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Radical I/Mg- and I/Zn-Exchange Reactions of Alkyl Iodides and Co-Catalyzed Cross-Couplings Using Organozinc Reagents

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Erklärung

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Diese Dissertation wurde eigenständig und ohne unerlaubte Hilfe erarbeitet.

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Alisa Sunagatullina

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Parts of this thesis have been published:

1. **A. Sunagatullina**[‡], M. S. Hofmayer[‡], D. Brösamlen, P. Mauker, P. Knochel, Stereoselective Cobalt-Catalyzed Cross-Coupling Reactions of Arylzinc Chlorides with α-Bromolactones and Related Derivatives, *Org. Lett.* **2020***, 22,* 1286-1289.

2. **A. S. Sunagatullina**, F. H. Lutter, P. Knochel, Preparation of Primary and Secondary Dialkylmagnesiums by a Radical I/Mg-Exchange Reaction Using *s*Bu_2Mg in Toluene, *Angew. Chem. Int. Ed.* **2022**, e202116625.

3. **A. S. Sunagatullina**, K. Karaghiosoff, P. Knochel, Iron-Catalyzed Radical Zincations of Alkyl Iodides, *Adv. Synth. Catal.* **2022**, DOI: 10.1002/adsc.202200907.

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4. S. K. Rout, A. Kastrati, H. Jangra, K. Schwärzer, **A. S. Sunagatullina**, M. Garny, F. Lima, C. E. Brocklehurst, K. Karaghiosoff, H. Zipse, P. Knochel, Reliable Functionalization of 5,6-Fused Bicyclic *N*-Heterocycles Pyrazolopyrimidines and Imidazopyridazines *via* Zinc and Magnesium Organometallics, *Chem. Eur. J.* **2022**, *28*, e202200733.

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

Fais ce que dois, advienne que pourra

List of Abbreviations

Ac	acetyl
acac	acetylacetonate
Alk	alkyl
aq.	aqueous
Ar	aryl
Boc	*tert*-butyloxycarbonyl
bipy	2,2'-bipyridine
Bu	butyl
calc.	calculated
Cy	cyclohexyl
δ	chemical shifts in ppm (parts per million)
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMPU	*N*,*N*'-dimethylpropyleneurea
EI	electron impact ionization
equiv	equivalent
ESI	electrospray ionization
Et	ethyl
GC	gas chromatography
HRMS	high resolution mass spectrometry
*i*Pr	*iso*-propyl
IR	infared
J	coupling constant (NMR)
M	molarity
m.p.	melting point
Me	methyl
MS	mass spectrometry
NMP	*N*-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
Ph	phenyl
ppm	parts per million
R	organic substituent
rt	room emperature
sat.	saturated
*s*Bu	*sec*-butyl
T	temperature

TBS	*tert*-butyldimethylsilyl
*t*Bu	*tert*-butyl
TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxyl
Th	thienyl
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMEDA	*N*,*N*,*N*',*N*'-tetramethylethylenediamine
TMP	2,2,6,6-tetramethylpiperidyl
TMS	trimethylsilyl
Ts	4-toluenesulfonyl

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I Introduction

1 Preparation of Organomagnesium Reagents

Discovered by *Victor Grignard* at the University of Lyon in France in 1900,[1] Grignard reagents became one of the most used organometallic reagents. Easily prepared and with broad potential for application in organic synthesis, these new organomagnesium reagents turned out to be very successful. The importance of this contribution to synthetic chemistry was recognized early and rewarded with the Nobel Prize in Chemistry in 1912 for *Victor Grignard "for the discovery of the so-called Grignard reagent, which in recent years has greatly advanced the progress of organic chemistry"*. Today, organomagnesium reagents have found numerous applications in industrial processes and a variety of these organometallics have become commercially available. Several comprehensive reviews and books have been published about the preparation and use of Grignard reagents[2] as well as their chemical and physical properties.[3] In addition, mechanistic investigations of the formation and studies of the structures in solution and in solid state have been described in the literature.[2,3,4]

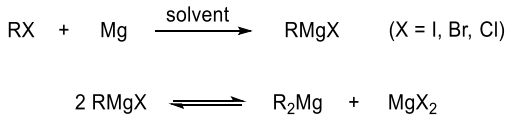
[1] a) V. Grignard, *Compt. Hebd. Séances Acad. Sci.* **1900**, *130*, 1322; b) V. Grignard, Dissertation "*Thèses sur les combinaisons organomagnesienes mixtes et leur application à des synthèses*", University of Lyon, Lyon, France, **1901**.
[2] a) H. G. Richey Jr, *Grignard Reagents: New Developments*, Wiley-VCH, Weinheim, **2000**; b) M. S. Kharasch, O. Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, New York, **1954**; c) G. S. Silverman, P. E. Rakita, *Handbook of Grignard Reagents*, Marcel Dekker, New York, **1996**; d) P. Knochel, *Handbook of Functionalized Organometallics*, Wiley-VCH, Weinheim, **2005**.
[3] W. E. Lindsell, *Comprehensive Organometallic Chemistry II*, Vol. 1, Pergamon Press, Oxford, **1995**, Chapter 3, pp. 72-78 and references therein, b) F. H. Lutter, M. S. Hofmayer, J. M. Hammann, V. Malakhov, P. Knochel in *Organic Reactions, Vol. 100* (Ed.: S. E. Denmark), Wiley, Hoboken, **2019**, pp.63-116.
[4] Z. Rappoport, I. Marek, *The Chemistry of Organomagnesium Compounds*, Wiley-VCH, Weinheim, **2008**.

1.1 Direct Oxidative Addition of Magnesium to Organic Halides

Due to their high reactivity organomagnesium species are very sensitive to air and moisture. Therefore, organomagnesium reagents are only stable and can be handled in an inert atmosphere. Most Grignard reagents of type RMgX are prepared by direct oxidative addition of magnesium turnings to organic halides (R-X) in aprotic polar solvents[2,5] such as diethyl ether or THF (Scheme 1).

Magnesium turnings are normally covered by “an oxide” film which passivates the metal surface. That is why during preparation of Grignard reagents a typical induction period after which an exothermic reaction starts is observed. Usually, small amounts of 1,2-dibromoethane or I_2 are used to initiate radical reaction.[2,6]

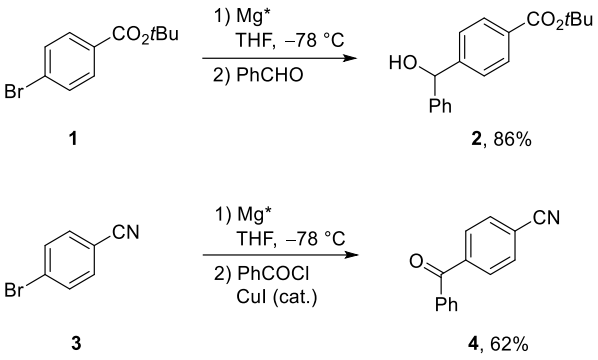
In 1929 *Schlenk* and his son discovered that Grignard reagents are present in solution as an equilibrium with the corresponding diorganomagnesium R_2Mg and magnesium dihalide MgX_2 (so-called “*Schlenk equilibrium*”) (Scheme 1).[7] Their ratio is highly dependent on the solvent, temperature and nature of the halide. For example, in 1,4-dioxane MgX_2 is precipitating and the equilibrium is shifted to R_2Mg.



Scheme 1. Preparation of Grignard reagents by oxidative addition and Schlenk equilibrium.

However, the preparation *via* direct oxidative addition is not compatible with many sensitive functional groups. In addition, it is also not very suitable for industry due to the exothermic nature of the reaction which makes it more difficult to control and the needed flammable solvents. A higher tolerance of functional groups can be achieved using “*pre-activated*” metal species, such as Rieke magnesium (Mg*). Thus, treating ester **1** with Rieke magnesium in THF at −78 °C followed by reaction with benzaldehyde led to alcohol **2** in 86% yield (Scheme 2).[8] The nitrile group of aryl bromide **3** was also tolerated in this reaction and after copper-catalyzed acylation gave ketone **4** in 62% yield (Scheme 2).[8]

[5] D. Seyferth, *Organometallics* **2009**, *28*, 1598-1605.
[6] W. E. Lindsell, *Comprehensive Organometallic Chemistry I*, *Vol. 1*, Pergamon Press, Oxford, **1982**.
[7] W. Schlenk, W. Schlenk, Jr., *Ber. Dtsch. Chem. Ges.* **1929**, *62*, 920.
[8] a) R. D. Rieke, *Science* **1989**, *246*, 1260-1264; b) T. P. Burns, R. D. Rieke, *J. Org. Chem.* **1987**, *52*, 3674-3680; c) J. Lee, R. Velarde-Ortiz, A. Guijarro, J. R. Wurst, R. D. Rieke, *J. Org. Chem.* **2000**, *65*, 5428-5430.

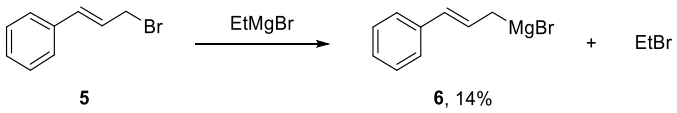


Scheme 2. Preparation of functionalized Grignard reagents using Rieke magnesium (Mg*).

1.2 Halogen/Magnesium-Exchange Reactions

The halogen/lithium-exchange reaction discovered by *Wittig*[9] and *Gilman*[10] allows the preparation of various organolithium compounds starting from commercially available alkyllithium reagents and the corresponding organic halides, mainly bromides and iodides.[11] This reaction is very fast and proceeds typically at −78 °C. In contrast to the halogen/magnesium-exchange, which is much slower and therefore offers greater tolerance to functional groups below 0 °C.

