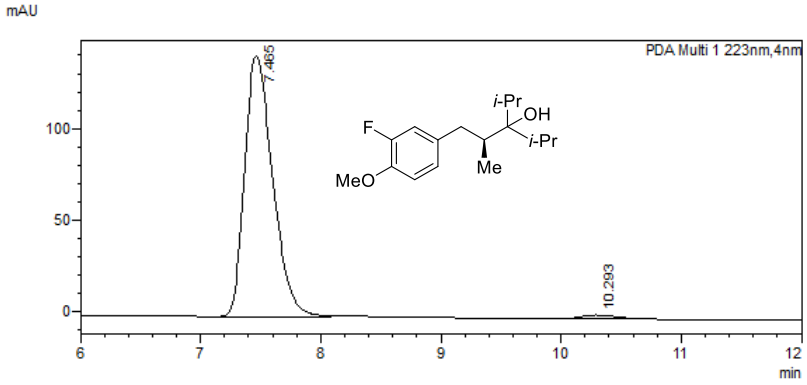
(*R*)-Enantiomer: t_R (min) = 7.6 ((*S*)-enantiomer, minor), 10.5 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	7.598	834337	53826	5.334
2	10.512	14807319	686574	94.666
Total		15641656	740400	100.000

The enantiomeric excess of (*R*)-**152af** was determined to 90%.

(*S*)-Enantiomer: t_R (min) = 7.5 ((*S*)-enantiomer, major), 10.3 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	7.465	2313292	142420	98.103
2	10.293	44728	2202	1.897
Total		2358021	144622	100.000

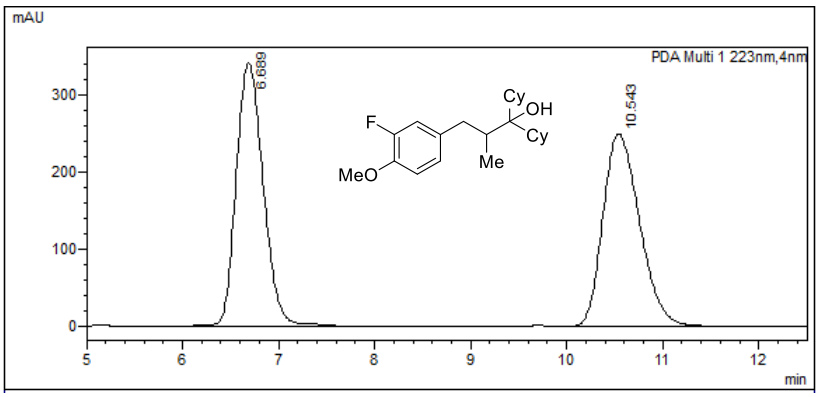
The enantiomeric excess of (*S*)-**152af** was determined to 96%.

(*R*)-152ag

The enantiomeric excess of (*R*)-**152ag** was determined by chiral HPLC analysis.

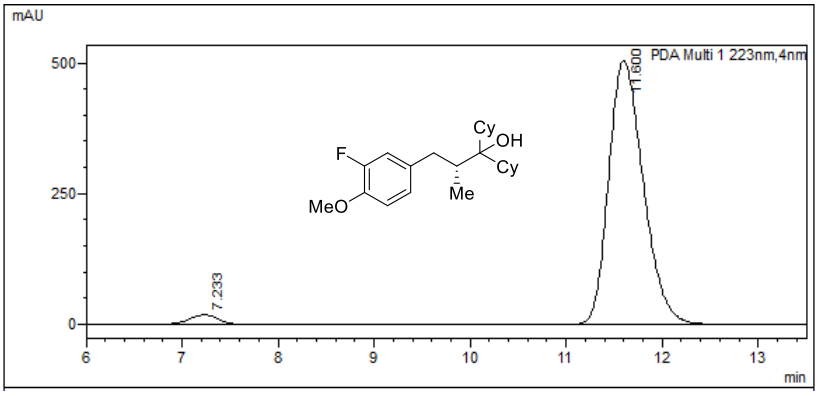
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	6.689	6756096	341383	50.331
2	10.543	6667141	249348	49.669
Total		13423237	590732	100.000

(*R*)-Enantiomer: t_R (min) = 7.2 ((*S*)-enantiomer, minor), 11.6 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	7.233	359754	17576	2.765
2	11.600	12649111	504139	97.235
Total		13008866	521714	100.000

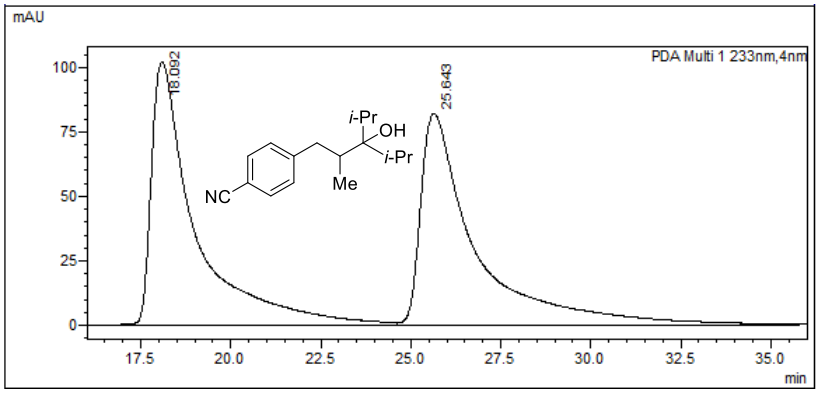
The enantiomeric excess of (*R*)-**152ag** was determined to 94%.

(*S*)-152ai

The enantiomeric excess of (*S*)-**152ai** was determined by chiral HPLC analysis.

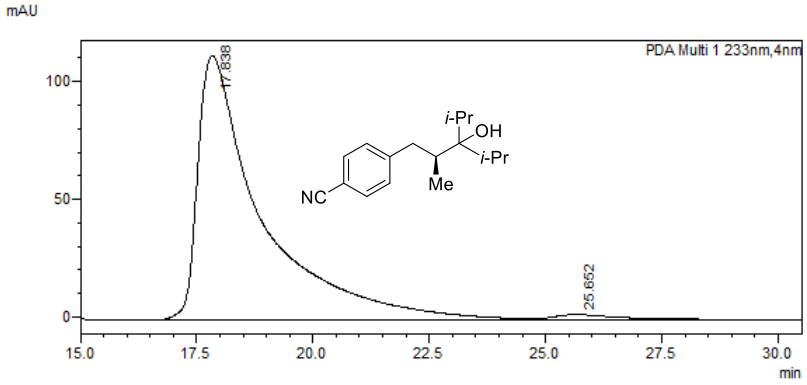
HPLC (column: OD-H; *n*-heptane/2-propanol = 98.0:2.0, 1.0 mL/min).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	18.092	8621827	101846	49.555
2	25.643	8776639	82095	50.445
Total		17398466	183942	100.000

(*S*)-Enantiomer: t_R (min) = 17.8 ((*S*)-enantiomer, major), 25.7 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	17.838	10702060	112029	97.609
2	25.652	262197	2310	2.391
Total		10964257	114339	100.000

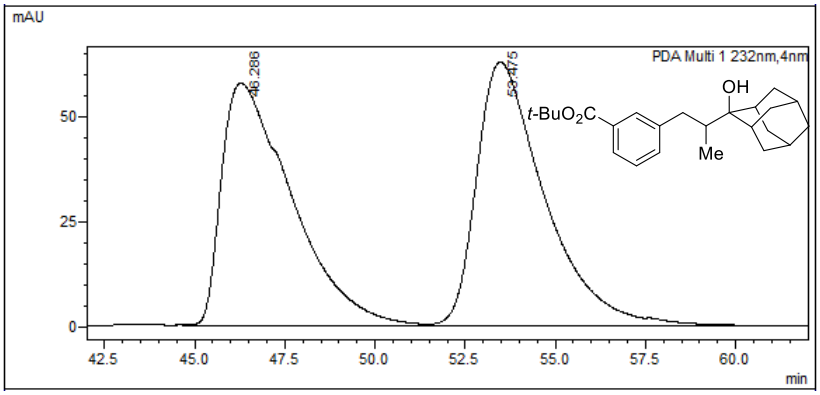
The enantiomeric excess of (*S*)-**152ai** was determined to 95%.

(*R*)- and (*S*)-152aj

The enantiomeric excess of (*R*)- and (*S*)-**152aj** was determined by chiral HPLC analysis.

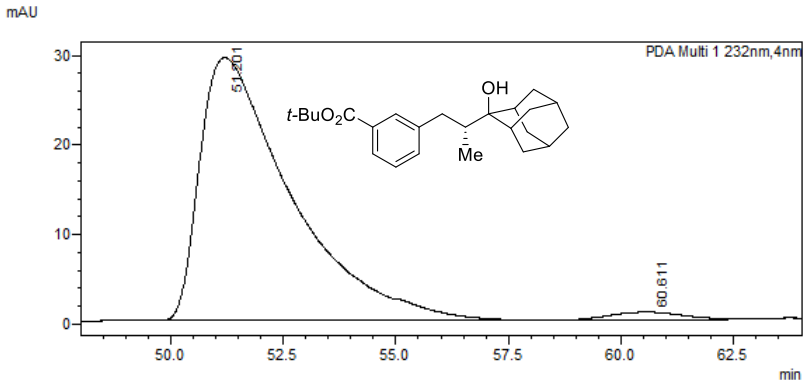
HPLC (column: OD-H; *n*-heptane/2-propanol = 98.0:2.0, 1.0 mL/min).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	46.286	7805678	57664	48.721
2	53.475	8215514	62691	51.279
Total		16021193	120354	100.000

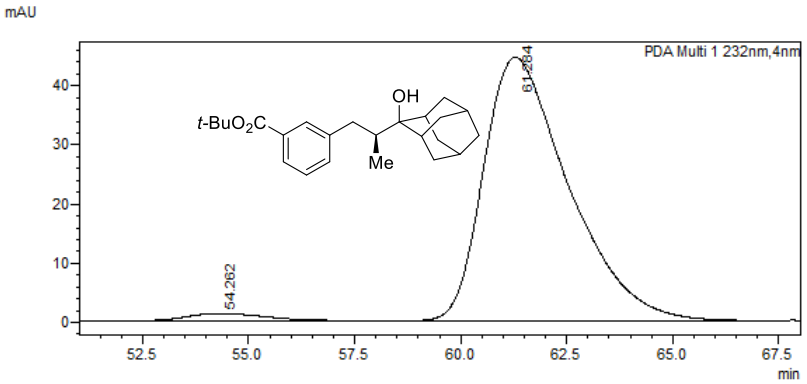
(*R*)-Enantiomer: t_R (min) = 51.2 ((*R*)-enantiomer, major), 60.6 ((S)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	51.201	4120292	29363	97.409
2	60.611	109578	917	2.591
Total		4229870	30281	100.000

The enantiomeric excess of (*R*)-**152aj** was determined to 95%.

(*S*)-Enantiomer: t_R (min) = 54.3 ((*R*)-enantiomer, minor), 61.3 ((S)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	54.262	168061	1280	2.640
2	61.284	6197548	44543	97.360
Total		6365609	45823	100.000

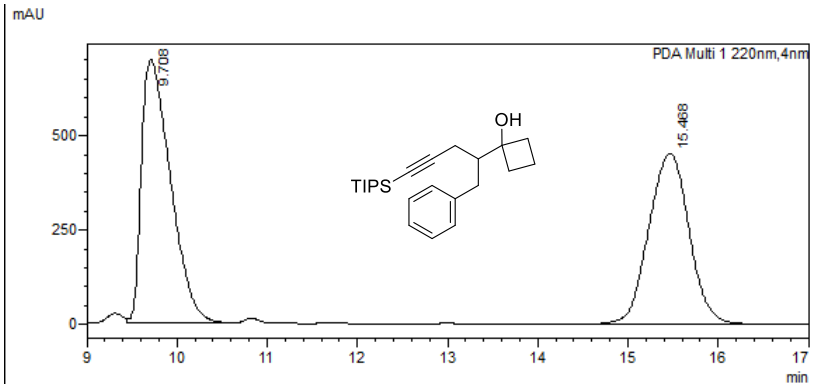
The enantiomeric excess of (*S*)-**152aj** was determined to 95%.

(*S*)-152al

The enantiomeric excess of (*S*)-**152al** was determined by chiral HPLC analysis.

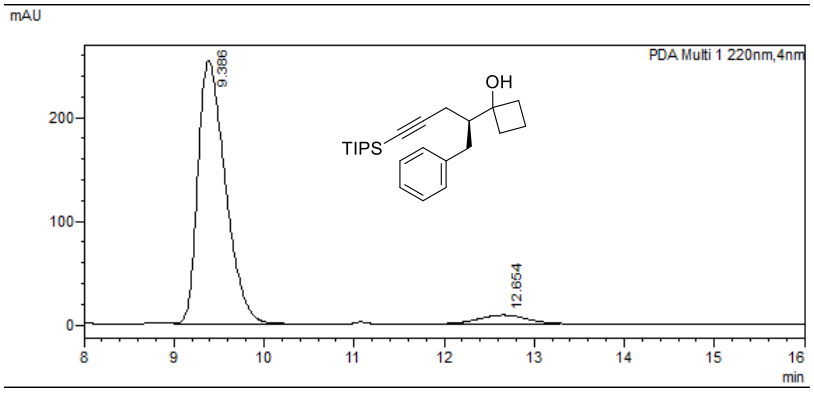
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.5:0.5, 1 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	9.708	15646432	697141	52.734
2	15.468	14024273	451585	47.266
Total		29670705	1148726	100.000

(*S*)-Enantiomer: t_R (min) = 9.4 ((*S*)-enantiomer, major), 12.7 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	9.386	5368419	253377	94.892
2	12.654	288979	8140	5.108
Total		5657398	261516	100.000

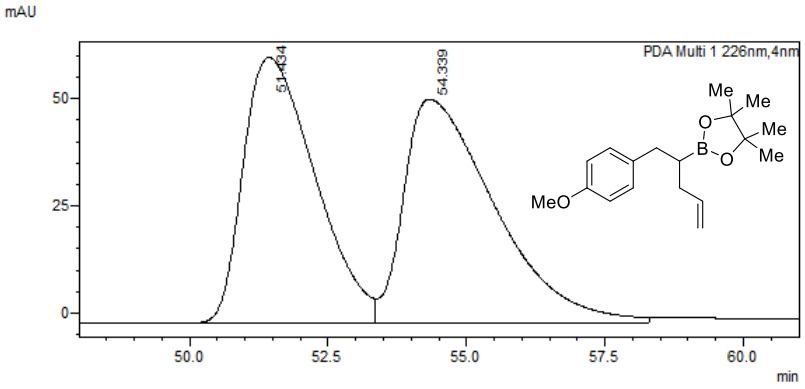
The enantiomeric excess of (*S*)-**152al** was determined to 90%

(*S*)-152am

The enantiomeric excess of (*S*)-**152am** was determined by chiral HPLC analysis.

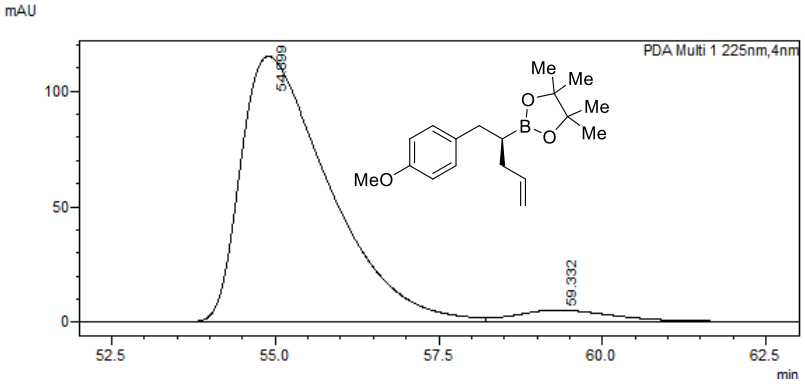
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 0.3 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	51.434	5608152	62144	48.216
2	54.339	6023257	52386	51.784
Total		11631409	114530	100.000

(*S*)-Enantiomer: t_R (min) = 54.9 ((*S*)-enantiomer, major), 59.3 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	54.899	10786604	114881	95.247
2	59.332	538278	5071	4.753
Total		11324881	119952	100.000

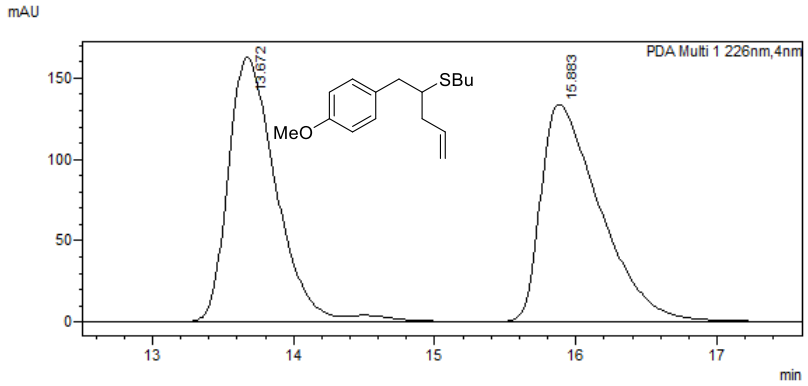
The enantiomeric excess of (*S*)-**152am** was determined to 90%

(*S*)-152an

The enantiomeric excess of (*S*)-**152an** was determined by chiral HPLC analysis.