The first halogen/magnesium-exchange was discovered by *Prévost* in 1931 by reacting cinnamyl bromide **5** with ethylmagnesium bromide leading to magnesium reagent **6** (Scheme 3).[12]



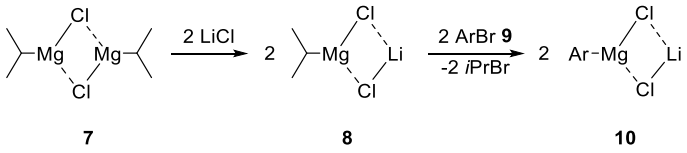
Scheme 3. First example of a halogen/magnesium-exchange.

The halogen/magnesium-exchange is an equilibrium process in which, the stability of the formed organometallic species depends on its hybridization (sp > sp^2_{vinyl} > sp^2_{aryl} > sp^3_{prim} > sp^3_{sec}). Thus, the newly formed organomagnesium species are more thermodynamically stable than the exchange reagent itself.[13] Albeit the mechanism of

[9] G. Wittig, U. Pockels, H. Dröge, *Chem. Ber.* **1938**, *71*, 1903.
[10] a) R. G. Jones, H. Gilman, *Org. Reactions* **1951**, *6*, 339; b) H. Gilman, W. Langham, A. L. Jacoby, *J. Am. Chem. Soc.* **1939**, *61*, 106-109.
[11] a) W. E. Parham, L. D. Jones, *J. Org. Chem.* **1976**, *41*, 1187-1191; b) W. E. Parham, L. D. Jones, Y. Sayed, *J. Org. Chem.* **1975**, *40*, 2394-2399; c) W. E. Parham, L. D. Jones, *J. Org. Chem. 1976*, **41**, 2704-2706; d) W. E. Parham, D. W. Boykin, *J. Org. Chem.* **1977**, *42*, 260-263; e) W. E. Parham, R. M. Piccirilli, *J. Org. Chem.* **1977**, *42*, 257-260; f) C. E. Tucker, T. N. Majid, P. Knochel, *J. Am. Chem. Soc.* **1992**, *114*, 3983-3985.
[12] C. Prévost, *Bull. Soc. Chim. Fr.* **1931**, 1372.
[13] D. Hauk, S. Lang, A. Murso, *Org. Process Res. Dev.* **2006**, *10*, 733-738.

this reaction is not fully clarified yet, but it is assumed that a halogen-ate complex is an intermediate.[14]

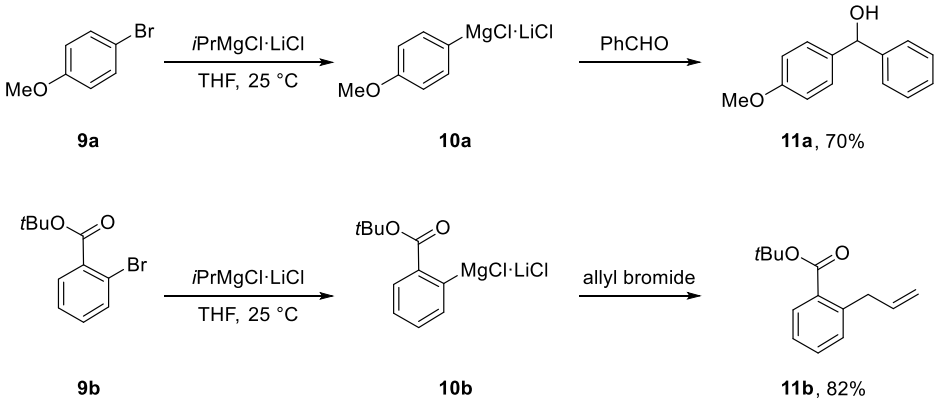
Starting from 1998, *Knochel* and co-workers described I/Mg-exchange reactions using *i*PrMgBr and PhMgCl as exchange reagents on functionalized aryl iodides at low temperatures.[15] In 2004, they have further improved halogen/magnesium-exchanges by using the so-called "*Turbo-Grignard*" – *i*PrMgCl·LiCl, obtained by adding stoichiometric amounts of LiCl to *i*PrMgCl **7** (Scheme 4).[16] It showed an improved reactivity due to the generation of a magnesium-lithium ate complex (**8**) which reacted with aryl bromides of type **9** giving the corresponding magnesium species of type **10**.



7 **8** **10**

Scheme 4. Formation of magnesium-lithium ate complex **8** by addition of LiCl to *i*PrMgCl aggregate **7**.

By using *i*PrMgCl·LiCl as exchange reagent at 25 °C, many aryl bromides bearing functional groups such as methoxy- on **9a**, ester- on **9b** and chloro- on **9c** as well as heterocycles such as **9d** were suitable substrates leading to organomagnesium species **10a-d** (Scheme 5). Trapping of the obtained organomagnesiums with aldehydes or allylations of **10a-d** afforded the corresponding products **11a-d** in 70-87% yield.



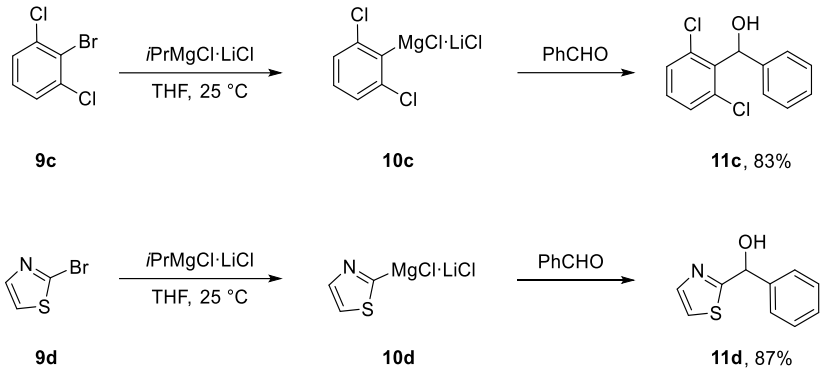
9a **10a** **11a**, 70%

9b **10b** **11b**, 82%

[14] a) R. W. Hoffmann, M. Bönstrup, M. Müller, *Org. Lett.* **2003**, *5*, 313-316; b) V. P. W. Böhm, V. Schulze, M. Bönstrup, M. Müller, R. W. Hoffmann, *Organometallics* **2003**, *22*, 2925-2930.

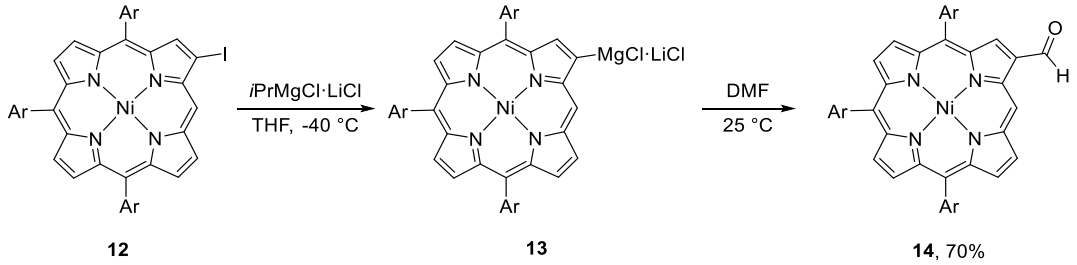
[15] a) L. Boymond, M. Rottländer, G. Cahiez, P. Knochel, *Angew. Chem. Int. Ed.* **1998**, *37*, 1701-1703; b) I. Sapountzis, P. Knochel, *Angew. Chem. Int. Ed.* **2002**, *41*, 1610-1611; c) A. E. Jensen, W. Dohle, I. Sapountzis, D. M. Lindsay, V. A. Vu, P. Knochel, *Synthesis* **2002**, 565-569.

[16] a) A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333-3336; b) A. Krasovskiy, B. F. Straub, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 159-162; c) H. Ren, P. Knochel, *Chem. Commun.* **2006**, 726-728; d) C.-Y. Liu, P. Knochel, *Org. Lett.* **2005**, *7*, 2543-2546; e) F. Kopp, A. Krasovskiy, P. Knochel, *Chem. Commun.* **2004**, 2288-2289.



Scheme 5. Br/Mg-exchanges on (hetero)aryl bromides bearing sensitive functional groups.