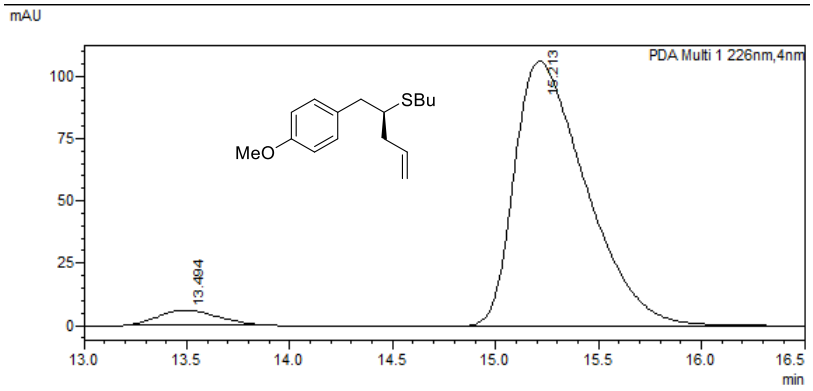
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.9:0.1, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	13.672	3865943	162731	49.654
2	15.883	3919808	133682	50.346
Total		7785751	296414	100.000

(*S*)-Enantiomer: t_R (min) = 13.5 ((*R*)-enantiomer, minor), 15.2 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	13.494	124496	6195	4.594
2	15.213	2585645	106379	95.406
Total		2710142	112574	100.000

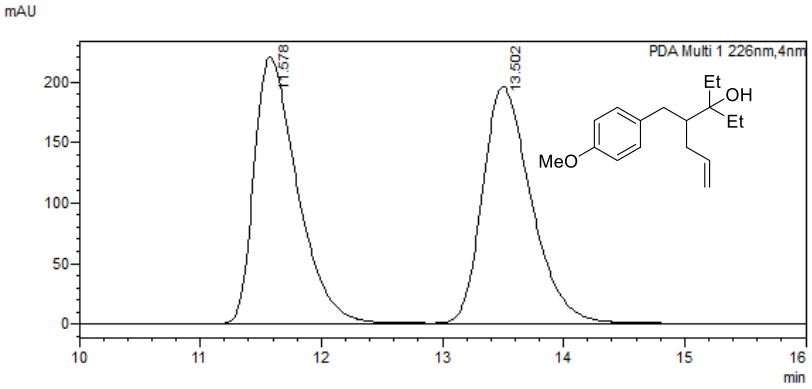
The enantiomeric excess of (*S*)-**152an** was determined to 91%

(*S*)-152ao

The enantiomeric excess of (*S*)-**152ao** was determined by chiral HPLC analysis.

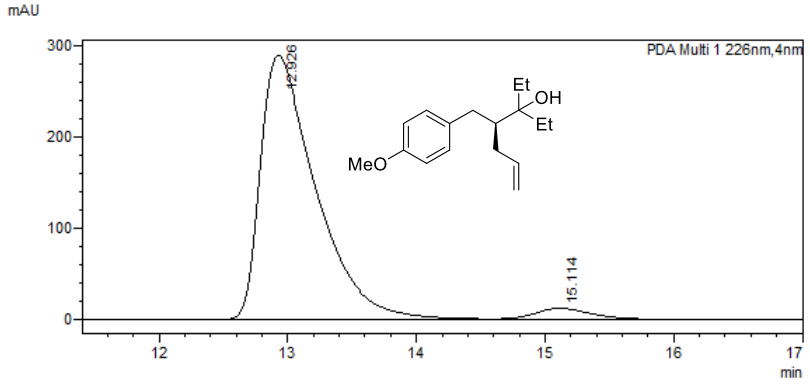
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	11.578	5482372	220428	49.805
2	13.502	5525348	196240	50.195
Total		11007719	416668	100.000

(*S*)-Enantiomer: t_R (min) = 12.9 ((*S*)-enantiomer, major), 15.1 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	12.926	8645122	289691	96.032
2	15.114	357186	12043	3.968
Total		9002308	301734	100.000

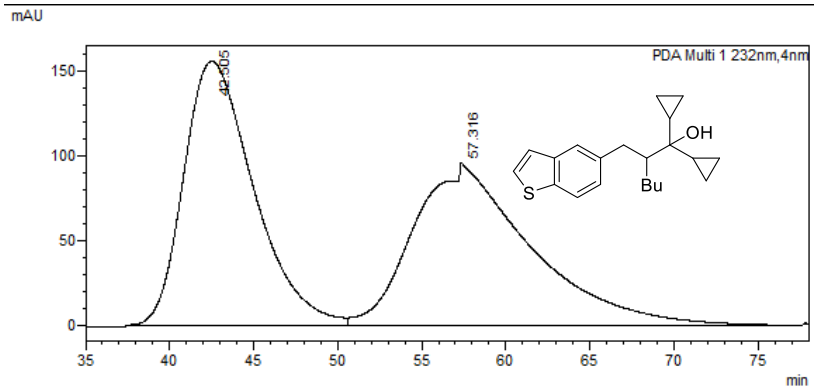
The enantiomeric excess of (*S*)-**152ao** was determined to 92%.

(*S*)-152ap

The enantiomeric excess of (*S*)-**152ap** was determined by chiral HPLC analysis.

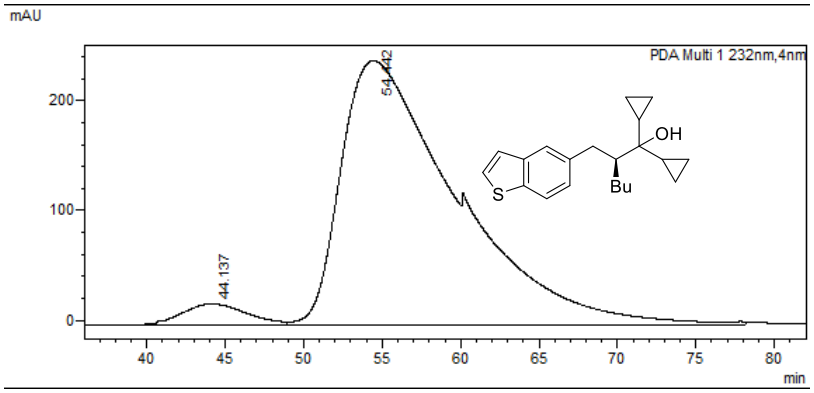
HPLC (column: OJ-H; *n*-heptane/2-propanol = 99.9:0.1, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	42.505	44742322	155090	49.493
2	57.316	45658948	95075	50.507
Total		90401270	250165	100.000

(*S*)-Enantiomer: t_R (min) = 44.1 ((*R*)-enantiomer, minor), 54.4 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	44.137	5387921	18967	4.183
2	54.442	123419504	239975	95.817
Total		128807426	258942	100.000

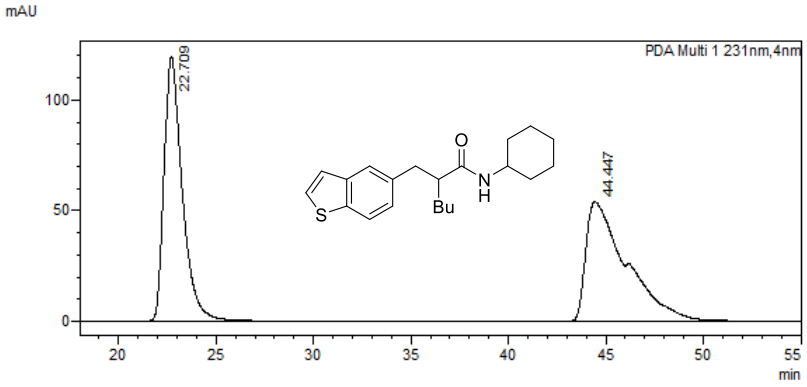
The enantiomeric excess of (*S*)-**152ap** was determined to 92%

(*S*)-152aq

The enantiomeric excess of (*S*)-**152aq** was determined by chiral HPLC analysis.

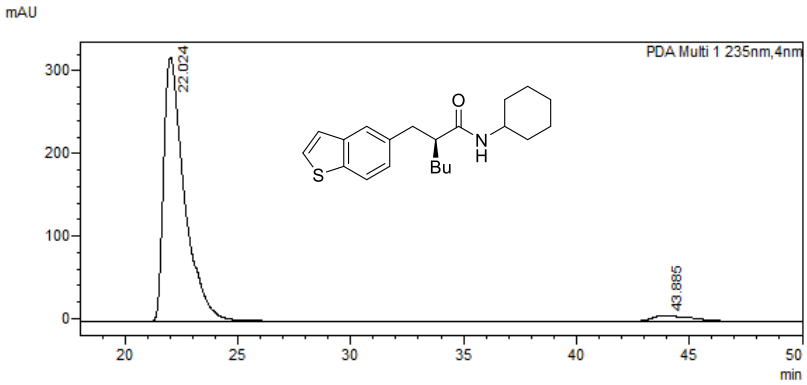
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	22.709	7845420	119685	49.956
2	44.447	7859324	53835	50.044
Total		15704744	173521	100.000

(*S*)-Enantiomer: t_R (min) = 22.0 ((*S*)-enantiomer, major), 43.9 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	22.024	20550376	319333	95.792
2	43.885	902636	7245	4.208
Total		21453013	326578	100.000

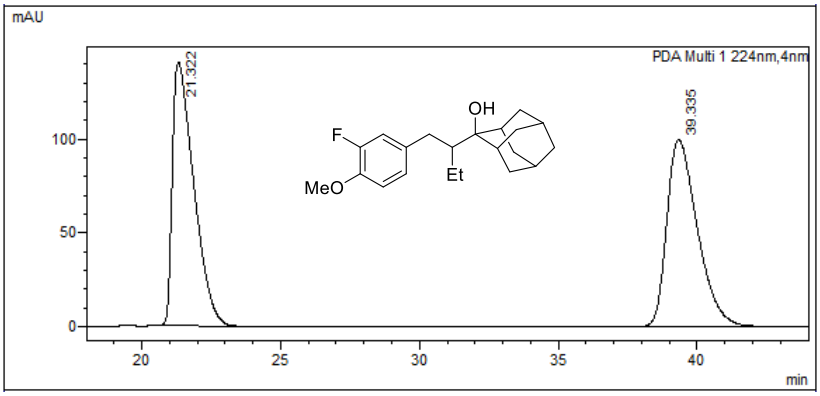
The enantiomeric excess of (*S*)-**152aq** was determined to 92%

(*R*)- and (*S*)-152at

The enantiomeric excess of (*R*)- and (*S*)-**152at** was determined by chiral HPLC analysis.

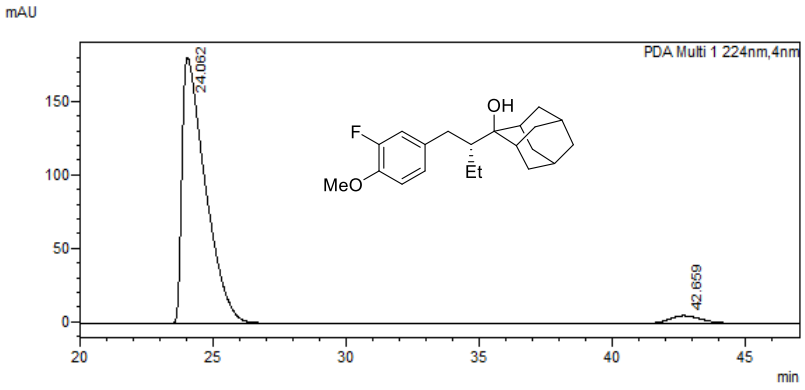
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.7:0.3, 1.0 mL/min).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	21.322	7544544	140574	49.857
2	39.335	7587960	99748	50.143
Total		15132504	240322	100.000

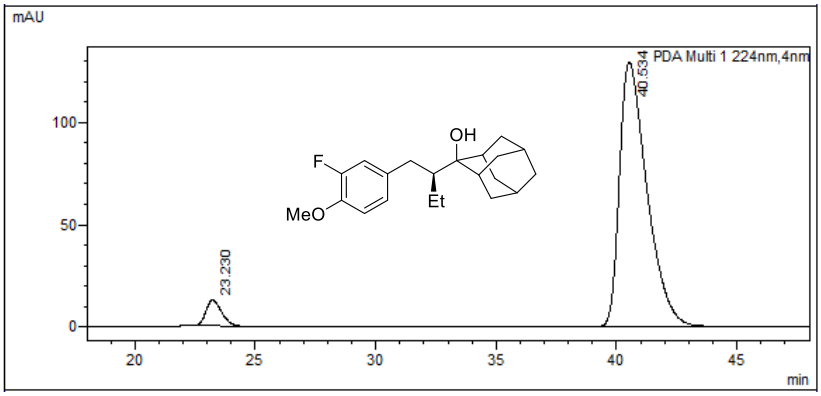
(*R*)-Enantiomer: t_R (min) = 24.1 ((*R*)-enantiomer, major), 42.7 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	24.062	11028711	180702	96.102
2	42.659	447302	5303	3.898
Total		11476014	186006	100.000

The enantiomeric excess of (*R*)-**152at** was determined to 92%.

(*S*)-Enantiomer: t_R (min) = 23.2 ((*R*)-enantiomer, minor), 40.5 ((*S*)-enantiomer, major).

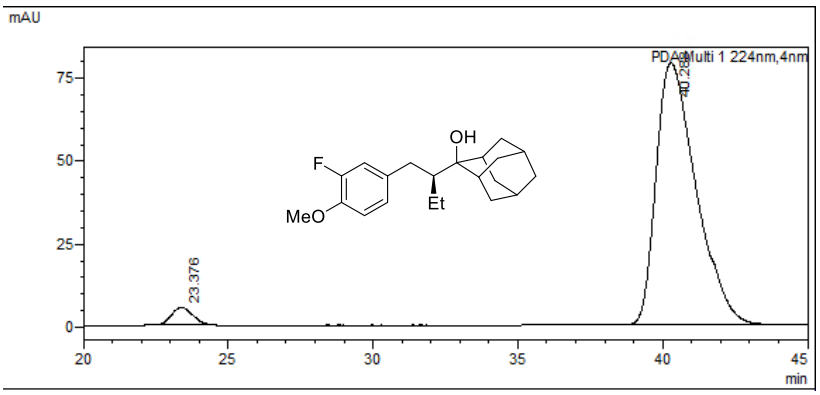


Peak#	Ret. Time	Area	Height	Area%
1	23.230	566854	12555	5.241
2	40.534	10248481	129304	94.759
Total		10815335	141859	100.000

The enantiomeric excess of (*S*)-**152at** was determined to 90%.

Determination of the enantiomeric excess of (*S*)-**152at** by chiral HPLC analysis obtained after reaction in continuous flow:

(*S*)-Enantiomer: t_R (min) = 23.4 ((*R*)-enantiomer, minor), 40.3 ((*S*)-enantiomer, major).



PDA Ch1 224nm

Peak#	Ret. Time	Area	Height	Area%
1	23.376	268661	5277	3.417
2	40.288	7592738	78990	96.583
Total		7861398	84267	100.000

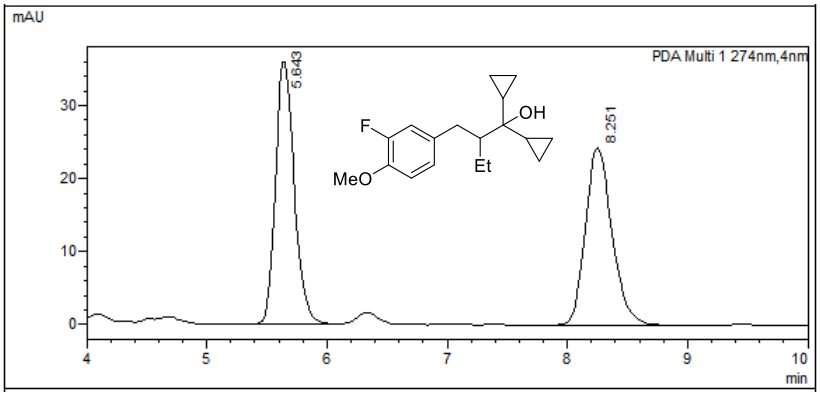
The enantiomeric excess of (*S*)-**152at** was determined to 93%.