Several research groups have applied this method for the convenient and expedient preparation of highly functionalized aryl or heteroaryl compounds.[17] Thus, iodoporphyrin **12** also smoothly underwent the iodine/magnesium-exchange with *i*PrMgCl·LiCl at −40 °C giving magnesium reagent **13** without decomposition of the porphyrin core and further reacted with various carbonyl compounds leading to aldehyde **14** in 70% yield (Scheme 6).[18]



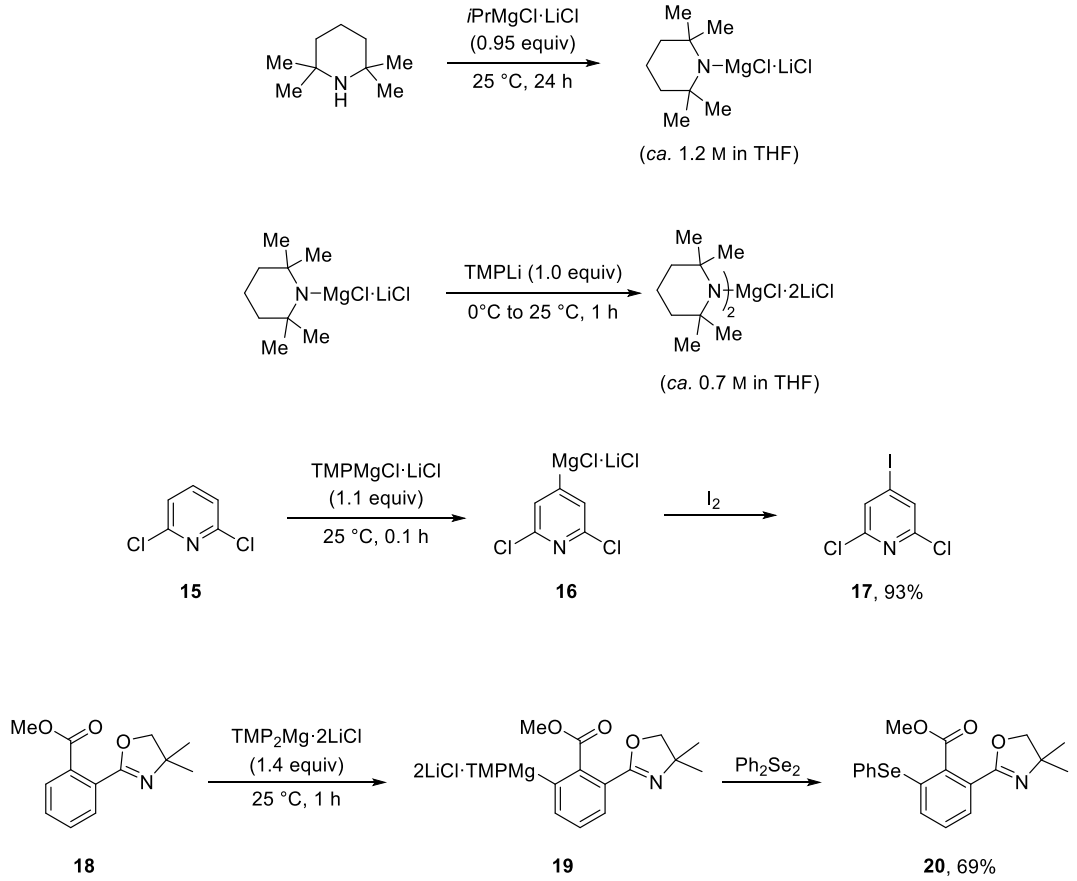
Scheme 6. Preparation and reaction of *β*-magnesiated porphyrins.

1.3 Directed Metalation with TMP-bases Complexed with LiCl

Since pioneering work of *Gilman*[19] and *Wittig*[20] directed *ortho* metalation became widely used as convenient method for regioselective functionalization of aromatic compounds. Strong bases such as alkyl lithium reagents and lithium amides have been used traditionally. However, several undesired side-reactions can occur, due to the high reactivity and nucleophilicity of the obtained organolithiums, hampering broad application of these methods.

[17] R. L.-Y. Bao, R. Zhao, L. Shi, *Chem. Commun.* **2015**, *51*, 6884-6900.
[18] K. Fujimoto, H. Yorimitsu, A. Osuka, *Eur. J. Org. Chem.* **2014**, 4327-4334.
[19] H. Gilman, R. L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109-112.
[20] G. Wittig, G. Fuhrmann, *Ber. Dtsch. Chem. Ges.* **1940**, *73*, 1197-1218.

Recently, *Knochel* and co-workers described magnesium bases such as TMPMgCl·LiCl[21] (TMP = 2,2,6,6-tetramethylpiperidyl) prepared by treating 2,2,6,6-tetramethylpiperidine with *i*PrMgCl·LiCl and $TMP_2Mg·2LiCl$.[22] $TMP_2Mg·2LiCl$ is usually prepared by treating TMPMgCl·LiCl with TMPLi. These bases allowed the directed magnesiation of sensitive aromatic and heterocyclic derivatives (Scheme 7). For example, 2,6-dichloropyridine (**15**) underwent a regioselective metalation with TMPMgCl·LiCl at room temperature within 5 min giving **16.** After iodination, the functionalized iodide **17** was obtained in 93% yield.[21a] Also, oxazoline derivative **18** was treated with $TMP_2Mg·2LiCl$ at room temperature leading to **19**, which after reaction with diphenyl diselenide gave **20** in 69% yield.[22c]

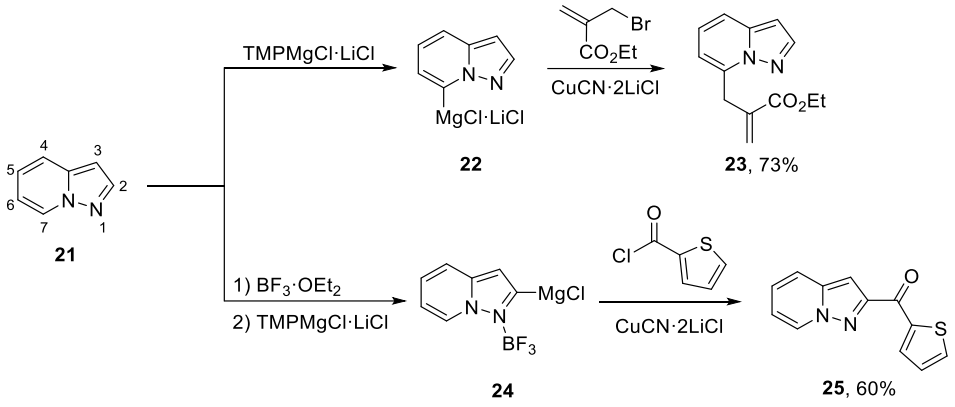


Scheme 7. Preparation of TMP-magnesium bases and their use for directed magnesiation of sensitive (hetero)aryls.

Using this mild method, the regioselective metalation of aromatics and heterocycles has been intensively studied.[2d] New regioselectivities can be observed by using strong Lewis

[21] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958-2961; b) C. Krinninger, *Spec. Chem. Mag.* **2010**, *30*, 20-21; c) A. Unsinn, C. J. Rohbogner, P. Knochel, *Adv. Synth. Catal.* **2013**, *355*, 1553-1560; d) K. Schwärzer, C. P. Tüllmann, S. Graβl, B.Górski, C. E. Brocklehurst, P. Knochel, *Org. Lett.* **2020**, *22*, 1899-1902.
[22] a) G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681-7684; b) M.Balkenhohl, R. Greiner, I. S. Makarov, B. Heinz, K. Karaghiosoff, H. Zipse, P. Knochel, *Chem. Eur. J.* **2017**, *23*, 13046-13050; c) L. A. Bozzini, T. dos Santos, V. E. Murie, M. B. M. de Mello, R. Vessecchi, G. C. Clososki, *J. Org. Chem.* **2021**, *86*, 1204-1215.

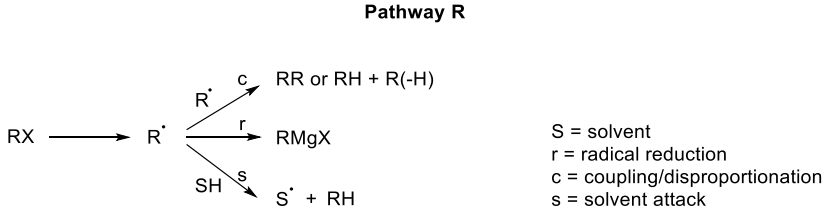
acids such as $BF_3 \cdot OEt_2$.[23] For example, reaction of pyrazolo[1,5-*a*]pyridine (**21**) with TMPMgCl·LiCl selectively gave the C7-metalated species **22** which after transmetalation with CuCN·2LiCl readily reacted with ethyl 2-(bromomethyl)acrylate furnishing **23** in 73% yield. However, when **21** was treated with $BF_3 \cdot OEt_2$ prior to the addition of base, the C2-position was metalated due to coordination of BF_3 to N1 leading to increased acidity of the C2-hydrogen. The obtained magnesium reagent **24** underwent a copper-catalyzed acylation with 2-thiophenecarbonyl chloride leading to ketone **25** in 60% yield (Scheme 8).[24]



Scheme 8. Regioselective metalations of pyrazolo[1,5-*a*]pyridine (**21**).

2 Mechanism of Grignard Reagent Formation

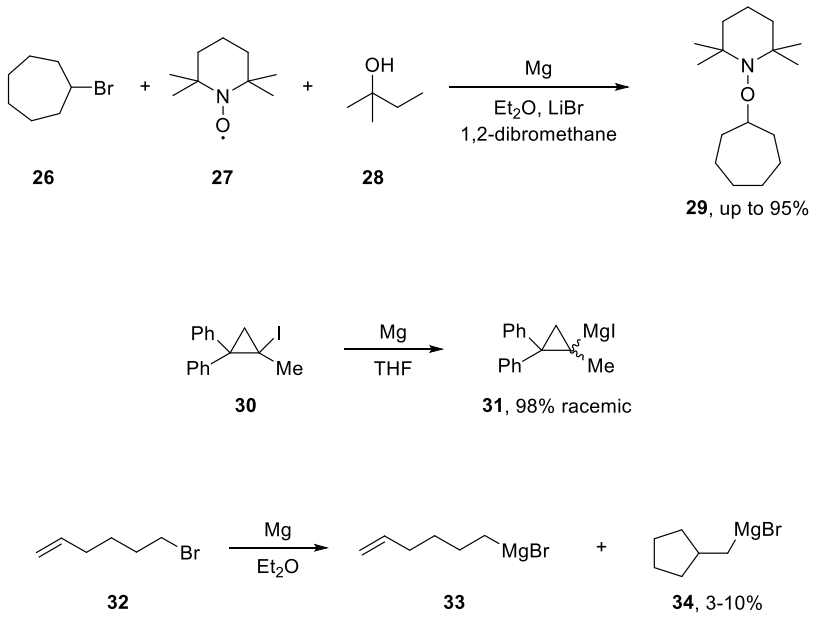
Suggestions for the mechanism of Grignard reagents formation can be divided into organic and inorganic explanations.[2] Mostly, organic chemists explain that Grignard reagent formation proceeds through intermediate radicals R· and a so-called "*pathway R*" (Scheme 9).[2,25]



Scheme 9. Radical mechanism of Grignard reagent formation.

[23] A. Kremsmair, A. Hess, B. Heinz, P. Knochel, *Chem. Eur. J.* **2022**, *28*, e202103269.
[24] M. Balkenhohl, B. Salgues, T. Hirai, K. Karaghiosoff, P. Knochel, *Org. Lett.* **2018**, *20*, 3114-3118.
[25] M. S. Kharasch, O. Reinmuth, *Grignard reactions of nonmetallic substances*, Prentice-Hall, New York, **1954**.

The existence of R· radicals was proven in numerous experiments. For example, the radical trapping of a Grignard reagent obtained *in situ* from bromocycloheptane **26** with TEMPO **27** in the presence of the tertiary alcohol **28** led to TEMPO-derivative **29** in up to 95% yield.[26] Furthermore, formation of Grignard reagent from substituted iodocyclopropane **30** was accompanied with almost complete racemization of **31**.[27] Also, hexenyl bromide **32** gave the corresponding magnesium reagent **33** as a mixture with 3-10% of cyclized product **34** (Scheme 10).[28]



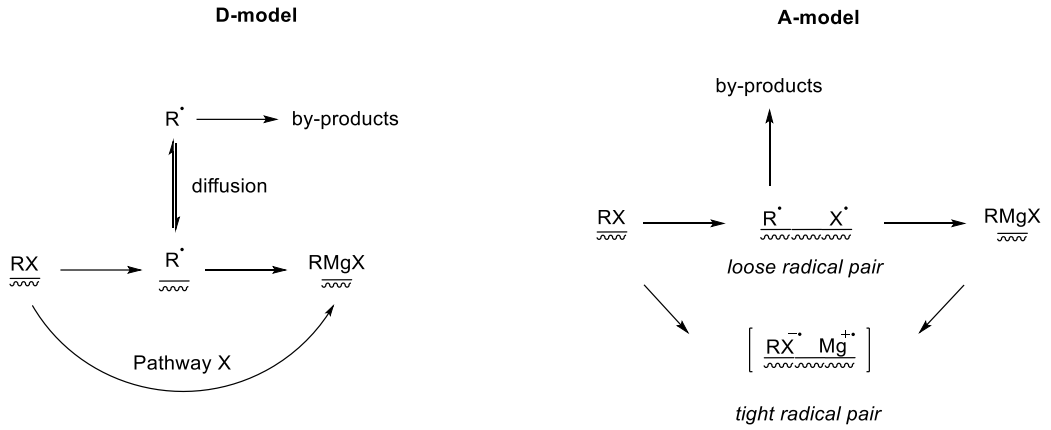
Scheme 10. Radical trapping and isomerization during Grignard reagents formation as an explanation for the occurrence of radical intermediates.

However, no chemically induced dynamic nuclear polarization was observed, which would be expected, if RMgX was formed by coupling of R· and MgX·.[29] Furthermore, it was shown, that MgX· is very unstable. So the nature of these radical intermediates was rather disputed.

The key problems of Grignard reagent formation are: the different product distribution of alkyl, alkenyl and aromatic halides, and the kinetics of the elimination of the induction period in the formation of the Grignard reagents.

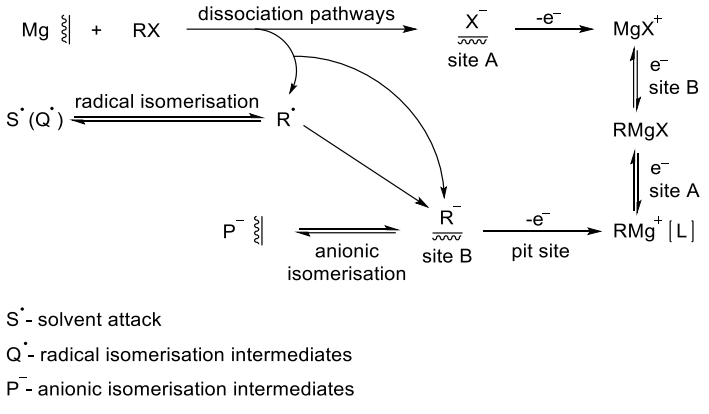
[26] a) E. C. Ashby, J. Oswald, *J. Org. Chem.* **1988**, *53*, 6068-6076; b) K. S. Root, C. L. Hill, L. M. Lawrence, G. M. Whitesides, *J. Am. Chem. Soc.* **1989**, *111*, 5405-5412; c) L. M. Lawrence, G. M. Whitesides, *J. Am. Chem. Soc.* **1980**, *102*, 2493-2494; d) I. M. Lawrence, G. M. Whitesides, *J. Am. Chem. Soc.* **1980**, *102*, 2493-2494; e) K. S. Root, C. L. Hill, L. M. Lawrence, G. M. Whitesides, *J. Am. Chem. Soc.* **1989**, *111*, 5405-5412.
[27] a) J. F. Garst, J. E. Deutch, G. M. Whitesides, *J. Am. Chem. Soc.* **1986**, *108*, 2490-2491; b) H. M. Walborsky, M. S. Aronoff, *J. Organomet. Chem.* **1973**, *51*, 31-53; c) R. C. Lamb, P. W. Ayers, M. K. Toney, J. F. Garst, *J. Am. Chem. Soc.* **1980**, *102*, 2493-2494; d) H. G. Jr. Richey, T. C. Rees, *Tetrahedron Lett.* **1966**, 4297-4301.
[28] J. F. Garst, F. Ungvary, R. Batlaw, K. E. Lawrence, *J. Am. Chem. Soc.* **1991**, *113*, 5392-5397.
[29] a) J. F. Garst, M. P. Soriaga, *Coord. Chem. Rev.* **2004**, *248*, 623-652; b) H. J. Bodewitz, C. Blomberg, F. Bickelhaupt, *Tetrahedron Lett.* **1972**, *13*, 281-284.

Garst et al.[29] predicted various isomerization products for alkane Grignard reagent formation with a radical diffusion model (D-model). However, the D-model failed in explanation of alkenyl and aromatic Grignard reagent formation, as this model predicts more side-products than it is observed. On the contrary, *Walborsky* et al.[30] proposed an adsorption model (A-model) which attributes the unusual configuration retention to surface-constrained radicals. However, the A-model lacks solid evidence for the assumed surface radical species and fails in prediction of many Grignard reagents formation reactions (Scheme 11).[31]



Scheme 11. A-model and D-model of radical pathway of Grignard reagents formation.

Due to its relevance for industrial processes, the mechanism of Grignard formation as well as the mechanism of Grignard reaction is still under discussion.[32] Recently, *Liu* and co-workers[31] reported a unified ionic model (Scheme 12).



Scheme 12. Ionic model of Grignard reagents formation.

[30] a) H. M. Walborsky, J. Rachon, J. *Am. Chem. Soc.* **1989**, *111*, 1896-1897; b) H. M. Walborsky, C. Zimmermann, *J. Am. Chem. Soc.* **1992**, *114*, 4996-5000; c) C. Hamdouchi, M. Topolski, V. Goedken, H. M. Walborsky, *J. Org.Chem.* **1993**, *58*, 3148-3155; d) H. M. Walborsky, *Acc. Chem. Res.* **1990**, *23*, 286-293.
[31] Y. Shao, Z. Liu, P. Huang, B. Liu, *Phys. Chem. Chem. Phys.* **2018**, *20*, 11100-11108.
[32] R. M. Peltzer, J. Gauss, O. Eisenstein, M. Cascella, *J. Am. Chem. Soc.* **2020**, *142*, 2984-2994.

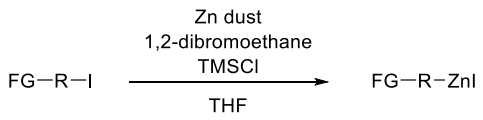
3 Preparation of Organozinc Reagents

The first organozinc compound, diethylzinc, was prepared by *Frankland* in 1849 in Marburg, Germany.[33] Since then organozinc reagents became a useful tool in organic synthesis and have been key precursors in the Reformatsky reaction,[34] the Simmons-Smith cyclopropanation[35] and the Negishi reaction.[36]

There are three important classes of organozinc reagents: organozinc halides of the general formula RZnX, diorganozincs R^1ZnR^2 and zincates of the general formula $R^1(R^2)(R^3)ZnMet$, where the metal (Met) is usually Li or MgX.

3.1 Oxidative Insertion of Zinc Dust to Organic Halides

The oxidative addition of zinc dust into functionalized organic halides allows the mild preparation of various organozinc iodides (Scheme 13).[37] This type of preparation requires activation of zinc dust due to zinc alkoxides and zinc oxide hampering the reaction. Thus, a very efficient procedure is to treat the zinc dust with 1,2-dibromoethane followed by the addition of TMSCl.[41a,38]



FG = CO_2R, enoate, CH, halide, $(RCO_2)N$, $(TMS)_2N$, RNH, NH_2, RCONH, $(RO)_3Si$, $(RO)_2PO$, RS, etc.