(*R*)- and (*S*)-152au

The enantiomeric excess of (*R*)- and (*S*)-**152au** was determined by chiral HPLC analysis.

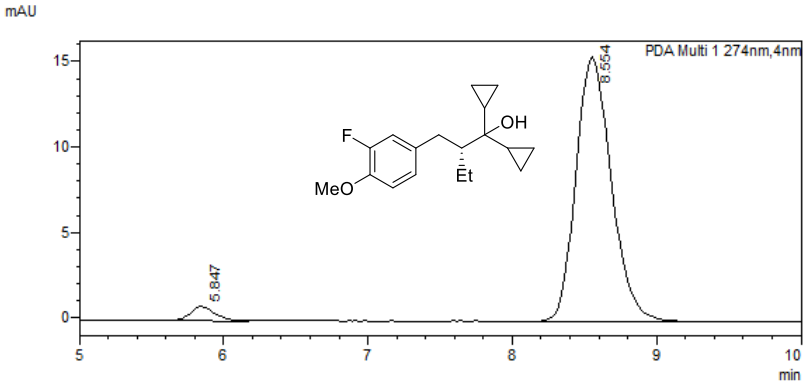
HPLC (column: OD-H; *n*-heptane/2-propanol = 95.0:5.0, 1.0 mL/min).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	5.643	388704	35861	51.197
2	8.251	370530	24237	48.803
Total		759234	60099	100.000

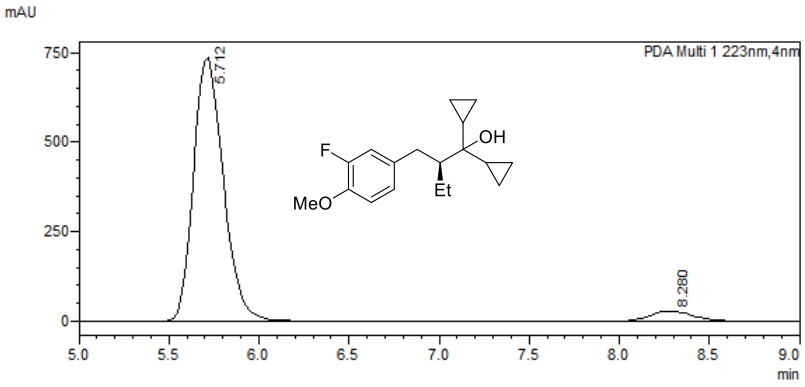
(*R*)-Enantiomer: t_R (min) = 5.8 ((*S*)-enantiomer, minor), 8.6 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	5.847	9488	826	3.465
2	8.554	264358	15482	96.535
Total		273846	16308	100.000

The enantiomeric excess of (*R*)-**152au** was determined to 93%.

(*S*)-Enantiomer: t_R (min) = 5.7 ((*S*)-enantiomer, major), 8.3 ((*R*)-enantiomer, minor).

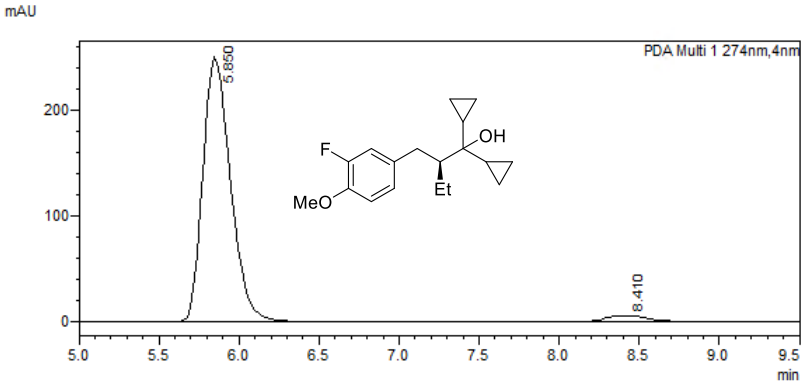


Peak#	Ret. Time	Area	Height	Area%
1	5.712	8486583	737084	94.913
2	8.280	454850	28265	5.087
Total		8941434	765349	100.000

The enantiomeric excess of (*S*)-**152au** was determined to 90%.

Determination of the enantiomeric excess of (*S*)-**152au** by chiral HPLC analysis obtained after reaction in continuous flow:

(*S*)-Enantiomer: t_R (min) = 5.9 ((*S*)-enantiomer, major), 8.4 ((*R*)-enantiomer, minor).



PDA Ch1 274nm

Peak#	Ret. Time	Area	Height	Area%
1	5.850	3008775	251057	96.843
2	8.410	98096	5903	3.157
Total		3106872	256960	100.000

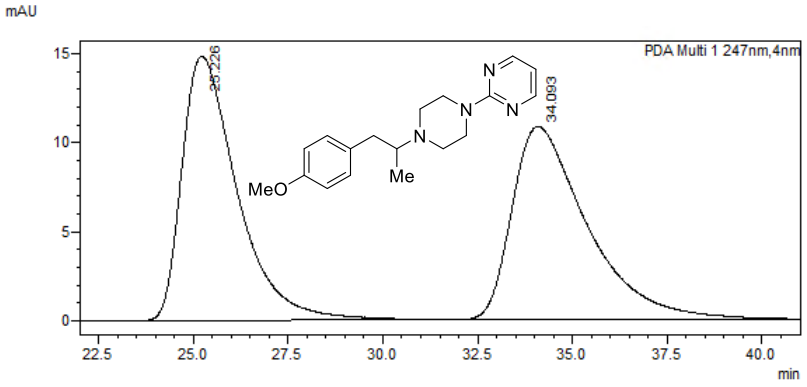
The enantiomeric excess of (*S*)-**152au** was determined to 94%.

(*R*)- and (*S*)-155a

The enantiomeric excess of (*R*)- and (*S*)-**155a** was determined by chiral HPLC analysis.

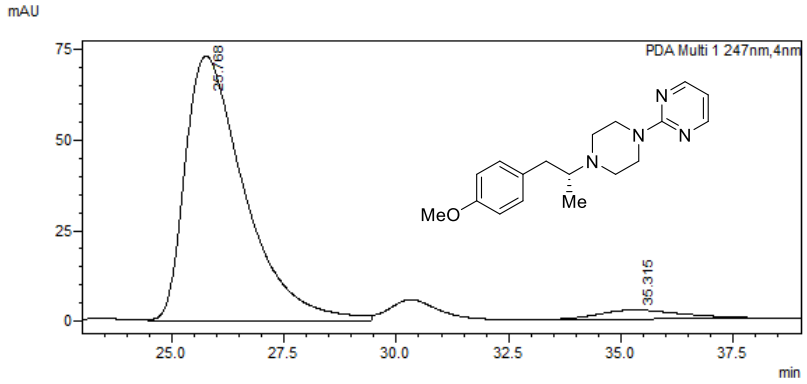
HPLC (column: OJ-H; *n*-heptane/2-propanol = 98.0:2.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	25.226	1507633	14852	50.044
2	34.093	1504959	10857	49.956
Total		3012592	25709	100.000

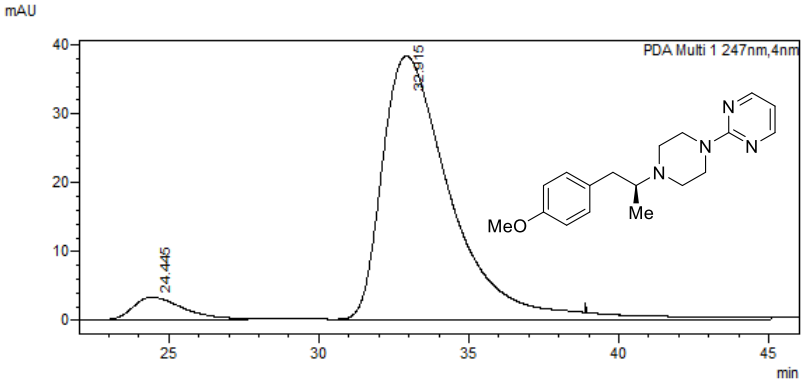
(*R*)-Enantiomer: t_R (min) = 25.8 ((*R*)-enantiomer, major), 35.3 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	25.768	6715045	72849	95.466
2	35.315	318885	2485	4.534
Total		7033929	75334	100.000

The enantiomeric excess of (*R*)-**155a** was determined to 91%.

(*S*)-Enantiomer: t_R (min) = 24.5 ((*R*)-enantiomer, minor), 32.9 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	24.445	392946	3308	6.015
2	32.915	6139817	38292	93.985
Total		6532763	41600	100.000

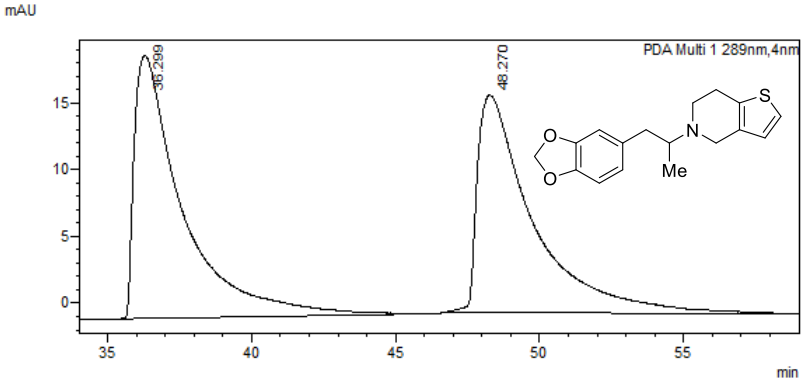
The enantiomeric excess of (*S*)-**155a** was determined to 88%.

(*R*)- and (*S*)-155c

The enantiomeric excess of (*R*)- and (*S*)-**155c** was determined by chiral HPLC analysis.

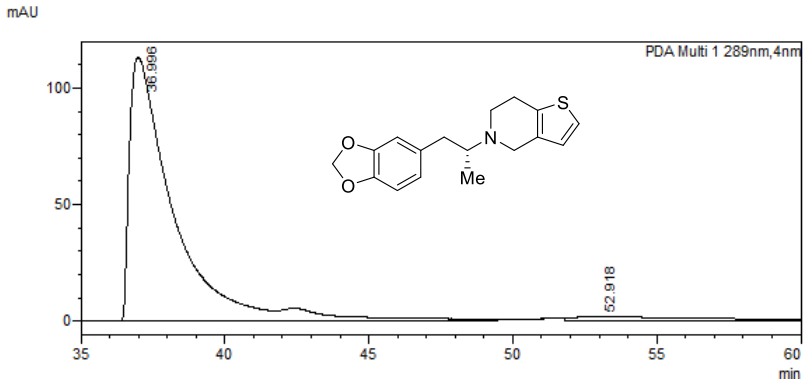
HPLC (column: OD-H; *n*-heptane/2-propanol = 99.5:0.5, 0.5 mL/min): t_R (min) = 36.3 ((*R*)-enantiomer, major), 52.9 ((*S*)-enantiomer, minor).

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	36.299	2286647	19680	51.045
2	48.270	2192981	16293	48.955
Total		4479628	35972	100.000

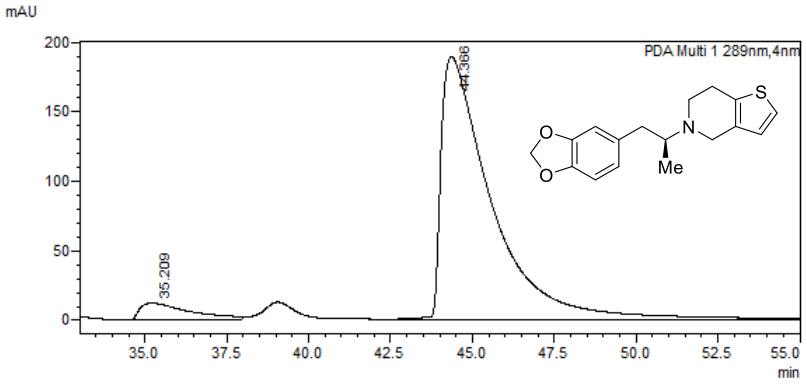
(*R*)-Enantiomer: t_R (min) = 37.0 ((*R*)-enantiomer, major), 52.9 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	36.996	12239819	113204	93.422
2	52.918	861890	1940	6.578
Total		13101709	115144	100.000

The enantiomeric excess of (*R*)-**155c** was determined to 87%.

(*S*)-Enantiomer: t_R (min) = 35.2 ((*R*)-enantiomer, minor), 44.4 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	35.209	1339039	12239	5.973
2	44.366	21078107	189469	94.027
Total		22417146	201707	100.000

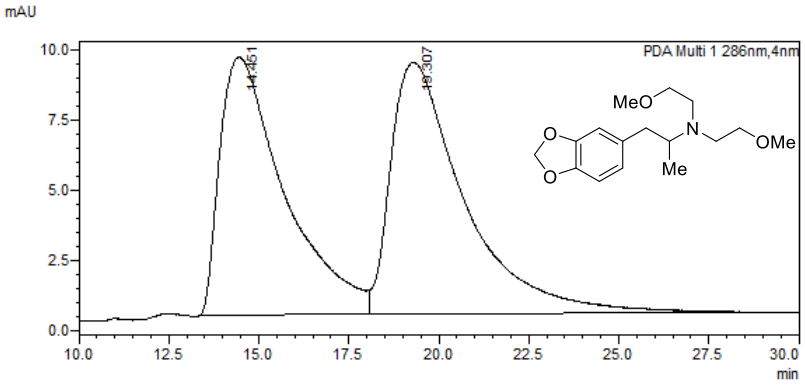
The enantiomeric excess of (*S*)-**155c** was determined to 88%.

(*R*)- and (*S*)-155d

The enantiomeric excess of (*R*)- and (*S*)-**155d** was determined by chiral HPLC analysis.

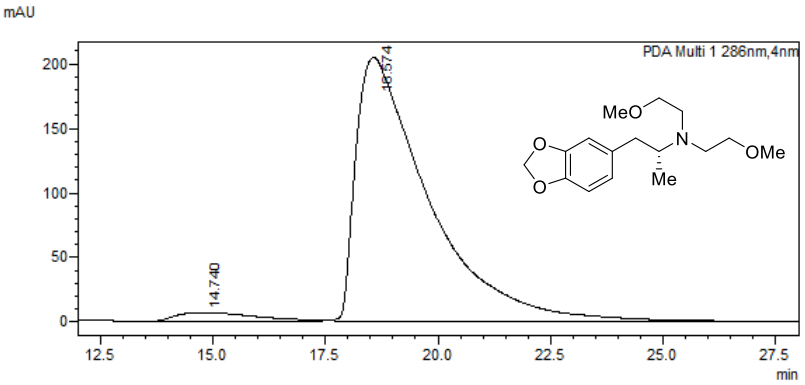
HPLC (column: OJ-H; *n*-heptane/2-propanol = 99.0:1.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	14.451	1139197	9177	47.241
2	19.307	1272242	8961	52.759
Total		2411439	18138	100.000

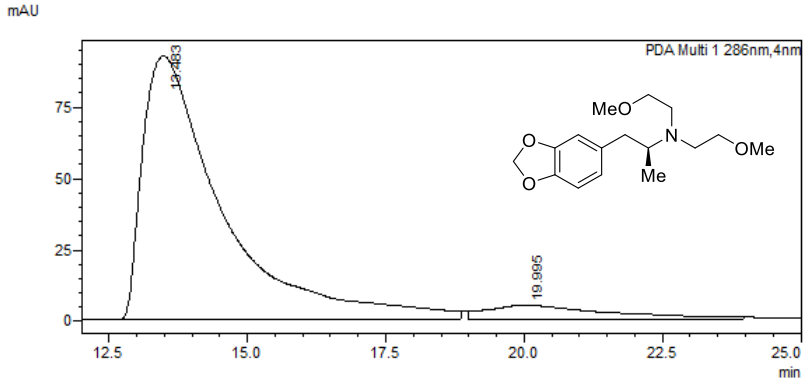
(*R*)-Enantiomer: t_R (min) = 14.7 ((*S*)-enantiomer, minor), 18.6 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	14.740	875442	6935	3.662
2	18.574	23032019	204681	96.338
Total		23907461	211616	100.000

The enantiomeric excess of (*R*)-**155d** was determined to 93%.