R = alkyl, aryl, benzyl, allyl

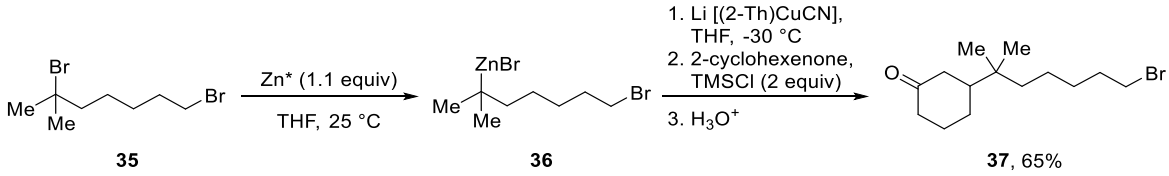
Scheme 13. Preparation of functionalized organozinc compounds by oxidative addition.

Addition of lithium chloride for activation of the zinc surface enabled the preparation of even more highly functionalized alkyl-, alkenyl-, aryl- and heteroarylzinc reagents.[39]

In the case of less reactive alkyl bromides such as tertiary bromide **35**, Rieke-zinc was used. The obtained zinc reagent **36** underwent transmetalation to the corresponding

[33] E. Frankland, *Liebigs Ann. Chem.* **1849**, *71*, 171 and 213.
[34] S. Reformatsky, *Chem. Ber.* **1887**, *20*, 1210-1211.
[35] a) H. E. Simmons, R. D. Smith, *J. Am. Chem. Soc.* **1958**, *80*, 5323-5321; b) H. E. Simmons, T. L. Cairns, A. Vladuchick, C. M. Hoiness, *Org. React.* **1972**, *20*, 1-131.
[36] a) E. Negishi, L. F. Valente, M. Kobayashi, *J. Am. Chem. Soc.* **1980**, *102*, 3298-3299; b) E. Erdik, *Tetrahedron* **1992**, *48*, 9577-9648.
[37] a) P. Knochel, M. C. P. Yeh, S.C. Berk, J. Talbert, *J. Org. Chem.* **1988**, *53*, 2390-2392; b) H. P. Knoess, M. T. Furlong, M. J. Rozema, P. Knochel, *J. Org. Chem.* **1991**, *56*, 5974-5978; c) S. C. Berk, M. C. P. Yeh, N. Jeong, P. Knochel, *Organometallics* **1990**, *9*, 3053-3064.
[38] a) M. Gaudemar, *Bull. Soc. Chim. Fr.* **1962**, 974; b) E. Erdik, *Tetrahedron* **1987**, *43*, 2203-2212; c) J. K. Gawronsky, *Tetrahedron Lett.* **1984**, *25*, 2605-2608; d) G. Picotin, P. Miginiac, *Tetrahedron Lett.* **1987**, *28*, 4551-4552.
[39] A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040-6044.

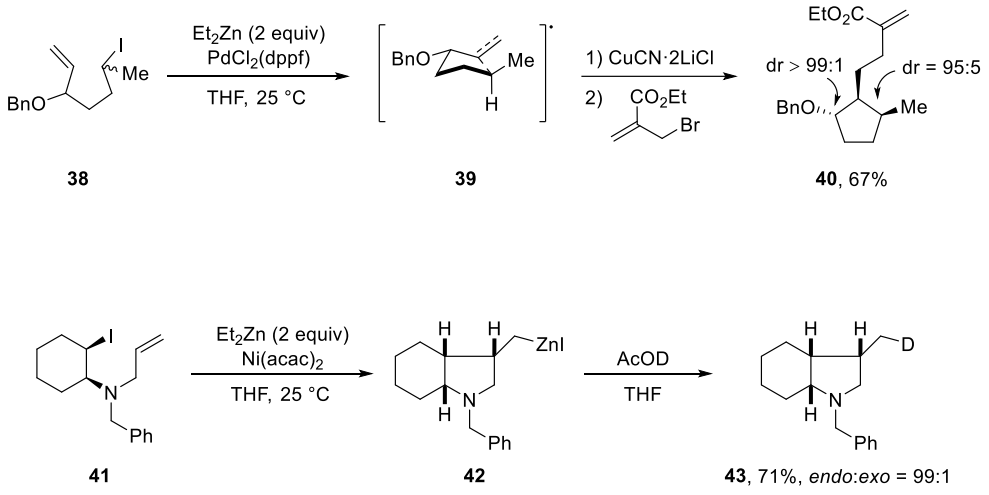
copper derivative and after treatment with 2-cyclohexenone in the presence of TMSCl led to functionalized alkyl bromide **37** in 65% yield (Scheme 14).[40]



35 **36** **37**, 65%

Scheme 14. Preparation of organozinc halides using Rieke-zinc. 2-Th = 2-thienyl.

Also, transition metals may catalyze the zinc insertion reaction. Thus, $PdCl_2$(dppf) and $Ni(acac)_2$ catalyze zinc insertion leading to organometallic products *via* radical formation. For example, treatment of alkenyl iodide **38** with Et_2Zn in the presence of $PdCl_2$(dppf) gave radical **39** which after copper-catalyzed allylation affording enantiomerically pure cyclopentane derivative **40** in 67% yield. Nickel-catalyzed I/Zn-exchange reaction of iodide **41** afforded zinc species **42** after radical cyclization followed by deuterolysis furnishing cyclized product **43** in 71% yield (Scheme 15).[41]



38 **39** **40**, 67%

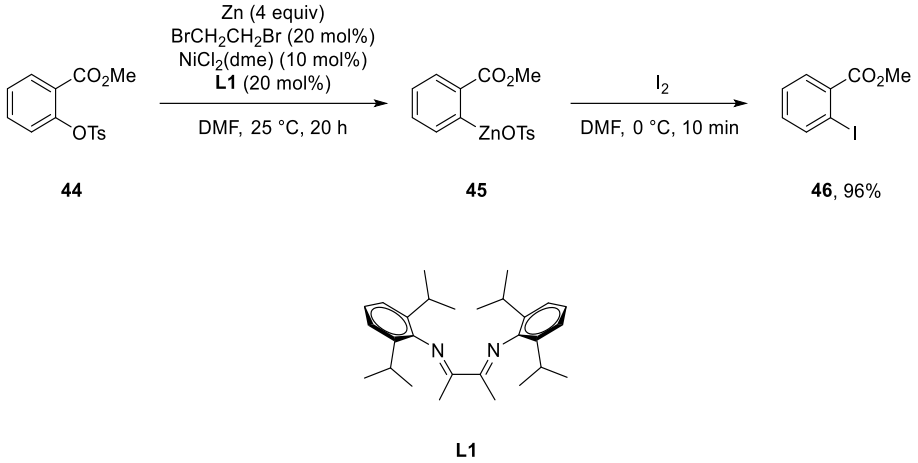
41 **42** **43**, 71%, *endo*:*exo* = 99:1

Scheme 15. Pd- and Ni-catalyzed preparation of organozinc compounds.

Recently, nickel-catalyzed insertion of zinc dust into aryl sulfonates was reported. For example, aryl tosylate **44** was converted into zinc species **45** in the presence of

[40] a) R. D. Rieke, *Science* **1989**, *246*, 1260-1264; b) R. D. Rieke, S.-H. Kim, X. Wu, *J. Org. Chem.* **1997**, *62*, 6921-6927; c) A. Guijarro, R. D. Rieke, *Angew. Chem. Int. Ed.* **1998**, *37*, 1679-1681; d) E. M. Hanada, T. K. S. Togawa, M. Kawada, S. A. Blum, *J. Am. Chem. Soc.* **2022**, *144*, 12081-12091.
[41] a) H. Stadtmüller, A. Vaupel, C. E. Tucker, T. Stüdemann, P. Knochel, *Chem. Eur. J.* **1996**, *2*, 1204-1220; b) A. Vaupel, P. Knochel, *J. Org. Chem.* **1996**, *61*, 5743-5753.

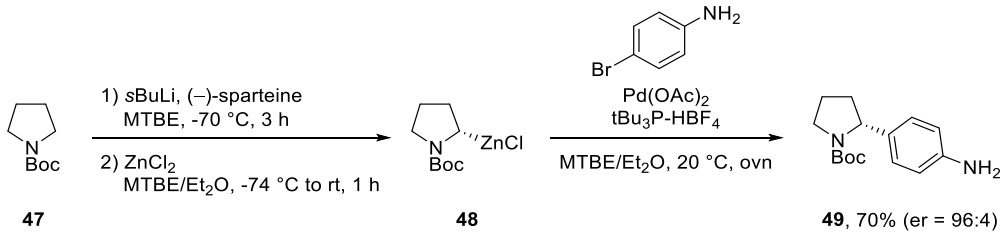
$NiCl_2$(dme) and **L1**. After addition of iodide methyl 2-iodobenzoate **46** was obtained in 96% yield (Scheme 16).[42]



Scheme 16. Nickel-catalyzed zinc insertion into aryl tosylates.