(*S*)-Enantiomer: 13.5 ((*S*)-enantiomer, major), 20.0 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	13.483	9266843	92307	92.065
2	19.995	798689	5029	7.935
Total		10065532	97336	100.000

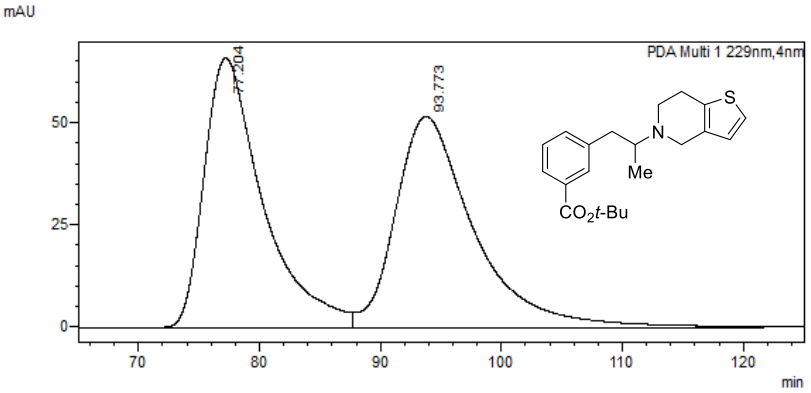
The enantiomeric excess of (*S*)-**155d** was determined to 84 %

(*R*)-155e

The enantiomeric excess of (*R*)-**155e** was determined by chiral HPLC analysis.

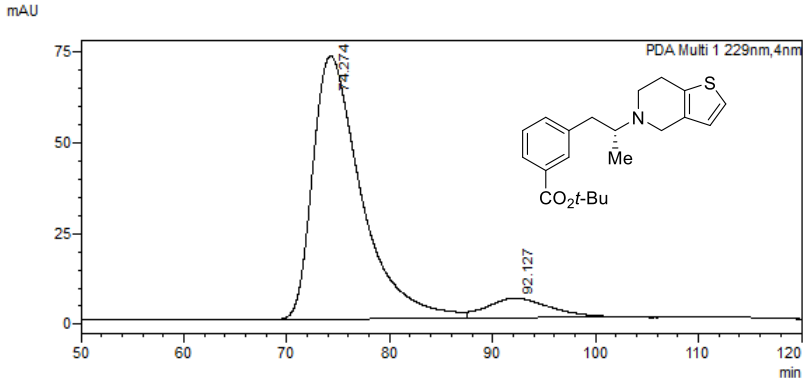
HPLC (column: OJ-H; *n*-heptane/2-propanol = 99.5:0.5, 0.25 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	77.204	22217014	65965	48.646
2	93.773	23453753	51671	51.354
Total		45670767	117635	100.000

(*R*)-Enantiomer: t_R (min) = 74.3 ((*R*)-enantiomer, major), 92.2 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	74.274	23728923	72461	91.506
2	92.127	2202713	5300	8.494
Total		25931636	77761	100.000

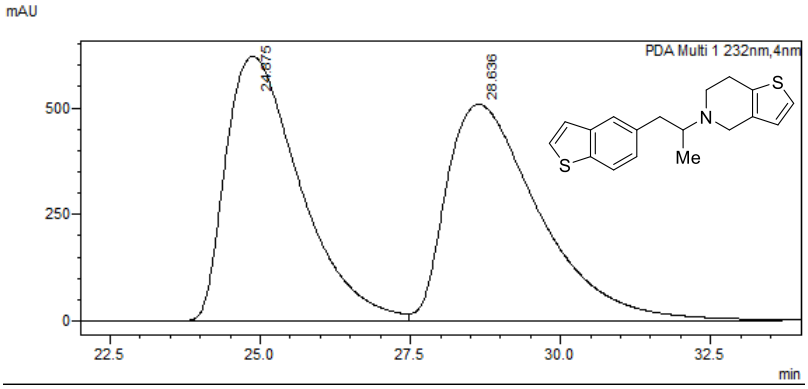
The enantiomeric excess of (*R*)-**155e** was determined to 83%.

(*R*)- and (*S*)-155f

The enantiomeric excess of (*R*)- and (*S*)-**155f** was determined by chiral HPLC analysis.

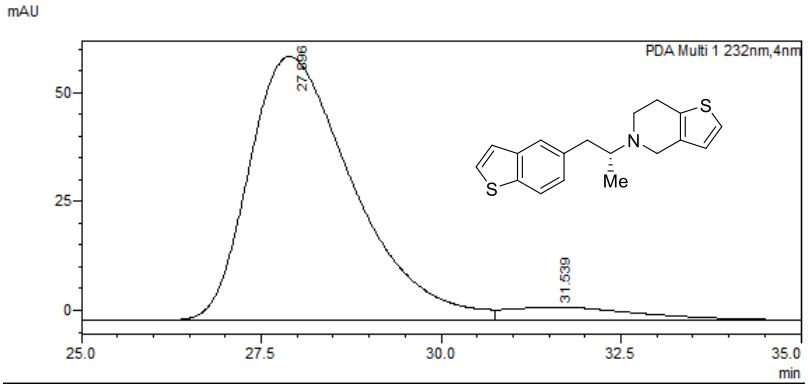
HPLC (column: OJ-H; *n*-heptane/2-propanol = 98.0:2.0, 1.0 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	24.875	53428670	620346	49.335
2	28.636	54869965	508120	50.665
Total		108298635	1128466	100.000

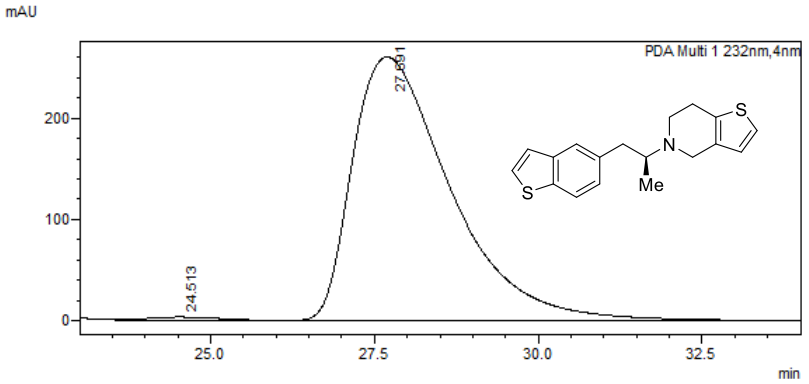
(*R*)-Enantiomer: t_R (min) = 27.9 ((*R*)-enantiomer, major), 31.5 ((*S*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	27.896	6097529	60542	94.037
2	31.539	386647	3052	5.963
Total		6484176	63594	100.000

The enantiomeric excess of (*R*)-**155f** was determined to 88%.

(*S*)-Enantiomer: t_R (min) = 24.5 ((*R*)-enantiomer, minor), 27.7 ((*S*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	24.513	306019	3694	1.112
2	27.691	27214904	260851	98.888
Total		27520924	264545	100.000

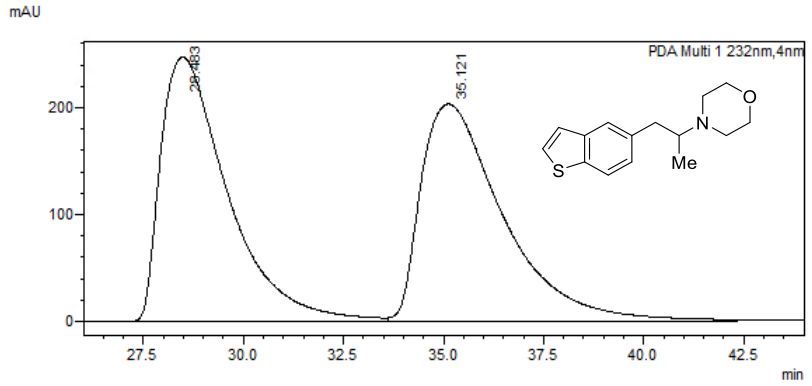
The enantiomeric excess of (*S*)-**155f** was determined to 97%.

(*R*)- and (*S*)-155g

The enantiomeric excess of (*R*)- and (*S*)-**155g** was determined by chiral HPLC analysis.

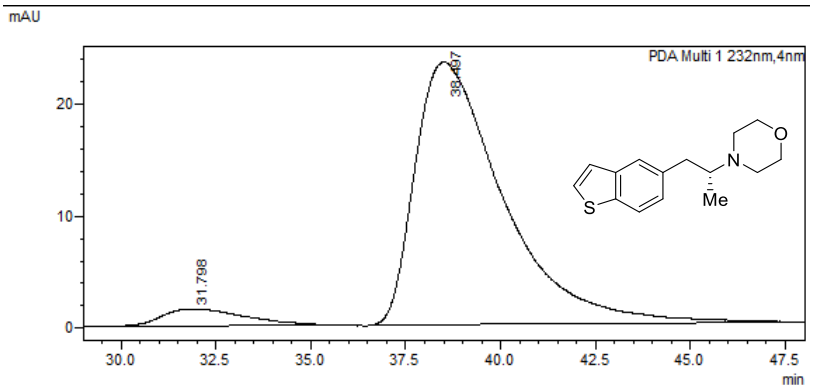
HPLC (column: OJ-H; *n*-heptane/2-propanol = 99.3:0.7, 1.25 mL/min):

Racemate:



Peak#	Ret. Time	Area	Height	Area%
1	28.483	28872265	247432	49.594
2	35.121	29344801	203583	50.406
Total		58217066	451015	100.000

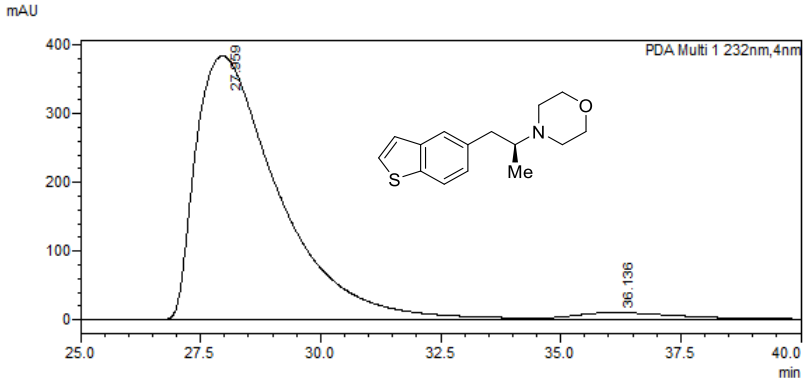
(*R*)-Enantiomer: t_R (min) = 31.8 ((*S*)-enantiomer, minor), 38.5 ((*R*)-enantiomer, major).



Peak#	Ret. Time	Area	Height	Area%
1	31.798	229991	1482	5.728
2	38.497	3785273	23435	94.272
Total		4015263	24916	100.000

The enantiomeric excess of (*R*)-**155g** was determined to 89%.

(*S*)-Enantiomer: t_R (min) = 28.0 ((*S*)-enantiomer, major), 36.1 ((*R*)-enantiomer, minor).



Peak#	Ret. Time	Area	Height	Area%
1	27.959	46032973	383821	96.908
2	36.136	1468773	9662	3.092
Total		47501746	393483	100.000

The enantiomeric excess of (*S*)-**155g** was determined to 94%.

8 Appendix

8.1 Single Crystal X-Ray Diffraction Studies of (*S*)-155g

Single crystals of compound (*S*)-**155g** as hydrochloride derivative, suitable for X-ray diffraction, were obtained by slow evaporation of water. The crystals were introduced into perfluorinated oil and a suitable single crystal was carefully mounted on the top of a thin glass wire. Data collection was performed with an Oxford Xcalibur 3 diffractometer equipped with a Spellman generator (50 kV, 40 mA) and a Kappa CCD detector, operating with Mo-K_α radiation (λ = 0.71071 Å).

Data collection and data reduction were performed with the CrysAlisPro software.[189] Absorption correction using the multiscan method[189] was applied. The structures were solved with SHELXS-97,[190] refined with SHELXL-97[191] and finally checked using PLATON.[192] Details for data collection and structure refinement are summarized in Table S13.

CCDC-**2110720** contains supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Table S13. Details for X-ray data collection and structure refinement for compound (*S*)-**155g**.

	1
Empirical formula	$C_{15}H_{20}ClNOS$
Formula mass	297.83
T[K]	123(2)
Crystal size [mm]	0.35 × 0.20 × 0.02
Crystal description	colorless platelet
Crystal system	orthorhombic
Space group	*P*212121
a [Å]	7.2165(2)

[189] Program package 'CrysAlisPro 1.171.39.46e (Rigaku OD, 2018)'.
[190] Sheldrick, G. M. (1997) SHELXS-97: Program for Crystal Structure Solution, University of Göttingen, Germany.
[191] Sheldrick, G. M. (1997) SHELXL-97: Program for the Refinement of Crystal Structures, University of Göttingen, Germany.
[192] Spek, A. L. (1999) PLATON: A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands.

b [Å]	12.5371(4)
c [Å]	16.4763(6)
α [°]	90.0
β [°]	90.0
γ [°]	90.0
V [Å^3]	1490.68(8)
Z	4
$\rho_{calcd.}$ [g cm^{-3}]	1.327
μ [mm^{-1}]	0.388
F(000)	632
Θ range [°]	2.04 – 25.24
Index ranges	$-10 \leq h \leq 10$
	$-17 \leq k \leq 17$
	$-23 \leq l \leq 23$
Reflns. collected	30202
Reflns. obsd.	4002
Reflns. unique	4545
	(R_{int} = 0.0539)
R_1, wR_2 (2σ data)	0.0382, 0.0823
R_1, wR_2 (all data)	0.0470, 0.0862
GOOF on F^2	1.058
Peak/hole [e Å^{-3}]	0.385 / -0.203

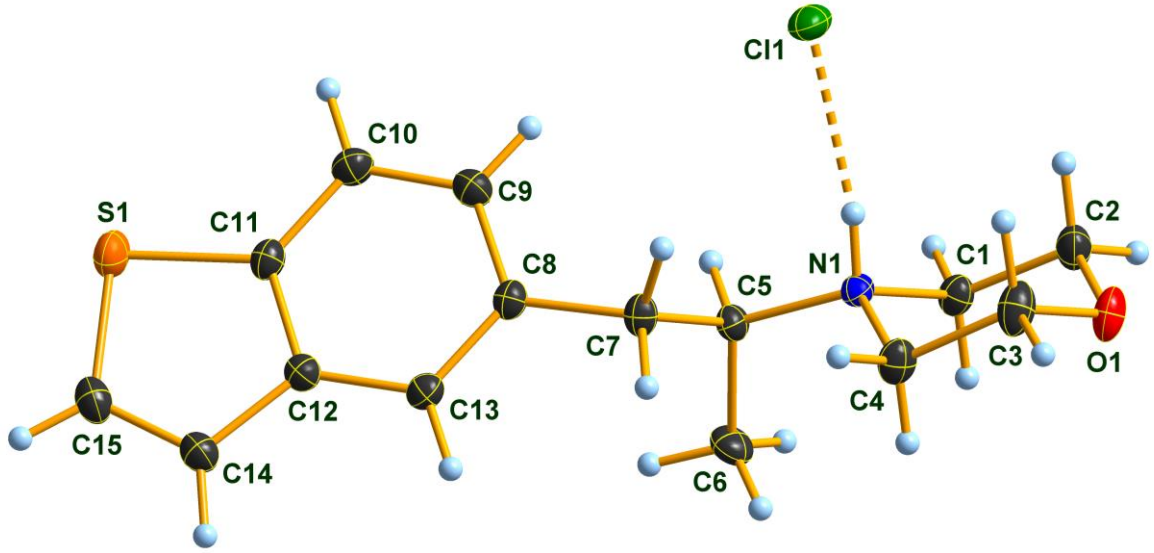


Figure 1. Molecular structure of compound (*S*)-**155g** in the crystal. DIAMOND.[193] representation; thermal ellipsoids are drawn at 50 % probability level. Symmetry code for chloride anion: -0.5+x, 1.5-y, 1-z.

Table S14. Selected bond lengths (Å) of compound (*S*)-**155g**.

S1 – C15	1.724(3)	C9 – C10	1.380(3)
S1 – C11	1.737(2)	C14 – C15	1.354(3)
C1 – N1	1.495(3)	C14 – C12	1.439(3)
C1 – C2	1.512(3)	C13 – C12	1.405(3)
C5 – C6	1.520(3)	C8 – C9	1.410(3)
C5 – N1	1.522(3)	C8 – C7	1.510(3)
C5 – C7	1.533(3)	O1 – C3	1.421(3)
C11 – C10	1.395(3)	O1 – C2	1.426(3)
C11 – C12	1.412(3)	C4 – N1	1.496(3)
C8 – C13	1.386(3)	C4 – C3	1.519(3)

[193] DIAMOND, Crystal Impact GbR., Version 3.2i.