3.2 Transmetalation

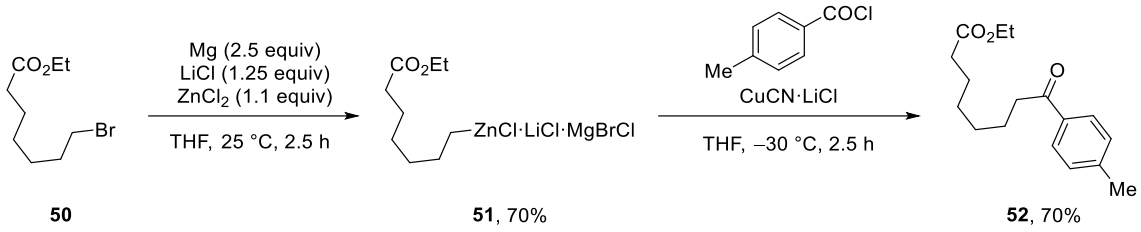
Lithium and magnesium organometallics undergo fast transmetalation with zinc salts due to the formation of a more thermodynamically stable carbon-metal bond.[43] This allows the convenient and mild preparation of organozinc compounds. A very elegant example of transmetalating lithium species prepared by treating *N*-Boc pyrrolidine (**47**) with *s*BuLi in the presence of (−)-sparteine to zinc halide **48** was reported by *Campos* and co-workers in 2006. Subsequent Pd-catalyzed Negishi cross-coupling gave the corresponding product **49** in 70% yield and er = 96:4 (Scheme 17).[44]



Scheme 17. Lithiation of *N*-Boc pyrrolidine (**47**) and subsequent transmetalation to the corresponding zinc reagent.

[42] a) P. Klein, V. D. Lechner, T. Schimmel, L. Hintermann, *Chem. Eur. J.* **2020**, *26*, 176-180; b) K. Yamada, T. Yanagi, H. Yorimitsu, *Org. Lett.* **2020**, *22*, 9712-9718.
[43] P. Knochel, H. Leuser, L-Z. Gong, S. Perrone, F. F. Kneisel, *Polyfunctional Zinc Organometallics for Organic Synthesis in Handbook of Functionalized Organometallics,* (Ed.: P. Knochel), Wiley-VCH, Weinheim, **2005**.
[44] K. R. Campos, A. Klapars, J. H. Waldman, P. G. Dormer, C.-Y. Chen, *J. Am. Chem. Soc.* **2006**, *128*, 3538-3539.

Also, the magnesium insertion into (hetero)aryl halides in the presence of $ZnCl_2$ allowed the efficient preparation of various polyfunctional zinc organometallics.[45] Later, this method was extended to alkylzinc reagents bearing sensitive functional groups. For example, alkyl bromide **50** was smoothly converted into the corresponding zinc species **51** in 70% yield. After transmetalation with CuCN·2LiCl solution and subsequent acylation with *p*-toluoyl chloride ketone **52** was obtained in 70% yield (Scheme 18).[46]



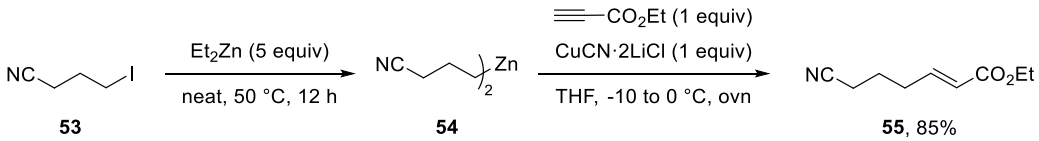
50 **51**, 70% **52**, 70%

Scheme 18. Magnesium insertion of alkyl bromides followed by *in situ* transmetalation with $ZnCl_2$.

3.3 The Halogen/Zinc-Exchange

Functionalized alkyl-, alkenyl-, aryl- and heteroarylzinc reagents can also be prepared from the corresponding halides *via* halogen/zinc-exchange using diorganozinc reagents or zincates.[47] Due to the covalent character of the carbon-zinc bond an exchange reaction is comparably slow and requires polar solvents or rather harsh reaction conditions.[3b]

Thus, 4-iodobutyronitrile **53** underwent an I/Zn-exchange using Et_2Zn at 50 °C for 12 h affording bis zinc species **54** which was transmetalated to copper-derivative and reacted with ethyl propiolate leading to (*E*)-alkene **55** in 85% yield.[48]



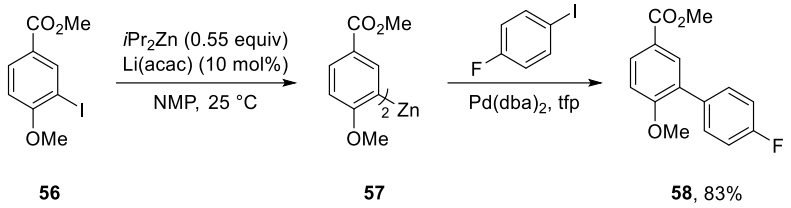
53 **54** **55**, 85%

Scheme 19. Preparation of diorganozincs *via* iodine/zinc-exchange using Et_2Zn.

Also, nucleophilic catalysis using Li(acac) in polar solvent such as *N*-methylpyrrolidone was reported. Thus, aryl iodide **56** was treated with *i*Pr_2Zn in the presence of Li(acac) in

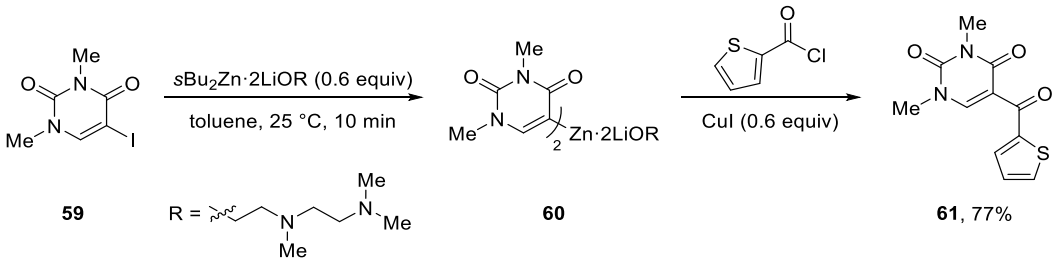
[45] a) F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 6802-6806; b) F. M. Piller, A. Metzger, M. A. Schade, B. A. Haag, A. Gavryushin, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 7192-7202.
[46] T. D. Blümke, F. M. Piller, P. Knochel, *Chem. Commun.* **2010**, *46*, 4082-4084.
[47] M. Balkenhohl, P. Knochel, *Chem. Eur. J.* **2020**, *26*, 3688-3697.
[48] M. J. Rozema, A. Sidduri, P. Knochel, *J. Org. Chem.* **1992**, *57*, 1956-1958.

NMP leading to organozinc reagent **57**. Subsequent palladium-catalyzed Negishi cross-coupling with 4-fluorophenyl iodide afforded **58** in 83% yield (Scheme 20).[49]



Scheme 20. Nucleophilic catalysis using Li(acac) for I/Zn-exchange reactions.

In 2019, *s*Bu_2Zn·2LiOR was reported as a highly reactive and selective exchange reagent for the preparation of di(hetero)aryl zinc reagents from various electron-rich as well as -deficient halo arenes. Hence, iodo uracil **59** underwent an iodine/zinc-exchange leading to **60** within 10 min. Copper-catalyzed acylation furnished the functionalized heterocycle **61** in 77% yield (Scheme 21). This method also enabled the first halogen/zinc-exchange reaction using aryl bromides.[50]



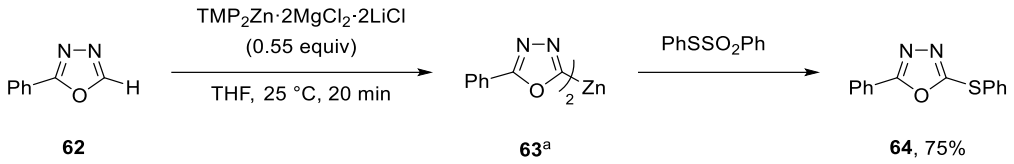
Scheme 21. Preparation of diorganozincs using *s*Bu_2Zn·2LiOR.

3.4 Directed Metalation

Another approach to prepare organozinc species is directed metalation.[51] Among others, the most common reagents for the mild deprotonation of various sensitive aromatics and heterocyclic substrates are $TMP_2Zn·2MgCl_2·2LiCl$[52] and TMPZnCl·LiCl.[53] These bases are readily prepared from the corresponding Mg- or Li-amide *via* transmetalation in the presence of Zn salts. Sensitive oxadiazole derivative **62** reacted with $TMP_2Zn·2MgCl_2·2LiCl$ affording **63** in 20 min at room temperature without any

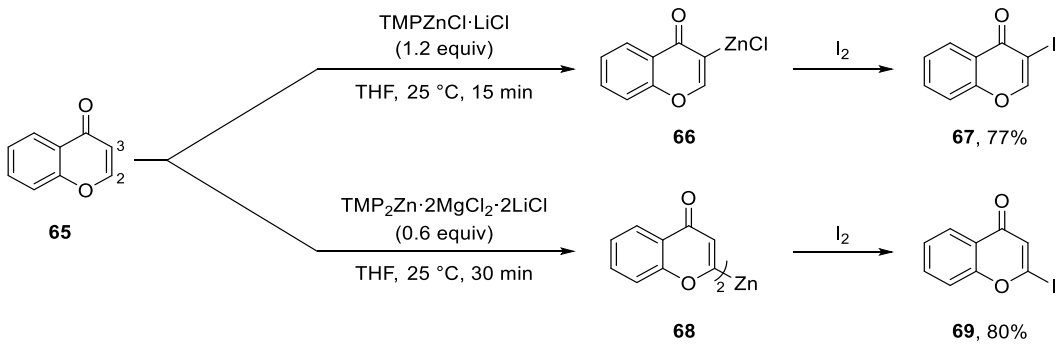
[49] F. F. Kneisel, M. Dochnahl, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 1017-1021.
[50] M. Balkenhohl, D. S. Ziegler, A. Desaintjean, L. J. Bole, A. R. Kennedy, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58*, 12898-12902.
[51] a) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879-933; b) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794-9824; c) M. Balkenhohl, P. Knochel, *SynOpen* **2018**, *2*, 78-95.
[52] S. H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7685-7688.
[53] M. Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837-1840.

fragmentation of the metalated heterocycle. After quenching **63** with $PhSSO_2Ph$ **64** was isolated in 75% yield (Scheme 22).[52]



Scheme 22. Metalation of azole with $TMP_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$. [a]Salts are omitted for clarity.

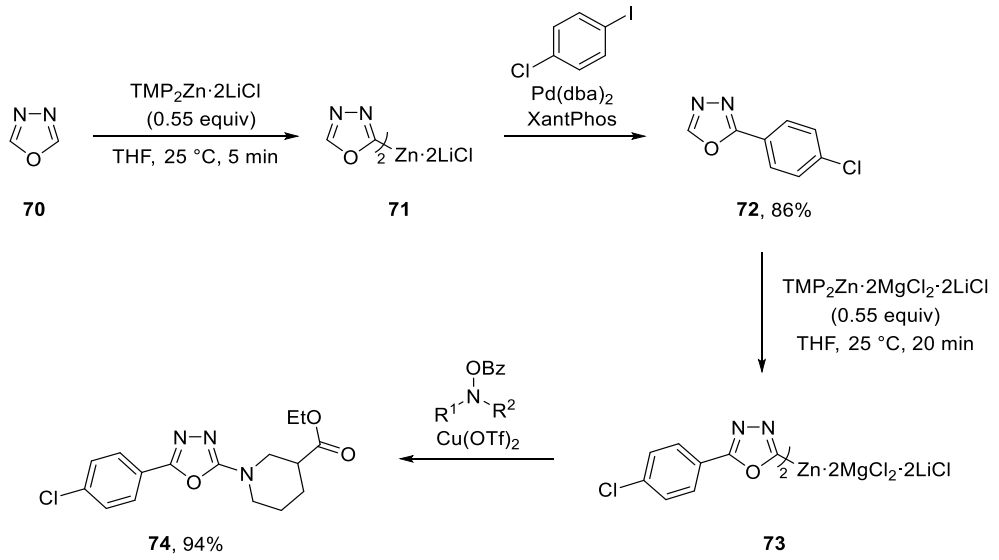
Furthermore, an elegant example for the change in regioselectivity achieved by using different bases was demonstrated on chromone **65**. Metalation using TMPZnCl·LiCl afforded C3-zincated species **66** which was trapped with I_2 giving **67** in 77% yield. However, using $TMP_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ allowed C2-zincation due to complexation of $MgCl_2$ to the ketone blocking the C3-position. After trapping **68** with I_2 the corresponding iodo derivative **69** was obtained in 80% yield (Scheme 23).[54]



Scheme 23. Regioselective metalations of chromone.

Recently, 1,3,4-oxadiazole was functionalized using TMP zinc bases. Therefore, **70** was treated with $TMP_2Zn{\cdot}2LiCl$ at room temperature leading within 5 min to zinc species **71** which underwent Pd-catalyzed Negishi cross-coupling giving **72** in 86% yield. Then, **72** was further zincated with another TMP base ($TMP_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$) furnishing **73**, which was subsequently submitted to copper-catalyzed electrophilic amination leading to functionalized heterocycle **74** in 94% yield (Scheme 24).[55]

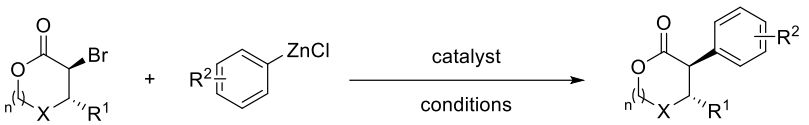
[54] L. Klier, T. Bresser, T. A. Nigst, K. Karaghiosoff, P. Knochel, *J. Am. Chem. Soc.* **2012**, *134*, 13584-13587.
[55] K. Schwärzer, C. P. Tüllmann, S. Grassl, B. Górski, C. E. Brocklehurst, P. Knochel, *Org. Lett.* **2020**, *22*, 1899-1902.



Scheme 24. Stepwise functionalization of 1,3,4-oxadiazole.

II Objectives

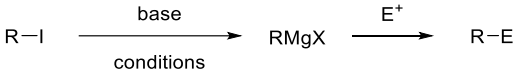
Transition-metal-catalyzed cross-couplings are one of the most used C-C-bond forming reactions in modern organic chemistry. Cobalt salts proved to be a cheap alternative to palladium and nickel catalysts. As described before, organozinc reagents tolerate a broad range of sensitive functional groups and *trans*-diastereoselective cobalt-catalyzed Negishi cross-coupling reactions of 1,2-substituted alkyl halides have been reported. However, for the preparation of chiral agrochemicals and pharmaceuticals a general and efficient method is missing. Thus, enantiomerically enriched *α*-bromolactones should be tested for their suitability to undergo Co-catalyzed Negishi cross-coupling with various arylzinc reagents (Scheme 25).[56]



X = CH_2, O; n = 0, 1

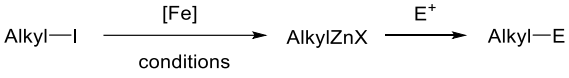
Scheme 25. Stereoselective cobalt-catalyzed cross-coupling of *α*-bromolactones with arylzinc reagents.

Furthermore, I/Mg-exchange reactions of iodo alkanes are scarcely described and have to date only been achieved using niche exchange reagents in combination with tailored substrates. Therefore, the straightforward and convenient preparation of various alkyl magnesium species *via* iodine/magnesium-exchange should be investigated (Scheme 26).



Scheme 26. Preparation of organomagnesium reagents *via* I/Mg-exchange.

Iodine/zinc-exchange reactions are known for the preparation of organozinc species but require polar solvents, tailored organozinc exchange reagents or transition metal catalysts. The aim of the last part of this thesis was to examine less toxic and cheap iron catalysts for the zincation of alkyl iodides followed by various trapping reactions (Scheme 27).



Scheme 27. Iron-catalyzed iodine/zinc-exchange reactions of alkyl iodides.

[56] This project was developed in cooperation with Maximilian S. Hofmayer, see: M. S. Hofmayer‡, A. Sunagatullina‡, D. Brösamlen, P. Mauker, P. Knochel, *Org. Lett.* **2020***, 22,* 1286-1289 and Maximilian S. Hofmayer, PhD Dissertation, **2020**, LMU Munich.

III Results and Discussion

1 Stereoselective Cobalt-Catalyzed Cross-Coupling Reactions of Arylzinc Chlorides with *α*-Bromolactones and Related Derivatives[57]

1.1 Introduction

The preparation of chiral agrochemicals and pharmaceuticals requires general and efficient asymmetric syntheses.[58] Recently, several advances involving Pd- and Ni-catalyzed asymmetric carbon-carbon bond forming reactions have been reported.[59] These transition-metal-catalyzed asymmetric cross-couplings involve expensive[60] or toxic[61] Ni- or Pd-catalysts. Also, reactions involving alkyl-palladium intermediates are often of limited scope due to *β*-hydrogen elimination side reactions.[62] It was shown that relatively inexpensive and less toxic $CoCl_2$ does efficiently catalyze cross-couplings.[63] Also, organozinc compounds are excellent nucleophilic reagents for various Co-catalyzed cross-coupling reactions, as a broad range of sensitive functional groups are tolerated in these organometallics.[3,50,64] 1,2-Substituted alkyl halides were used as