Table S15. Selected bond angles (°) of compound (*S*)-**155g**.

C15 – S1 – C11	91.5(1)	C9 – C10 – C11	118.2(2)
N1 – C1 – C2	109.7(2)	C15 – C14 – C12	112.6(2)
C6 – C5 – N1	112.6(2)	C1 – N1 – C4	108.8(2)
C6 – C5 – C7	113.4(2)	C1 – N1 – C5	113.3(2)
N1 – C5 – C7	108.0(2)	C4 – N1 – C5	115.4(2)
C10 – C11 – C12	121.4(2)	C8 – C13 – C12	120.1(2)
C10 – C11 – S1	127.5(2)	O1 – C2 – C1	111.9(2)
C12 – C11 – S1	111.1(2)	C14 – C15 – S1	113.4(2)
C13 – C8 – C9	119.5(2)	C13 – C12 – C11	118.9(2)
C13 – C8 – C7	120.7(2)	C13 – C12 – C14	129.5(2)
C9 – C8 – C7	119.7(2)	C11 – C12 – C14	111.6(2)
C3 – O1 – C2	110.3(2)	O1 – C3 – C4	111.8(2)
N1 – C4 – C3	108.5(2)	C8 – C7 – C5	114.1(2)
C10 – C9 – C8	121.9(2)		

Table S16. Selected torsion angles (°) of compound (*S*)-**155g**.

C15 – S1 – C11 – C10	-178.0(2)	C7 – C5 – N1 – C4	53.1(2)
C15 – S1 – C11 – C12	-0.3(2)	C9 – C8 – C13 – C12	-0.3(3)
C13 – C8 – C9 – C10	0.3(3)	C7 – C8 – C13 – C12	175.8(2)
C7 – C8 – C9 – C10	-175.9(2)	C3 – O1 – C2 – C1	-58.2(3)
C13 – C8 – C7 – C5	113.6(2)	N1 – C1 – C2 – O1	57.5(3)

C9 – C8 – C7 – C5	-70.3(3)	C12 – C14 – C15 – S1	0.4(3)
C6 – C5 – C7 – C8	-75.6(3)	C11 – S1 – C15 – C14	-0.1(2)
N1 – C5 – C7 – C8	158.9(2)	C8 – C13 – C12 – C11	0.0(3)
C8 – C9 – C10 – C11	0.0(3)	C8 – C13 – C12 – C14	-177.8(2)
C12 – C11 – C10 – C9	-0.3(3)	C10 – C11 – C12 – C13	0.3(3)
S1 – C11 – C10 – C9	177.3(2)	S1 – C11 – C12 – C13	-177.6(2)
C2 – C1 – N1 – C4	-56.9(2)	C10 – C11 – C12 – C14	178.4(2)
C2 – C1 – N1 – C5	173.4(2)	S1 – C11 – C12 – C14	0.5(2)
C3 – C4 – N1 – C1	57.5(2)	C15 – C14 – C12 – C13	177.3(2)
C3 – C4 – N1 – C5	-174.0(2)	C15 – C14 – C12 – C11	-0.6(3)
C6 – C5 – N1 – C1	53.4(2)	C2 – O1 – C3 – C4	59.6(3)
C7 – C5 – N1 – C1	179.4(2)	N1 – C4 – C3 – O1	-59.7(3)
C6 – C5 – N1 – C4	-72.9(2)		

8.2 Single Crystal X-Ray Diffraction Studies for (*S*)-152v

Single crystals of compound (*S*)-**152v**, suitable for X-ray diffraction, were obtained by slow evaporation of an etheral solution of (*S*)-**152v**. The crystals were introduced into perfluorinated oil and a suitable single crystal was carefully mounted on the top of a thin glass wire. Data collection was performed with an Oxford Xcalibur 3 diffractometer equipped with a Spellman generator (50 kV, 40 mA) and a Kappa CCD detector, operating with Mo-K_α radiation ($\lambda = 0.71071$ Å).

Data collection and data reduction were performed with the CrysAlisPro software.[189] Absorption correction using the multiscan method[189] was applied. The structures were solved with SHELXS-97,[190] refined with SHELXL-97[191] and finally checked using PLATON.[192] Details for data collection and structure refinement are summarized in Table S17.

CCDC-2210094 contains supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Table S17. Details for X-ray data collection and structure refinement for compound (*S*)-**152v**.

	1
Empirical formula	$C_{20}H_{26}O_3$
Formula mass	314.41
T[K]	123(2)
Crystal size [mm]	0.40 × 0.40 × 0.10
Crystal description	colorless block
Crystal system	triclinic
Space group	*P*1
a [Å]	9.0348(3)
b [Å]	9.1064(4)
c [Å]	11.2425(4)
α [°]	100.035(3)
β [°]	104.789(3)
γ [°]	111.434(4)
V [Å^3]	794.85(6)
Z	2
$\rho_{calcd.}$ [g cm^{-3}]	1.314
μ [mm^{-1}]	0.086
F(000)	340
Θ range [°]	1.96 – 25.24
Index ranges	$-12 \leq h \leq 12$
	$-12 \leq k \leq 12$
	$-14 \leq l \leq 14$

Reflns. collected	13967
Reflns. obsd.	7043
Reflns. unique	7816
	(R_{int} = 0.0218)
R_1, wR_2 (2σ data)	0.0489, 0.1200
R_1, wR_2 (all data)	0.0554, 0.1263
GOOF on F^2	1.020
Peak/hole [e Å^{-3}]	0.434 / -0.188

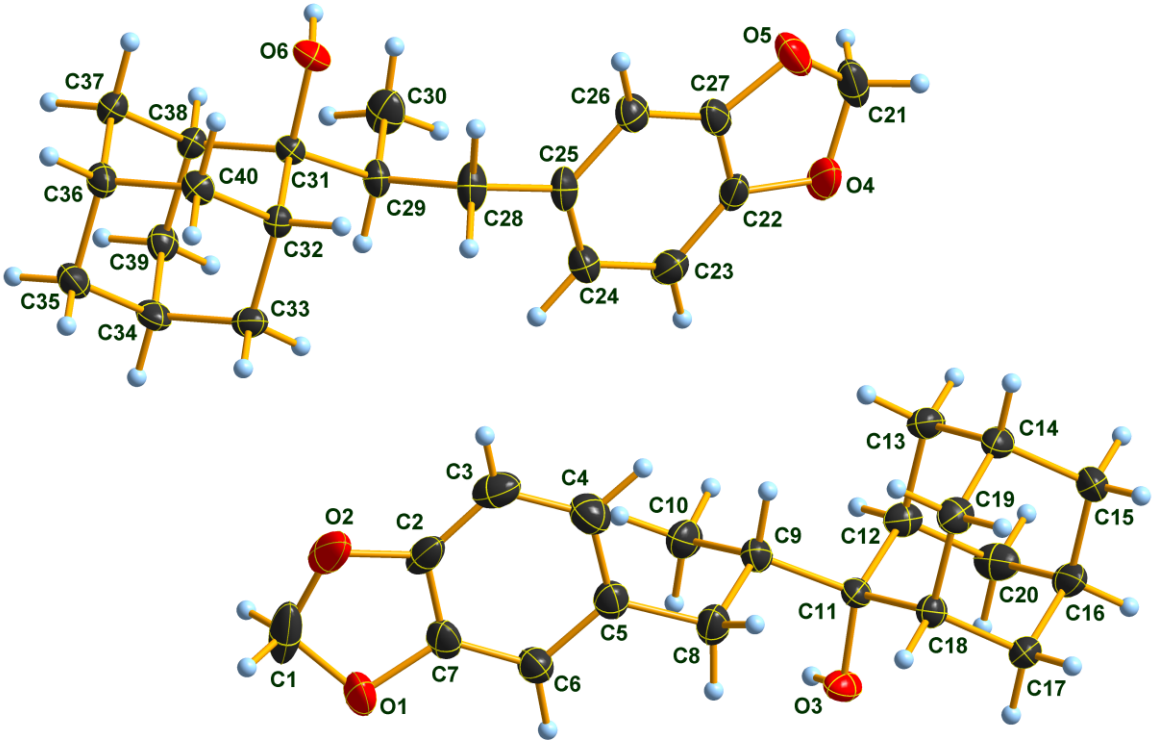


Figure 1. Molecular structure of compound (*S*)-**152v** in the crystal. View of the two crystallographically independent molecules. DIAMOND[193] representation; thermal ellipsoids are drawn at 50 % probability level.

Table S18. Selected bond lengths (Å) of compound (*S*)-**152v**.

O6 – C31	1.452(3)	C25 – C24	1.383(4)
C32 – C40	1.531(3)	C25 – C26	1.410(4)
C32 – C31	1.543(3)	C25 – C28	1.506(4)
C32 – C33	1.543(3)	C14 – C19	1.529(4)
O3 – C11	1.434(3)	C14 – C15	1.539(4)
C31 – C38	1.543(3)	C16 – C20	1.522(5)
C31 – C29	1.558(3)	C16 – C17	1.527(4)
C9 – C10	1.531(4)	C16 – C15	1.529(4)
C9 – C8	1.539(4)	C12 – C20	1.532(4)
C9 – C11	1.552(4)	C27 – C26	1.366(4)
C18 – C17	1.525(4)	O1 – C7	1.382(4)
C18 – C19	1.537(4)	O1 – C1	1.428(5)
C18 – C11	1.554(3)	C6 – C7	1.380(4)
C37 – C36	1.533(4)	C6 – C5	1.407(4)
C37 – C38	1.534(4)	C23 – C24	1.404(4)
C39 – C34	1.534(4)	C4 – C5	1.399(4)
C39 – C38	1.536(4)	C4 – C3	1.400(5)
C35 – C34	1.533(4)	C7 – C2	1.381(5)
C35 – C36	1.540(4)	C5 – C8	1.509(4)
C29 – C30	1.520(4)	O2 – C2	1.375(4)
C29 – C28	1.551(4)	O2 – C1	1.428(6)
C11 – C12	1.556(4)	C2 – C3	1.357(5)
O4 – C22	1.385(3)	C36 – C40	1.530(4)

O4 – C21	1.435(4)	C13 – C14	1.534(4)
C22 – C23	1.366(4)	C13 – C12	1.536(4)
C22 – C27	1.383(5)	O5 – C27	1.380(4)
C34 – C33	1.532(4)	O5 – C21	1.427(5)

Table S19. Selected bond angles (°) of compound (*S*)-**152v**.

C40 – C32 – C31	111.4(2)	C20 – C16 – C17	108.5(2)
C40 – C32 – C33	108.1(2)	C20 – C16 – C15	109.7(2)
C31 – C32 – C33	109.4(2)	C17 – C16 – C15	110.1(3)
O6 – C31 – C32	106.4(2)	C18 – C17 – C16	110.0(2)
O6 – C31 – C38	108.3(2)	C20 – C12 – C13	108.8(2)
C32 – C31 – C38	107.6(2)	C20 – C12 – C11	109.9(2)
O6 – C31 – C29	108.1(2)	C13 – C12 – C11	110.4(2)
C32 – C31 – C29	112.3(2)	C26 – C27 – O5	127.7(3)
C38 – C31 – C29	113.8(2)	C26 – C27 – C22	122.2(3)
C10 – C9 – C8	110.1(2)	O5 – C27 – C22	110.0(3)
C10 – C9 – C11	112.2(2)	C14 – C19 – C18	109.8(2)
C8 – C9 – C11	111.1(2)	C7 – O1 – C1	104.8(3)
C17 – C18 – C19	108.5(2)	C27 – C26 – C25	117.9(3)
C17 – C18 – C11	110.4(2)	C7 – C6 – C5	116.6(3)
C19 – C18 – C11	110.2(2)	C22 – C23 – C24	116.9(3)
C36 – C37 – C38	109.8(2)	C36 – C40 – C32	109.9(2)
C34 – C39 – C38	109.0(2)	C5 – C4 – C3	122.9(3)
C34 – C35 – C36	108.9(2)	C6 – C7 – C2	123.1(3)

C30 – C29 – C28	113.2(2)	C6 – C7 – O1	127.0(3)
C30 – C29 – C31	112.4(2)	C2 – C7 – O1	109.8(3)
C28 – C29 – C31	110.6(2)	C4 – C5 – C6	119.2(3)
O3 – C11 – C9	108.9(2)	C4 – C5 – C8	121.5(3)
O3 – C11 – C18	104.9(2)	C6 – C5 – C8	119.3(3)
C9 – C11 – C18	114.0(2)	C16 – C15 – C14	109.1(2)
O3 – C11 – C12	110.8(2)	C16 – C20 – C12	110.2(2)
C9 – C11 – C12	111.1(2)	C2 – O2 – C1	104.9(3)
C18 – C11 – C12	107.0(2)	C25 – C24 – C23	122.4(3)
C22 – O4 – C21	104.6(2)	C25 – C28 – C29	115.7(2)
C23 – C22 – C27	121.4(3)	C5 – C8 – C9	114.5(2)
C23 – C22 – O4	129.0(3)	O5 – C21 – O4	108.3(2)
C27 – C22 – O4	109.6(3)	C3 – C2 – O2	128.3(3)
C33 – C34 – C35	109.5(2)	C3 – C2 – C7	121.6(3)
C33 – C34 – C39	110.2(2)	O2 – C2 – C7	110.0(3)
C35 – C34 – C39	109.3(2)	C2 – C3 – C4	116.6(3)
C40 – C36 – C37	109.0(2)	O2 – C1 – O1	108.6(3)
C40 – C36 – C35	109.6(2)	C39 – C38 – C31	110.4(2)
C37 – C36 – C35	109.4(2)	C24 – C25 – C26	119.2(3)
C14 – C13 – C12	109.4(2)	C24 – C25 – C28	121.5(3)
C34 – C33 – C32	109.6(2)	C26 – C25 – C28	119.3(3)
C27 – O5 – C21	104.7(2)	C19 – C14 – C13	110.5(2)
C37 – C38 – C39	108.7(2)	C19 – C14 – C15	108.9(2)
C37 – C38 – C31	110.6(2)	C13 – C14 – C15	108.8(2)

Table S20. Selected torsion angles (°) of compound (*S*)-**152v**.

C40 – C32 – C31 – O6	57.5(2)	C18 – C11 – C12 – C13	-60.9(3)
C33 – C32 – C31 – O6	177.0(2)	C21 – O5 – C27 – C26	-171.3(3)
C40 – C32 – C31 – C38	-58.4(2)	C21 – O5 – C27 – C22	10.9(3)
C33 – C32 – C31 – C38	61.1(2)	C23 – C22 – C27 – C26	-0.9(4)
C40 – C32 – C31 – C29	175.6(2)	O4 – C22 – C27 – C26	-179.1(3)
C33 – C32 – C31 – C29	-64.9(2)	C23 – C22 – C27 – O5	177.1(3)
O6 – C31 – C29 – C30	-66.3(3)	O4 – C22 – C27 – O5	-1.1(3)
C32 – C31 – C29 – C30	176.6(2)	C13 – C14 – C19 – C18	58.3(3)
C38 – C31 – C29 – C30	54.1(3)	C15 – C14 – C19 – C18	-61.2(3)
O6 – C31 – C29 – C28	61.4(3)	C17 – C18 – C19 – C14	60.8(3)
C32 – C31 – C29 – C28	-55.7(3)	C11 – C18 – C19 – C14	-60.2(3)
C38 – C31 – C29 – C28	-178.3(2)	O5 – C27 – C26 – C25	-176.6(3)
C10 – C9 – C11 – O3	-62.7(3)	C22 – C27 – C26 – C25	0.9(4)
C8 – C9 – C11 – O3	61.1(3)	C24 – C25 – C26 – C27	-0.3(4)
C10 – C9 – C11 – C18	-179.4(2)	C28 – C25 – C26 – C27	179.4(3)
C8 – C9 – C11 – C18	-55.6(3)	C27 – C22 – C23 – C24	0.2(4)
C10 – C9 – C11 – C12	59.6(3)	O4 – C22 – C23 – C24	178.0(3)
C8 – C9 – C11 – C12	-176.6(2)	C37 – C36 – C40 – C32	-58.9(3)
C17 – C18 – C11 – O3	58.3(3)	C35 – C36 – C40 – C32	60.8(3)
C19 – C18 – C11 – O3	178.2(2)	C31 – C32 – C40 – C36	59.6(3)
C17 – C18 – C11 – C9	177.4(2)	C33 – C32 – C40 – C36	-60.6(3)
C19 – C18 – C11 – C9	-62.7(3)	C5 – C6 – C7 – C2	-1.1(4)
C17 – C18 – C11 – C12	-59.4(3)	C5 – C6 – C7 – O1	-176.1(3)

C19 – C18 – C11 – C12	60.5(3)	C1 – O1 – C7 – C6	-176.8(3)
C21 – O4 – C22 – C23	172.9(3)	C1 – O1 – C7 – C2	7.6(3)
C21 – O4 – C22 – C27	-9.1(3)	C3 – C4 – C5 – C6	1.3(5)
C36 – C35 – C34 – C33	59.9(3)	C3 – C4 – C5 – C8	-178.3(3)
C36 – C35 – C34 – C39	-60.9(3)	C7 – C6 – C5 – C4	-0.7(4)
C38 – C39 – C34 – C33	-58.5(3)	C7 – C6 – C5 – C8	178.9(3)
C38 – C39 – C34 – C35	61.8(3)	C20 – C16 – C15 – C14	60.0(3)
C38 – C37 – C36 – C40	59.8(3)	C17 – C16 – C15 – C14	-59.3(3)
C38 – C37 – C36 – C35	-60.0(3)	C19 – C14 – C15 – C16	59.9(3)
C34 – C35 – C36 – C40	-59.6(3)	C13 – C14 – C15 – C16	-60.7(3)
C34 – C35 – C36 – C37	59.8(3)	C17 – C16 – C20 – C12	60.5(3)
C35 – C34 – C33 – C32	-61.1(3)	C15 – C16 – C20 – C12	-59.8(3)
C39 – C34 – C33 – C32	59.1(3)	C13 – C12 – C20 – C16	59.6(3)
C40 – C32 – C33 – C34	60.8(3)	C11 – C12 – C20 – C16	-61.4(3)
C31 – C32 – C33 – C34	-60.7(3)	C26 – C25 – C24 – C23	-0.4(4)
C36 – C37 – C38 – C39	60.5(3)	C28 – C25 – C24 – C23	180.0(3)
C36 – C37 – C38 – C31	-60.9(3)	C22 – C23 – C24 – C25	0.4(4)
C34 – C39 – C38 – C37	-61.1(3)	C24 – C25 – C28 – C29	-63.8(4)
C34 – C39 – C38 – C31	60.3(3)	C26 – C25 – C28 – C29	116.6(3)
O6 – C31 – C38 – C37	-55.9(3)	C30 – C29 – C28 – C25	-38.0(4)
C32 – C31 – C38 – C37	58.8(3)	C31 – C29 – C28 – C25	-165.2(2)
C29 – C31 – C38 – C37	-176.1(2)	C4 – C5 – C8 – C9	-65.1(4)
O6 – C31 – C38 – C39	-176.2(2)	C6 – C5 – C8 – C9	115.3(3)
C32 – C31 – C38 – C39	-61.5(3)	C10 – C9 – C8 – C5	-47.9(3)

C29 – C31 – C38 – C39	63.5(3)	C11 – C9 – C8 – C5	-172.9(2)
C12 – C13 – C14 – C19	-58.3(3)	C27 – O5 – C21 – O4	-16.5(3)
C12 – C13 – C14 – C15	61.2(3)	C22 – O4 – C21 – O5	15.9(3)
C19 – C18 – C17 – C16	-59.7(3)	C1 – O2 – C2 – C3	174.1(3)
C11 – C18 – C17 – C16	61.2(3)	C1 – O2 – C2 – C7	-8.8(3)
C20 – C16 – C17 – C18	-60.3(3)	C6 – C7 – C2 – C3	2.3(5)
C15 – C16 – C17 – C18	59.8(3)	O1 – C7 – C2 – C3	178.1(3)
C14 – C13 – C12 – C20	-60.4(3)	C6 – C7 – C2 – O2	-175.0(3)
C14 – C13 – C12 – C11	60.4(3)	O1 – C7 – C2 – O2	0.8(4)
O3 – C11 – C12 – C20	-54.5(3)	O2 – C2 – C3 – C4	175.2(3)
C9 – C11 – C12 – C20	-175.7(2)	C7 – C2 – C3 – C4	-1.6(5)
C18 – C11 – C12 – C20	59.2(3)	C5 – C4 – C3 – C2	-0.2(5)
O3 – C11 – C12 – C13	-174.6(2)	C2 – O2 – C1 – O1	13.5(4)
C9 – C11 – C12 – C13	64.2(3)	C7 – O1 – C1 – O2	-13.1(3)

8.3 Single Crystal X-Ray Diffraction Studies for 168

Crystallographic data for Compound **168** (CSD number 2176477) was measured on a *RIGAKU Synergy S* area-detector diffractometer using mirror optics monochromated Cu *K*α radiation (λ = 1.54184 Å). Data reduction was performed using the *CrysAlisPro* program.[194] The intensities were corrected for Lorentz and polarization effects, and an absorption correction based on the multi-scan method using SCALE3 ABSPACK in *CrysAlisPro*[194] was applied..

The structure was solved by direct methods using *SHELXT*,[195] which revealed the positions of all non-hydrogen atoms of the title compounds. Refinement of the structures were carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. The weighting scheme was based on counting statistics and included a factor to downweight the intense reflections. All calculations were performed using the *SHELXL-2014/7*[195] program in OLEX2.[194]

A solvent mask was used to include the contribution of electron densities from void areas into the calculated structure factors. These correspond to two disordered THF solvent molecules where the most disordered one could be possibly coordinating Zn1.

Compound	**Compound 9**
CSD Number	2176477
Empirical formula	$C_{35}H_{55}Br_6LiN_6O_5Zn_4$
Mol. Mass	1387.73
Crystal system	Triclinic
a/Å	11.0839(10)
b/Å	14.1896(10)
c/Å	19.4995(10)
α/°	81.3200(10)
β/°	76.7700(10)
γ/°	89.0220(10)
V/Å^3	2950.73(4)
Z	2
□/Å	1.54184
Measured reflections	117516
Unique reflections	12042
*R*int	0.0461
Observed rflns [I > 2□(I)]	11701

[194] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.* **2009**, *42*, 339–341.

[195] G. M. Sheldrick, *Acta Crystallogr. Sect. C Struct. Chem.* **2015**, *C71*, 3–8.

Goof	1.065
R [on *F*, obs rflns only]	0.0342
□*R* [on F^2, all data]	0.0923
Largest diff. peak/hole e/Å^{-3}	0.8200/-0.7000

All calculations were conducted with the program package GAUSSIAN16[12].

8.4 Computational Studies

Calculation of Gibbs Free Energies:

Optimizations of minimum geometries were performed using the B3LYP functional[196] with the 6-311+G(d,p) basis set[197] for atoms C, H, O, Si and Cl, and the LANL2DZ[198] effective core potential for atoms Zn and Pd. Solvent effects were accounted for through the Polarizable Continuum Model (PCM)[199], using the adequate dielectric constant of the respective solvent (as indicated for each structure below). The minimum structures were verified by a frequency analysis on the same level of theory by the absence of negative modes. For each geometry, a thermochemical analysis was performed at room temperature, according to experiments. The Gibbs free energy G_{solv} in solution was extracted from the thermochemistry output for each structure ("Sum of electronic and thermal Free Energies") and is indicated below. To obtain the ΔG_{solv} values used in the main manuscript, they are compared to the Gibbs free energy of a reference structure (*anti*-**144a** for the Zn species in the transmetalation step and *anti*-**148a** for the Pd species in the reductive elimination step of the catalytic cross-coupling cycle) according to

$$\Delta G_{solv} = G_{solv} - G_{solv}^{ref} \quad . \qquad (1)$$

[196] a) Stephens, P. J., Devlin, F. J., Chabalowski, C. F. & Frisch, M. J. *J. Phys. Chem.* **98,** 11623–11627 (1994); b) Vosko, S. H., Wilk, L. & Nusair, M. Accurate spin-dependent electron liquid correlation energies for local spin density calculations: a critical analysis. *Can. J. Phys.* **58,** 1200–1211 (1980); c) Lee, C., Yang, W. & Parr, R. G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B* **37,** 785–789 (1988); d) Becke, A. D. Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **98,** 5648–5652 (1993).

[197] McLean, A. D. & Chandler, G. S. Contracted Gaussian basis sets for molecular calculations. I. Second row atoms, Z =11–18. *J. Chem. Phys.* **72,** 5639–5648 (1980).

[198] Hay, P. J. & Wadt, W. R. Ab initio effective core potentials for molecular calculations. Potentials for the transition metal atoms Sc to Hg. *J. Chem. Phys.* **82,** 270–283 (1985).

[199] a) Miertuš, S., Scrocco, E. & Tomasi, J. Electrostatic interaction of a solute with a continuum. A direct utilizaion of AB initio molecular potentials for the prevision of solvent effects. *Chem. Phys.* **55,** 117–129 (1981); b) *Continuum Solvation Models in Chemical Physics*. (John Wiley & Sons, Ltd, 2007). doi:10.1002/9780470515235; c) Tomasi, J., Mennucci, B. & Cammi, R. Quantum Mechanical Continuum Solvation Models. *Chem. Rev.* **105,** 2999–3094 (2005).

Calculation of transition state barriers:

The transition state *ts*-**144a** for the epimerization between *syn*-**144a** and *anti*-**144a** was optimized on the same level of electronic structure theory as above, with the frequency analysis exhibiting exactly one mode with negative frequency. The transition state was further verified by displacing the *ts*-**144a** structure along this mode's displacement vector in positive and negative direction, and subsequent geometry optimizations leading to *syn*-**144a** and *anti*-**144a**, respectively.

The transition states *ts*-**148a** and *ts*-**148b** were computed at the B3LYP/6-31G* level of theory, as a transition state optimization for this significantly larger structure turned out to be computationally too expensive for the 6-311+G* basis set. The Gibbs free energy of the transition state was compared to the *syn*- and *anti*- minimum structures on the same level of theory. To verify this, the B3LYP/6-31G* method was also used to compute the transition state barrier of the eperimerization of *anti*-**144a** *via ts*-**144a** to *syn*-**144a** to have a benchmark for the lower basis set. Both methods qualitatively yield similar epimerization barriers, and thus the B3LYP/6-31G* method is expected to give a reasonable value for the epimerization of *anti*-**148a,b** *via ts*-**148a,b** to *syn*-**148a,b**. All values are indicated in Table 1.

Calculation of bond energies:

Another pathway which could lead to loss of stereoinformation is the cleavage of the Zn-C bond in the transmetalation step or the Pd-C bond in the reductive elimination step. Bond dissociation energies (BDEs) can be calculated from the enthalpies of formation of the participating molecular moieties according to

$$\Delta H^{\circ}(298\mathrm{K}) = \sum_{\text{products}} \Delta \mathrm{H}^{\circ}_{\mathrm{prod}}(298\mathrm{K}) - \Delta \mathrm{H}^{\circ}_{\mathrm{reactant}}(298\mathrm{K})\,. \qquad (2)$$

In all species investigated here, $\Delta H^{\circ}_{reactant}$ is the enthalpy of formation of the complete molecule (AB), and $\Delta H^{\circ}_{prod}(298K)$ are the enthalpies of formation of the two radicals (A + B) after homolytic bond cleavage. These values can be extracted from the GAUSSIAN thermochemistry output ("Sum of electronic and thermal enthalpies).

To calculate BDEs, all molecules (AB) were optimized at the UB3LYP/6-311+G* level with subsequent frequency analysis. Afterwards, both radicals A and B were optimized separately using the same method to account for relaxation effects and extracting $\Delta H^{\circ}_{prod}(298K)$ from the thermochemistry output. BDEs were calculated according to Equation 2 and values are given in Table 2, together with the bond length of the bond before cleavage. All BDEs are well above thermally accessible energies at room temperature.

Table S21: Transition state barriers for the epimerization of **148a**, **148b** and **144a**. Gibbs free energies ΔG_{solv} are indicated in kcal/mol, with *anti*-**148a** as the reference for the top two rows, and *anti*-**144a** on

their respective level for the bottom two rows. For species **144a**, both basis sets qualitatively yield a similar barrier. Thus, the B3LYP/6-31G* method used for **148a** and **148b** are expected to yield reasonable values.

method	species	*anti* [kcal/mol]	*ts* [kcal/mol]	*syn* [kcal/mol]
B3LYP/6-31G*	**148a**	0.0	41.8	-1.0
B3LYP/6-31G*	**148b**	3.8	39.7	5.6
B3LYP/6-31G*	**144a**	0.0	97.0	1.5
B3LYP/6-311+G*	**144a**	0.0	95.9	2.7

Table S22: Bond dissociation energies (BDEs) of Zn-C bonds and Pd-C bonds of investigated molecular species. BDE values are calculated according to Equation 2. ΔG_{solv} is given according to Equation 1, with *anti*-**144a** as the reference for the Zinc species and *anti*-**148a** as the reference for the Palladium species.

molecule	bond type	bond length [pm]	BDE [kcal/mol]	ΔG_{solv} [kcal/mol]
anti-**144a**	Zn-C	207.5	53.1	0.0
syn-**144a**	Zn-C	207.2	49.6	2.7
anti-**144a** + 1 Ether	Zn-C	209.6	54.0	2.4
syn-**144a** + 1 Ether	Zn-C	209.2	51.8	4.2
anti-**144a** + 2 Ether	Zn-C	210.9	55.3	13.8
anti-**148a**	Pd-C	212.1	47.2	0.0
syn-**148a**	Pd-C	211.1	47.7	-0.4
anti-**148b**	Pd-C	220.6	41.6	4.3
syn-**148b**	Pd-C	220.8	40.1	6.1

Optimized molecular geometries:

syn-144a

B3LYP // 6-311+G(d,p) (C,H,Si) // LANL2DZ (Zn) // PCM (*n*-pentane) // 298.15 °C

Sum of electronic and thermal free energies = -942.253754 a.u.

C	-2.82766400	1.11136400	0.28838300
C	-1.38804300	0.49954100	0.21026600
H	-1.47198000	-0.48059500	-0.27084600
H	-1.04030000	0.29941600	1.23322400
C	-0.33885400	1.33004700	-0.55636800
C	-3.90212200	0.04881900	0.11493200
C	-4.04085000	-1.00419000	1.03089000
C	-4.77843700	0.08693100	-0.97532900
C	-5.01894700	-1.98159800	0.86177400
H	-3.37665100	-1.06435200	1.88685300
C	-5.76108800	-0.88872600	-1.14964200
H	-4.69095300	0.89242800	-1.69803300
C	-5.88537200	-1.92826300	-0.23078600
H	-5.10618800	-2.78621700	1.58413700
H	-6.42806600	-0.83479100	-2.00342900
H	-6.64757800	-2.68810200	-0.36233200
C	-3.05821600	1.91396000	1.58393700
H	-4.04773600	2.38004800	1.58589900
H	-2.99604200	1.26413900	2.46203100
H	-2.31107000	2.70099800	1.70170000
H	-2.92850400	1.80288800	-0.55633100
C	3.09729300	-0.90405500	-1.04257000
H	3.46713500	-0.71537500	-2.05865500
H	2.77220900	-1.95250000	-1.01651100
Si	4.46516000	-0.62619400	0.20275000
C	5.10635200	1.15490400	0.08223600
H	5.46228400	1.37844800	-0.92898900
H	4.33063700	1.88773500	0.32891100
H	5.94251600	1.32194800	0.76895300
C	3.82132800	-0.91840300	1.96356800
H	3.04446300	-0.19804000	2.24178600
H	3.39433300	-1.92155800	2.06720000
H	4.62699100	-0.82739200	2.69935000
C	5.93310000	-1.79517600	-0.07677400
H	6.73029100	-1.62188400	0.65416700
H	5.62436600	-2.84202100	0.00932700
H	6.36103400	-1.65955900	-1.07522200
Zn	1.40222500	0.23247000	-0.79599700
C	-0.06210400	2.72416300	0.03080300
H	0.29533600	2.66763200	1.06579400
H	0.70255600	3.25829900	-0.54340400
H	-0.95093000	3.36942500	0.03470400
H	-0.71539200	1.46570800	-1.58081300

***anti*-144a**

B3LYP // 6-311+G(d,p) (C,H,Si) // LANL2DZ (Zn) // PCM (*n*-pentane) // 298.15 °C

Sum of electronic and thermal free energies = -942.258064 a.u.

C	2.80932800	-0.94119600	0.59852400
C	1.43936400	-0.51608500	-0.01121000
H	1.60035900	-0.35471600	-1.08522400
H	1.18736200	0.46903200	0.40282900
C	0.25990900	-1.48554000	0.19584000
H	0.07067400	-1.58609700	1.27244200
C	0.51727400	-2.88842100	-0.38088600
H	0.72307300	-2.85111500	-1.45742600
H	1.37413100	-3.39308100	0.08663300
H	-0.34416400	-3.55037800	-0.24244500
C	3.89548600	0.04269700	0.19256200
C	3.94842100	1.34041500	0.72046600
C	4.86532400	-0.31906800	-0.75001100
C	4.93530500	2.24035600	0.32274800
H	3.21401200	1.65486700	1.45425500
C	5.85551700	0.57722800	-1.15276400
H	4.84613100	-1.31917700	-1.17241500
C	5.89476200	1.86275800	-0.61679800
H	4.95646700	3.23789000	0.74849100
H	6.59667800	0.26920500	-1.88247500
H	6.66405900	2.56198000	-0.92484800
C	2.73585400	-1.13301900	2.12244500
H	3.71321600	-1.40655900	2.52881800
H	2.40702500	-0.21988500	2.62827400
H	2.02993600	-1.92543300	2.38239100
H	3.08342500	-1.90555900	0.15834700
C	-3.23946900	0.16197600	-1.26372200
H	-3.72239100	-0.57676400	-1.91595700
H	-2.94421400	1.00312100	-1.90454000
Si	-4.43603300	0.74496600	0.05103800
C	-5.04625500	-0.72833800	1.07817700
H	-5.52445400	-1.48122200	0.44283900
H	-4.22854000	-1.22054100	1.61537100
H	-5.78275600	-0.41248000	1.82412900
C	-3.58339400	1.97929800	1.21333100
H	-2.75786700	1.51901600	1.76722700
H	-3.17433100	2.82894000	0.65639400
H	-4.28666800	2.37898400	1.95115900
C	-5.95239500	1.60558600	-0.69656700
H	-6.64883400	1.94100400	0.07947000
H	-5.65797700	2.48296900	-1.28148100
H	-6.49777900	0.93228900	-1.36563500
Zn	-1.49341000	-0.67659000	-0.56379900

***ts*-144a**

B3LYP // 6-311+G(d,p) (C,H,Si) // LANL2DZ (Zn) // PCM (*n*-pentane) // 298.15 °C

Sum of electronic and thermal free energies = -942.105132 a.u.

C	2.34233700	0.44842300	0.47200200
C	1.52453000	-0.51168200	-0.45256400
H	2.06215600	-1.47553300	-0.49793000
H	1.55471900	-0.09753800	-1.47130200
C	0.07171500	-0.66227700	-0.00248600
H	-0.49732500	-0.68899400	-0.99618900
C	-0.03947800	-1.79109400	1.06456000
H	0.46783200	-2.75179800	0.82566700
H	0.45682900	-1.40844600	1.97170900
H	-1.04995500	-2.06031600	1.44606500
C	3.83684900	0.34178200	0.19469200
C	4.37590800	0.71872100	-1.04165200
C	4.70974200	-0.14540300	1.17685600
C	5.74530200	0.61362100	-1.29402900
H	3.72586000	1.10085200	-1.82437400
C	6.08186500	-0.25179300	0.93110400
H	4.30734700	-0.44360800	2.14244300
C	6.61028800	0.12780600	-0.30289700
H	6.14555500	0.91263200	-2.25921900
H	6.73649000	-0.63024300	1.71171100
H	7.66814800	0.04734900	-0.49141100
C	1.82707000	1.89026600	0.36103100
H	2.32318400	2.54875800	1.08232700
H	2.00216200	2.30358000	-0.64548800
H	0.75051800	1.91133800	0.54196700
H	2.17738900	0.12274400	1.50790300
C	-3.94851900	-1.05744800	-0.24635900
H	-4.33702300	-1.68481000	0.57121500
H	-4.47362300	-1.35404600	-1.16346000
Si	-4.10678800	0.79007200	0.10715000
C	-3.35450500	1.18241900	1.79277500
H	-3.85138700	0.61950500	2.59706200
H	-2.28272000	0.93155000	1.80983400
H	-3.44717200	2.24932100	2.03282600
C	-3.11323500	1.68734900	-1.25223400
H	-2.06772200	1.22698300	-1.30692500
H	-3.60729700	1.55820600	-2.23937600
H	-2.98629100	2.79498000	-1.04652700
C	-5.93458000	1.30953400	0.07845100
H	-6.04178500	2.39005800	0.24733900
H	-6.40692600	1.07537300	-0.87941600
H	-6.49712900	0.79398400	0.86642400
Zn	-1.99161800	-1.48180800	-0.49694900

syn-**144a** + 1 diethyl ether
B3LYP // 6-311+G(d,p) (C,H,Si,O) // LANL2DZ (Zn) // PCM (*n*-pentane) // 298.15 °C
Sum of electronic and thermal free energies = -1175.870205 a.u.

C	2.77266100	-1.41704100	-0.93200100
C	1.39463000	-0.95442700	-0.34551900
H	1.58929500	-0.14481500	0.36628300
H	0.98160000	-1.77864900	0.25259100
C	0.34745200	-0.46833500	-1.36777300
C	3.94897100	-0.90398800	-0.11678600
C	4.09622300	-1.23354900	1.23880200
C	4.92374900	-0.08620300	-0.69955600
C	5.17632400	-0.76245400	1.98170900
H	3.35765800	-1.86532500	1.72141600
C	6.00890800	0.38828800	0.03911900
H	4.83323100	0.18052800	-1.74818600
C	6.13978900	0.05177400	1.38453400
H	5.26798200	-1.03222000	3.02850600
H	6.75126500	1.01886200	-0.43857600
H	6.98185200	0.41694500	1.96185800
C	2.85374700	-2.94857600	-1.09114300
H	3.79293600	-3.24726800	-1.56598500
H	2.80201200	-3.44393600	-0.11673700
H	2.02871100	-3.32581300	-1.69869400
H	2.86349700	-0.97334000	-1.93028000
C	-3.23479900	0.26719700	0.49433500
H	-3.87752100	0.94093400	-0.08874100
H	-3.10656100	0.73379600	1.48064900
Si	-4.07992200	-1.38479400	0.68658800
C	-4.40153100	-2.16754100	-1.01217800
H	-5.01087000	-1.50841100	-1.63984200
H	-3.46964400	-2.36754900	-1.55093000
H	-4.93726700	-3.11776600	-0.91719600
C	-3.00017000	-2.57004500	1.70321500
H	-2.05045800	-2.78486600	1.20206700
H	-2.76694800	-2.14584600	2.68575300
H	-3.50697700	-3.52618700	1.87015800
C	-5.75465900	-1.23834300	1.57361000
H	-6.24368600	-2.21258600	1.68252300
H	-5.63301300	-0.81331800	2.57545600
H	-6.43641300	-0.58391400	1.02035000
Zn	-1.35754600	0.26239700	-0.39966900
O	-0.76780700	2.56292300	-0.06287700
C	-1.76650200	3.57942000	0.15164600
H	-1.39521500	4.30428100	0.88344800
H	-2.61705600	3.06260500	0.59702000
C	-2.17552200	4.26876400	-1.14320300
H	-2.58232300	3.54573500	-1.85426200
H	-2.94765600	5.01594400	-0.93697400
H	-1.33376600	4.78068500	-1.61621800
C	0.59259400	3.03854500	-0.08513500
H	0.63607400	3.98879000	-0.62807300
H	1.14958800	2.30167700	-0.66466700
C	1.18269700	3.17795900	1.31155500

H	2.22270900	3.50932100	1.24125600
H	0.63830100	3.90975900	1.91361800
H	1.16742100	2.21958400	1.83561000
C	-0.02791400	-1.52422600	-2.42224100
H	-0.46456900	-2.42005100	-1.96405300
H	-0.76760900	-1.13811700	-3.13206800
H	0.82934800	-1.86083700	-3.02266700
H	0.78193500	0.38987100	-1.90149300

anti-**144a** + 1 diethyl ether

B3LYP // 6-311+G(d,p) (C,H,Si,O) // LANL2DZ (Zn) // PCM (*n*-pentane) // 298.15 °C

Sum of electronic and thermal free energies = -1175.873046 a.u.

C	-2.83768900	-0.93326400	1.18916900
C	-1.54705600	-0.33221500	0.55155500
H	-1.81246000	0.66387400	0.17423400
H	-1.31750600	-0.93162800	-0.33983800
C	-0.29990900	-0.23207400	1.44931000
H	-0.04149100	-1.24491200	1.78886700
C	-0.51969500	0.63448800	2.70091800
H	-0.77524700	1.66960200	2.44355000
H	-1.32796400	0.26495400	3.34886100
H	0.37965700	0.67733600	3.32471000
C	-4.01537600	-0.78199600	0.23955300
C	-4.10612600	-1.52536600	-0.94605300
C	-5.03563400	0.13748100	0.51217800
C	-5.17584600	-1.35624500	-1.82310200
H	-3.33495300	-2.24836400	-1.18936700
C	-6.10927700	0.31153300	-0.36150500
H	-4.98973800	0.72320600	1.42543700
C	-6.18383700	-0.43576600	-1.53520000
H	-5.22360700	-1.94556800	-2.73269700
H	-6.88784500	1.02824300	-0.12257900
H	-7.01750700	-0.30568000	-2.21625100
C	-2.63821800	-2.38884100	1.64288700
H	-3.55783700	-2.79515100	2.07282300
H	-2.34585700	-3.03336300	0.80799700
H	-1.85359000	-2.45595400	2.40020900
H	-3.07700600	-0.34084400	2.07848800
C	3.24639400	-0.12558500	-0.52955000
H	4.01374900	0.47010000	-0.01638000
H	3.20199900	0.24328900	-1.56326000
Si	3.74397100	-1.92341300	-0.52178400
C	3.87976800	-2.56464500	1.25955000
H	4.60535400	-1.97961400	1.83483200
H	2.91999400	-2.50819900	1.78352300
H	4.20726100	-3.60920600	1.28321700
C	2.45428800	-2.97016200	-1.44149300
H	1.47663500	-2.93241100	-0.94956100
H	2.32123100	-2.61747500	-2.46991700
H	2.75645800	-4.02141700	-1.49123700
C	5.42205300	-2.21806500	-1.36465300
H	5.70178300	-3.27724200	-1.35330300

H	5.40028800	-1.89092400	-2.40947700
H	6.21799300	-1.65840900	-0.86223400
Zn	1.40955500	0.29535500	0.35717800
O	1.16651200	2.55529000	-0.24633900
C	2.31690500	3.35869100	-0.58400300
H	2.06137200	4.01995200	-1.41818800
H	3.07112200	2.65428400	-0.93499600
C	2.83415700	4.15210400	0.60788600
H	3.12458600	3.48325400	1.42155400
H	3.71401000	4.73128100	0.31236700
H	2.08598000	4.85217000	0.98809100
C	-0.09832700	3.24363200	-0.32752300
H	0.02353900	4.26659800	0.04332800
H	-0.76182400	2.72013100	0.36092700
C	-0.67182900	3.23456300	-1.73738700
H	-1.63776700	3.74784800	-1.74660400
H	-0.01519800	3.74445900	-2.44669700
H	-0.82843400	2.21100700	-2.08530300

***syn*-148a**

B3LYP // 6-311+G(d,p) (C,H,N,Cl) // LANL2DZ (Pd) // PCM (*n*-pentane) // 298.15 °C

Sum of electronic and thermal free energies = -2422.005069 a.u.

Pd	0.00074800	-0.20897500	-0.78119800
C	-1.65225200	-1.39769900	0.03750300
C	-2.76568300	-2.84594800	1.42945600
C	-3.56858300	-2.61648000	0.37293500
H	-2.90663800	-3.45321300	2.30642800
H	-4.54841800	-2.99204200	0.13655500
N	-1.60408500	-2.10671000	1.21535200
N	-2.88837700	-1.73323400	-0.46505300
C	-3.50181300	-1.27479000	-1.69001000
C	-4.67036900	-0.49711400	-1.60230000
C	-2.98243000	-1.69239000	-2.92660400
C	-5.29538600	-0.11396100	-2.79349900
C	-3.64310500	-1.28649100	-4.08943600
C	-4.78850700	-0.50085500	-4.02825600
H	-6.18992100	0.49737000	-2.74301000
H	-3.24996600	-1.59671800	-5.05132600
H	-5.28578600	-0.19267000	-4.94109100
C	-0.49897400	-2.19124600	2.14119800
C	-0.19918900	-1.09955800	2.97184800
C	0.19211900	-3.41151400	2.23875400
C	0.83906000	-1.24681300	3.89718300
C	1.21683700	-3.51423000	3.18413900
C	1.54265400	-2.44144000	4.00604900
H	1.08669400	-0.41234800	4.54407300
H	1.76673900	-4.44552400	3.26571500
H	2.34349500	-2.53602000	4.73069500
C	-0.13654400	-4.59865800	1.36488800
H	0.71188900	-5.28375100	1.32511000
H	-0.99242400	-5.15999400	1.75301000
H	-0.38286900	-4.29746700	0.34589100
C	-0.95623400	0.19872100	2.88931700
H	-0.72099900	0.83148500	3.74644000
H	-0.69277600	0.73809600	1.97601200
H	-2.03655300	0.03716400	2.86975600
C	-1.74433800	-2.54229900	-3.03007200
H	-1.75891200	-3.36692300	-2.31283600
H	-1.64911900	-2.95776200	-4.03476600
H	-0.85893200	-1.93512800	-2.81630000
C	-5.28124800	-0.08410000	-0.28408000
H	-4.52792100	0.12637700	0.47395700
H	-5.88792700	0.81297700	-0.41512800
H	-5.93835600	-0.86556900	0.11178200
C	-0.99000600	1.62075600	-1.13518200
C	-2.22066300	1.93747100	-0.25583700
H	-3.13396500	1.87402300	-0.85972800
H	-2.33993300	1.20245700	0.54136100
C	-2.16867800	3.33727700	0.42155200
H	-1.24021400	3.36863200	1.00494600
C	-2.10994900	4.49945400	-0.58663800
H	-2.05334000	5.46053200	-0.06727700

H	-1.23261300	4.41158100	-1.23062800
H	-2.99468700	4.51856300	-1.22985000
C	-3.31300200	3.51804500	1.40857900
C	-3.06781000	3.56203900	2.78628900
C	-4.64220900	3.63967700	0.97884300
C	-4.10625600	3.71989400	3.70506000
H	-2.04650000	3.47628000	3.14430400
C	-5.68426500	3.79799400	1.89047000
H	-4.86760600	3.61463700	-0.08187300
C	-5.42149100	3.83792500	3.26033500
H	-3.88600600	3.75432400	4.76683800
H	-6.70370900	3.89354200	1.53146600
H	-6.23153500	3.96406200	3.97013500
C	2.58050900	-1.75623300	0.27557200
C	1.66628900	-2.99623700	-1.43151600
C	3.72088300	-2.55250000	0.27681400
H	2.48413700	-0.91871800	0.95321400
C	2.77867400	-3.82977300	-1.49214400
H	0.83011200	-3.14389300	-2.10237600
C	3.83797600	-3.60792500	-0.61876900
H	2.81546700	-4.63563800	-2.21473100
H	4.72502500	-4.22844600	-0.63377200
N	1.56438700	-1.97796500	-0.56742200
Cl	5.01254100	-2.20438700	1.41067100
C	1.64514400	0.74588100	-1.54803800
H	2.10593200	0.20267800	-2.38606600
C	2.30933300	1.83481500	-1.14113800
H	1.91753900	2.43336400	-0.31429000
C	3.60104600	2.36078400	-1.72669200
H	3.88028100	1.75272100	-2.59584800
H	3.44629700	3.38454200	-2.09997700
C	4.76914900	2.38841400	-0.72487500
H	4.96277900	1.36680400	-0.37504200
H	4.46861300	2.96200000	0.16181500
C	6.05817200	2.98601000	-1.30046000
H	6.35334100	2.41703100	-2.19208900
H	5.85905000	4.00901200	-1.64614500
C	7.22591300	3.00735900	-0.30767800
H	7.42624000	1.98461600	0.03782400
H	6.93238100	3.57657100	0.58430400
C	8.51497400	3.60503300	-0.88340600
H	8.80916800	3.03627500	-1.77412400
H	8.31556900	4.62717100	-1.22806100
C	9.67560600	3.62215900	0.11600400
H	9.92142700	2.60994800	0.45320100
H	10.57863400	4.05353000	-0.32562500
H	9.42450300	4.21316500	1.00274400
H	-0.20828500	2.33901900	-0.88483700
C	-1.29890600	1.75876700	-2.63056100
H	-1.99730300	0.99199000	-2.97577900
H	-1.76204300	2.73215400	-2.85422800
H	-0.38983600	1.67859600	-3.23079700

***anti*-148a**

B3LYP // 6-311+G(d,p) (C,H,N,Cl) // LANL2DZ (Pd) // PCM (*n*-pentane) // 298.15 °C

Sum of electronic and thermal free energies = -2422.004603 a.u.

Pd	0.14462100	0.17323100	-0.10155000
C	-1.36408700	-1.36220800	-0.60846700
C	-2.27445300	-3.43886600	-0.98727600
C	-2.88369000	-2.57962200	-1.82728700
H	-2.40429000	-4.49676800	-0.83848300
H	-3.65057600	-2.73661500	-2.56541500
N	-1.35784900	-2.69044400	-0.25282600
N	-2.33343400	-1.32152800	-1.58669400
C	-2.86354200	-0.16396600	-2.27267000
C	-4.18169300	0.22839100	-1.98086400
C	-2.10555700	0.47196300	-3.26844700
C	-4.72347800	1.29835500	-2.70034800
C	-2.68648600	1.53989300	-3.95769100
C	-3.98503500	1.95257300	-3.67899900
H	-5.73389700	1.62094100	-2.47605000
H	-2.11041700	2.04409600	-4.72589400
H	-4.42030200	2.78192800	-4.22546100
C	-0.54796200	-3.30275300	0.77181900
C	-0.91320600	-3.12894000	2.11693600
C	0.51451000	-4.13638700	0.38882700
C	-0.13336600	-3.75510300	3.09298500
C	1.26136500	-4.75121300	1.39957100
C	0.95054600	-4.55365100	2.74011300
H	-0.39080000	-3.62227000	4.13803400
H	2.09690300	-5.38593300	1.12570600
H	1.54643900	-5.03001100	3.51052200
C	0.83978900	-4.40767600	-1.06000700
H	1.86533800	-4.76698400	-1.15950200
H	0.18124200	-5.17932300	-1.47250900
H	0.72378100	-3.51683100	-1.67716000
C	-2.14200100	-2.34728000	2.50510900
H	-2.22043400	-2.26999000	3.59041500
H	-2.12809300	-1.34181500	2.08624200
H	-3.04762000	-2.84046800	2.13643900
C	-0.70129700	0.04379700	-3.59385600
H	-0.61897000	-1.04232200	-3.68399800
H	-0.36836200	0.49737500	-4.52911000
H	-0.02909400	0.35953500	-2.78947800
C	-5.02551800	-0.46299100	-0.93691400
H	-4.42771100	-0.82187200	-0.09946600
H	-5.77797600	0.22300500	-0.54661300
H	-5.55054000	-1.32652600	-1.35928400
C	-0.92834500	1.51658100	1.14106100
H	-0.53414800	2.49594200	0.86740700
C	-2.44767400	1.54341300	0.94258300
H	-2.68045100	1.74839700	-0.10641400
H	-2.87523500	0.56042000	1.16705900
C	-3.20665100	2.60034000	1.81339600
H	-2.97752900	2.38575100	2.86207200

C	-0.51665900	1.22345700	2.58816600
H	-0.92805500	1.96466100	3.29031200
H	-0.86181400	0.24201100	2.92668300
H	0.56827200	1.25005600	2.69714600
C	-2.73696100	4.03503900	1.52515500
H	-3.33216500	4.76375900	2.08294000
H	-1.69181200	4.16400400	1.81261200
H	-2.81168900	4.28013400	0.46125200
C	-4.71199400	2.43167100	1.67348800
C	-5.40310300	1.59109100	2.55765300
C	-5.45460100	3.07562200	0.67508200
C	-6.77919700	1.39634400	2.45226600
H	-4.85187300	1.08781300	3.34653500
C	-6.83281000	2.88806700	0.56588400
H	-4.95704100	3.73659300	-0.02498100
C	-7.50303900	2.04650800	1.45281500
H	-7.28725500	0.74476200	3.15540300
H	-7.38486300	3.40566400	-0.21182100
H	-8.57511900	1.90518700	1.37135900
C	2.70127600	-1.64834000	-0.01633500
C	2.46883900	-1.05720900	-2.22390900
C	3.97819500	-2.14469200	-0.25648400
H	2.27307100	-1.67408700	0.97699200
C	3.73808400	-1.53225400	-2.53875100
H	1.84791200	-0.60897600	-2.98765300
C	4.51998800	-2.09181800	-1.53440900
H	4.10911800	-1.45843200	-3.55352900
H	5.51532600	-2.46863700	-1.73268300
N	1.95283600	-1.11399100	-0.98931300
Cl	4.90003200	-2.82816500	1.07008100
C	1.56849100	1.64087500	0.05961400
H	1.40504400	2.49227700	-0.61470800
C	2.65632300	1.71429900	0.83459600
H	2.87468400	0.91414800	1.54754700
C	3.67103000	2.83704600	0.83827000
H	3.34132400	3.62456300	0.14976400
H	3.71130200	3.29525900	1.83813200
C	5.09337100	2.38800900	0.45917300
H	5.07347400	1.96287600	-0.55209700
H	5.40375600	1.57334000	1.12645400
C	6.13099500	3.51481700	0.52059100
H	5.81543900	4.33277800	-0.14052900
H	6.14879800	3.93477700	1.53492600
C	7.54647400	3.07185100	0.13325800
H	7.52935600	2.65170500	-0.88121900
H	7.86394600	2.25478700	0.79463500
C	8.58473000	4.19831900	0.19236600
H	8.26812500	5.01491900	-0.46811000
H	8.60394100	4.61755300	1.20580900
C	9.99489700	3.74530600	-0.19800900
H	10.01503700	3.35314000	-1.22006100
H	10.71024000	4.57114900	-0.14535500
H	10.35327600	2.95253800	0.46663800

***syn*-148b**

B3LYP // 6-311+G(d,p) (C,H,N,Cl) // LANL2DZ (Pd) // PCM (*n*-pentane) // 298.15 °C

Sum of electronic and thermal free energies = -2421.996657 a.u.

Pd	-0.12367300	0.09500100	0.39320800
C	0.74556700	-1.57669500	-0.32151300
C	1.34327300	-3.24176100	-1.76912100
C	1.77002400	-3.60823100	-0.54602000
H	1.42565500	-3.73259300	-2.72272700
H	2.29342200	-4.48720600	-0.21424500
N	0.71291000	-2.00702300	-1.62757400
N	1.40729000	-2.58786600	0.33370400
C	1.73985900	-2.66328500	1.73775600
C	3.09644700	-2.63778300	2.10774600
C	0.71737900	-2.86219400	2.68249500
C	3.40795200	-2.73831100	3.46778400
C	1.07967100	-2.95591000	4.02940000
C	2.41092900	-2.88305700	4.42444000
H	4.44873200	-2.70218600	3.77099900
H	0.30231100	-3.10193400	4.77146600
H	2.67115400	-2.95410900	5.47467100
C	0.03684000	-1.38715100	-2.74612700
C	0.57751300	-0.23319500	-3.33496800
C	-1.10805900	-2.01733600	-3.26365700
C	-0.08218900	0.31105400	-4.44053600
C	-1.73092500	-1.43885500	-4.37367500
C	-1.22971800	-0.28118200	-4.95617100
H	0.32056800	1.20543000	-4.90344300
H	-2.62458100	-1.90426100	-4.77506900
H	-1.72897200	0.15612000	-5.81373400
C	-1.98994900	1.83677800	2.10407900
C	-0.98736200	3.03414200	0.40522200
C	-2.69157700	2.95400300	2.53790100
H	-2.10281400	0.87747500	2.58879000
C	-1.67562300	4.18435900	0.77638200
H	-0.30092400	3.04129100	-0.42999200
C	-2.54064200	4.16105100	1.86221900
H	-3.35369000	2.87660600	3.39088800
H	-3.07638200	5.05149800	2.16517800
N	-1.14446300	1.87566700	1.06097200
Cl	-1.43170000	5.65786200	-0.13998600
C	-2.02049300	-0.71365400	-0.12803400
H	-2.15524500	-1.80047900	-0.07614600
C	-3.11851900	-0.05377000	-0.52502100
H	-3.09895300	1.03464900	-0.62828000
C	-4.45351300	-0.67066600	-0.88189100
H	-4.68912800	-0.45123100	-1.93452400
H	-4.38487500	-1.76218300	-0.79955000
C	-5.62137100	-0.16565200	-0.01626400
H	-5.65420600	0.93086300	-0.06142300
H	-5.42383900	-0.42207500	1.03218000
C	-6.98504400	-0.72871000	-0.43282500
H	-7.17815800	-0.46716200	-1.48159500
H	-6.94977800	-1.82560100	-0.39530100

C	-8.14872600	-0.23272900	0.43293800
H	-8.18655500	0.86406000	0.39456200
H	-7.95631300	-0.49320700	1.48218800
C	-9.51228600	-0.79713800	0.01750700
H	-9.47582500	-1.89275300	0.05763700
H	-9.70511300	-0.53778900	-1.03074800
C	-10.66824100	-0.29392400	0.88733800
H	-11.62495400	-0.71507000	0.56521600
H	-10.52123900	-0.56814200	1.93703200
H	-10.75261500	0.79660400	0.83991400
C	-1.67289600	-3.29107000	-2.68228400
H	-2.72930100	-3.38428000	-2.93923900
H	-1.15978100	-4.17296200	-3.08039600
H	-1.58367800	-3.31971900	-1.59683900
C	1.83285700	0.41446800	-2.81640800
H	2.17345700	1.18906500	-3.50539900
H	1.65881600	0.86737400	-1.83796100
H	2.64094700	-0.31133700	-2.69521900
C	-0.72923400	-3.00504400	2.28834900
H	-0.84765300	-3.68871600	1.44345800
H	-1.31156200	-3.39380700	3.12558400
H	-1.15364600	-2.04705400	1.98010500
C	4.22195500	-2.55486600	1.10395800
H	3.95999900	-1.96692100	0.22658200
H	5.10455100	-2.10540600	1.56163700
H	4.50948200	-3.55411100	0.75916300
C	1.69988600	1.11410200	1.10764900
C	3.11647900	0.78644800	0.58680000
H	3.67525800	0.24718600	1.36141000
H	3.08518900	0.11322600	-0.27305200
C	3.96123500	2.01908800	0.14934200
H	3.38414200	2.53622700	-0.62771700
C	4.20031400	3.03259700	1.28322500
H	4.77033500	3.89315800	0.92076900
H	3.25201400	3.39867400	1.68230100
H	4.75974400	2.58558200	2.11018700
C	5.27270200	1.59013700	-0.49305600
C	5.50279100	1.79542500	-1.85865200
C	6.28571700	0.96971200	0.25238500
C	6.69647200	1.39835800	-2.46299700
H	4.73620100	2.27762200	-2.45740100
C	7.48034900	0.57112700	-0.34399900
H	6.14218300	0.79789500	1.31380500
C	7.69193000	0.78280900	-1.70707400
H	6.84804400	1.57281800	-3.52301800
H	8.24927200	0.09595400	0.25617400
H	8.62205000	0.47450300	-2.17149300
H	1.46939500	2.13978400	0.78665600
C	1.65778700	1.07984800	2.64401100
H	1.80668200	0.06368600	3.02220100
H	2.44027800	1.70381200	3.10493600
H	0.70024500	1.43193600	3.03947400

***anti*-148b**

B3LYP // 6-311+G(d,p) (C,H,N,Cl) // LANL2DZ (Pd) // PCM (*n*-pentane) // 298.15 °C

Sum of electronic and thermal free energies = -2421,99907 a.u.

Pd	-0.14162800	0.46557300	0.15088700
C	0.59704600	-0.31822500	-1.55756200
C	0.93776500	-0.57474600	-3.80497100
C	1.06994800	-1.79152200	-3.24117400
H	1.02020400	-0.25496600	-4.82932100
H	1.29160800	-2.75191400	-3.67300400
N	0.65322600	0.31974700	-2.77423800
N	0.86858400	-1.63056700	-1.87020400
C	1.12518300	-2.72140000	-0.95192200
C	2.46679900	-3.05659700	-0.69359200
C	0.06058600	-3.48007500	-0.43658800
C	2.72472500	-4.11927700	0.17821600
C	0.36882400	-4.53450900	0.42971100
C	1.68592100	-4.84489100	0.74879500
H	3.75446400	-4.37604600	0.40073200
H	-0.44167700	-5.12553600	0.84226600
H	1.90233700	-5.66521400	1.42440800
C	0.58921200	1.74655600	-3.01101500
C	1.78731000	2.47824700	-2.91951500
C	-0.61095100	2.34034600	-3.43125700
C	1.74298400	3.85197100	-3.16611500
C	-0.60549800	3.71971400	-3.67400000
C	0.55162000	4.47382500	-3.52707300
H	2.65570100	4.43204400	-3.08565400
H	-1.52585700	4.19759100	-3.99200500
H	0.53175500	5.54146600	-3.71594100
C	-1.18660700	0.62919300	3.03324600
C	-1.61404300	2.55169200	1.82759800
C	-1.81814300	1.14106800	4.15969700
H	-0.74519900	-0.35844700	3.03557200
C	-2.24740200	3.12666400	2.92419100
H	-1.53238600	3.07931900	0.88730800
C	-2.36213100	2.42099300	4.11500600
H	-1.88044700	0.54437900	5.06083500
H	-2.85807700	2.85621800	4.97307600
N	-1.08714400	1.32055000	1.88619100
Cl	-2.90298400	4.74442800	2.77904000
C	-2.08024900	0.02556600	-0.62669100
H	-2.12825800	-0.48415100	-1.59440800
C	-3.29137900	0.26018000	-0.09596700
H	-3.39039500	0.75513300	0.87237800
C	-4.62230100	-0.11289000	-0.71374900
H	-5.22124900	0.79583000	-0.87949600
H	-4.45580100	-0.55977300	-1.70137800
C	-5.45203800	-1.07840800	0.15169800
H	-5.58092800	-0.64348700	1.15149300
H	-4.88432200	-2.00630300	0.29436400
C	-6.82864300	-1.40516200	-0.43833900
H	-7.39242700	-0.47321100	-0.57703900
H	-6.69947800	-1.83329700	-1.44120500
C	-7.65411700	-2.37117300	0.41903500

H	-7.78697700	-1.94265600	1.42128200
H	-7.09026700	-3.30279900	0.55993000
C	-9.02936300	-2.70109700	-0.17278400
H	-8.89704200	-3.13104200	-1.17325800
H	-9.59321200	-1.77083900	-0.31414100
C	-9.84690700	-3.66551900	0.69183300
H	-10.82054700	-3.87991500	0.24184700
H	-9.32435300	-4.61864500	0.82273600
H	-10.02605100	-3.24806300	1.68794900
C	-1.88401000	1.56247500	-3.64103600
H	-2.52756500	2.08233500	-4.35357000
H	-1.69489200	0.55693100	-4.02016400
H	-2.42873300	1.45308700	-2.70064100
C	3.10244600	1.80669300	-2.61677700
H	3.89750800	2.54752400	-2.52153800
H	3.05766900	1.23364100	-1.69094700
H	3.38403100	1.11376700	-3.41601600
C	-1.37452400	-3.22114700	-0.80709800
H	-1.48366100	-3.01769900	-1.87486800
H	-1.98891900	-4.08891800	-0.55961700
H	-1.77116800	-2.35164000	-0.27889500
C	3.62546800	-2.36061900	-1.36529100
H	3.41594700	-1.31519800	-1.58166200
H	4.51502800	-2.40638800	-0.73593600
H	3.86550700	-2.85070900	-2.31548900
C	1.71191400	1.02836100	1.20691000
H	1.34945700	0.90887000	2.23435100
C	2.96053200	0.15372900	1.07485700
H	2.69080100	-0.89845800	1.21875800
H	3.36772500	0.22499700	0.06153700
C	4.13725300	0.47587300	2.05679500
H	4.42723600	1.51900800	1.89191300
C	1.99918800	2.51816300	0.98629800
H	2.72522700	2.92964600	1.70645000
H	2.40163500	2.71458700	-0.01199800
H	1.09381000	3.12510500	1.08483100
C	3.72397900	0.34234000	3.53128900
H	4.57570900	0.51312200	4.19609900
H	2.94940600	1.07027900	3.78159600
H	3.31958600	-0.65094900	3.75024400
C	5.35599600	-0.36453300	1.71329100
C	6.38221700	0.17278800	0.92436000
C	5.48678000	-1.69667800	2.13071900
C	7.49605400	-0.58475300	0.56341100
H	6.30777800	1.20413800	0.59250500
C	6.59923400	-2.45903500	1.77576900
H	4.71385700	-2.14739800	2.74306400
C	7.61036300	-1.90764900	0.98880100
H	8.27693000	-0.13958800	-0.04417900
H	6.67829100	-3.48570400	2.11808200
H	8.47737600	-2.49903000	0.71597200