[57] Adapted with permission from (M. S. Hofmayer‡, A. Sunagatullina‡, D. Brösamlen, P. Mauker, P. Knochel, *Org. Lett.* **2020**, *22,* 1286-1289). Copyright (2020) American Chemical Society.
[58] (a) *Modern Drug Synthesis* (eds. J. J. Li, D. S. Johnson), Wiley-VCH: Weinheim, Germany, **2010**; (b) V. Yeh, W. A. Szabo in *Applications of Transition Metal Catalysis in Drug Discovery and Development* (eds. M. L. Crawley, B. M. Trost), John Wiley and Sons, **2012,** pp. 165-213; (c) *Innovative Drug Synthesis* (eds. J. J. Li, D. S. Johnson), Wiley-VCH: Weinheim, Germany, **2015**.
[59] (a) H. Horibe, Y. Fukuda, K. Kondo, H. Okuno, Y. Murakami, T. Aoyama, *Tetrahedron* **2004**, *60*, 10701-10709; (b) M. Genov, B. Fuentes, P. Espinet, B. Pelaz, *Tetrahedron: Asymmetry* **2006**, *17*, 2593-2595; (c) B. L. H. Taylor, E. R. Jarvo, *Synlett* **2011**, 2761-2765; (d) J. T. Binder, C. J. Cordier, G. C. Fu, *J. Am. Chem. Soc.* **2012**, *134*, 17003-17006; (e) J. Choi, G. C. Fu, *J. Am. Chem. Soc.* **2012**, *134*, 9102-9105; (f) C.-Y. Wang, J. Derosa, M. R. Biscoe, *Chem. Sci.* **2015**, *6*, 5105-5113; (g) M. S. Eno, A. Lu, J. P. Morken, *J. Am. Chem. Soc.* **2016**, *138*, 7824-7827; (h) X. Yang, G. Xu, W. Tang, *Tetrahedron* **2016**, *72*, 5178-5183; (i) G. J. Lovinger, M. D. Aparece, J. P. Morken, *J. Am. Chem. Soc.* **2017**, *139*, 3153-3160; (j) K. E. Poremba, N. T. Kadunce, N. Suzuki, A. H. Cherney, S. E. Reisman, *J. Am. Chem. Soc.* **2017**, *139*, 5684-5687; (k) Y. Uozumi, Y. Matsuura, T. Suzuka, T. Arakawa, Y. M. A. Yamada, *Synthesis* **2016**, *49*, 59-68; (l) J. A. Myhill, C. A. Wilhelmsen, L. Zhang, J. P. Morken, *J. Am. Chem. Soc.* **2018**, *140*, 15181-15185; (m) W. Huang, M. Hu, X. Wan, Q. Shen, *Nat. Commun.* **2019**, *10*, 2963; (n) Y. Jin, C. Wang, *Angew. Chem. Int. Ed.* **2019**, *58*, 6722-6726; (o) G. Wang, X. Xin, Z. Wang, G. Lu, Y. Ma, L. Liu, *Nat. Commun.* **2019**, *10*, 559; (p) M. D. Aparece, W. Hu, J. P. Morken, *ACS Catal.* **2019**, *9*, 11381-11385.
[60] World market prices for Pd: 51140 EUR/kg; for Co: 32 EUR/kg (retrieved Nov. 2019, http://www.infomine.com).
[61] (a) *Handbook on the Toxicology of Metals* (eds. L. Friberg, G. F. Nordberg, V. B. Vouk), Elsevier: Amsterdam, **1986**; (b) K. S. Egorova, V. P. Ananikov, *Angew. Chem. Int. Ed.* **2016**, *55*, 12150-12162.
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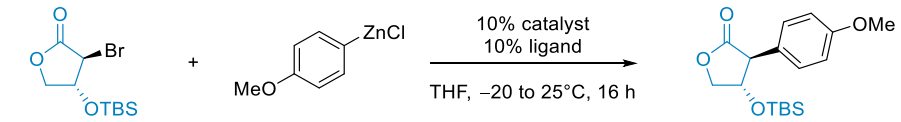
[63] (a) W. M. Czaplik, M. Mayer, A. Jacobi von Wangelin, *Synlett* **2009**, 2931-2934; (b) S. Gülak, O. Stepanek, J. Malberg, B. R. Rad, M. Kotora, R. Wolf, A. Jacobi von Wangelin, *Chem. Sci.* **2013**, *4*, 776-784; (c) J. Mao, F. Liu, M. Wang, L. Wu, B. Zheng, S. Liu, J. Zhong, Q. Bian, P. J. Walsh, *J. Am. Chem. Soc.* **2014**, *136*, 17662-17668; (d) F. Liu, Q. Bian, J. Mao, Z. Gao, D. Liu, S. Liu, X. Wang, Y. Wang, M. Wang, J. Zhong, *Tetrahedron: Asymmetry* **2016**, *27*, 663-669; (e) A. Rérat, C. Michon, F. Agbossou-Niedercorn, C. Gosmini, *Eur. J. Org. Chem.* **2016**, 4554-4560; (f) E. Barde, A. Guérinot, J. Cossy, *Org. Lett.* **2017**, *19*, 6068-6071; (g) F. Liu, J. Zhong, Y. Zhou, Z. Gao, P. J. Walsh, X. Wang, S. Ma, S. Hou, S. Liu, M. Wang, M. Wang, Q. Bian, *Chem. Eur. J.* **2018**, *24*, 2059-2064; (h) L. Thomas, F. H. Lutter, M. S. Hofmayer, K. Karaghiosoff, P. Knochel, *Org. Lett.* **2018**, *20*, 2441-2444; (i) S. Linke, S. M. Manolikakés, A. Auffrant, C. Gosmini, *Synthesis* **2018**, *50*, 2595-2600; (j) F. H. Lutter, S. Graßl, L. Grokenberger, M. S. Hofmayer, Y.-H. Chen, P. Knochel, *ChemCatChem* **2019**, *11*, 5188-5197; (k) X. Sun, X. Wang, F. Liu, Z. Gao, Q. Bian, M. Wang, J. Zhong, *Chirality* **2019**, *31*, 682-687; (l) C. Dorval, E. Dubois, Y. Bourne-Branchu, C. Gosmini, G. Danoun, *Adv. Synth. Catal.* **2019**, *361*, 1777-1780; (m) V. Koch, M. M. Lorion, E. Barde, S. Bräse, J. Cossy, *Org. Lett.* **2019**, *21*, 6241-6244; (n) T. Song, S. Arseniyadis, J. Cossy, *Org. Lett.* **2019**, *21*, 603-607.
[64] (a) J. M. Hammann, D. Haas, P. Knochel, *Angew. Chem. Int. Ed.* **2015**, *54*, 4478-4481; (b) D. Haas, J. M. Hammann, R. Greiner, P. Knochel, *ACS Catal.* **2016**, *6*, 1540-1552; (c) D. Haas, J. M. Hammann, F. H. Lutter, P. Knochel, *Angew. Chem. Int. Ed.* **2016**, *55*, 3809-3812; (d) J. M. Hammann, M. S. Hofmayer, F. H. Lutter, L. Thomas, P. Knochel, *Synthesis* **2017**, *49*, 3887-3894; (e) J. M. Hammann, F. H. Lutter, D. Haas, P. Knochel, *Angew. Chem.* **2017**, *129*, 1102-1106; (f) J. M. Hammann, L.Thomas, Y.-H. Chen, D. Haas, P. Knochel, *Org. Lett.* **2017**, *19*, 3847-3850; (g) M. S. Hofmayer, J. M.

electrophiles for *trans*-diastereoselective cobalt-catalyzed cross-coupling reactions.[6h,m,7a,65]

1.2 Optimization of the Reaction Conditions

In preliminary experiments, the readily available *α*-bromolactone **75**, which was prepared from *D*-isoascorbic acid in 99% *ee*,[66] was submitted to an arylation using 4-anisylzinc chloride (**76a**). The formation of product **77a** was optimized using various metallic salts (Table 1). Whereas $CuCl_2$, $CrCl_2$, $MnCl_2$, and $FeCl_2$ were not effective catalysts (entries 1-5), $CoCl_2$ gave excellent results compared to $CoBr_2$ or $Co(acac)_2$ (entries 6-8). The addition of a ligand, such as PPh_3, allowed further yield improvement (entries 9-12). $NiCl_2/PPh_3$ was equally efficient (entry 13).

Table 1. Reaction conditions optimization for the cross-coupling of *p*-anisylzinc chloride (**76a**) with *α*-bromolactone **75**.



75 (1.0 equiv)
dr = 99:1, 99% *ee*

76a (1.2 equiv)

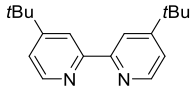
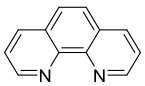
77a

entry	catalyst	ligand	yield[a]
1	-	-	3%
2	$CuCl_2$	-	-
3	$CrCl_2$	-	4%
4	$MnCl_2$	-	4%
5	$FeCl_2$	-	5%
6	$CoCl_2$	-	86% (83%)[b]
7	$CoBr_2$	-	77%
8	$Co(acac)_2$	-	75%
9	$CoCl_2$	TMEDA	56%
10	$CoCl_2$	L_1	30%
11	$CoCl_2$	L_2	65%
12	$CoCl_2$	PPh_3	98% (96%)[c]
13	$NiCl_2$	PPh_3	98%

Hammann, F. H. Lutter, P. Knochel, *Synthesis* **2017**, *49*, 3925-3930; (h) J. Li, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 11436-11440; (i) S. Graßl, C. Hamze, T. J. Koller, P. Knochel, *Chem. Eur. J.* **2019**, *25*, 3752-3755; (j) F. H. Lutter, L. Grokenberger, M. S. Hofmayer, P. Knochel, *Chem. Sci.* **2019**, *10*, 8241-8245.

[65] (a) J. M. Hammann, A. K. Steib, P. Knochel, *Org. Lett.* **2014**, *16*, 6500-6503; (b) J. M. Hammann, D. Haas, A. K. Steib, P. Knochel, *Synthesis* **2015**, *47*, 1461-1468.

[66] See Experimental Part.

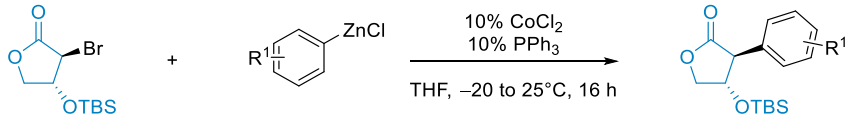
entry	catalyst	ligand	yield[a]
			
	L_1	L_2	

[a] Calibrated GC-yield using undecane as internal standard. [b] 99.99% $CoCl_2$ was used. [c] Isolated yield of analytically pure **77a** (dr = 99:1, 99% *ee*).

1.3 Stereoselective Cobalt-Catalyzed Cross-Coupling Reactions of Arylzinc Chlorides with α-Bromolactone 75

These optimized conditions were then applied to the arylation of *α*-bromolactone **75** using various arylzinc reagents of type **76** (Table 2). Thus, *p*-trifluoromethoxyphenylzinc chloride (**76b**) was cross-coupled with **75**, leading to the desired *α*-arylated lactone **77b** in 63% yield (dr = 99:1, 99% *ee*, entry 1). Similarly, the electron-poor organozinc reagent **76c** furnished the 4-trifluorotolyl substituted lactone **77c** in 62% yield (dr = 99:1, 99% *ee*, entry 2). Also, the *meta*-substituted arylzinc reagents **76d** and **76e**, bearing a MeS- and a TBSO-group in the *meta* position are satisfactory coupling partners. They afforded the optically pure products **77d** and **77e** in 63-77% yield (dr = 99:1, 99% *ee*, entries 3-4).

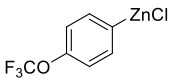
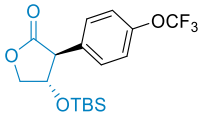
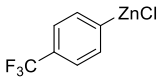
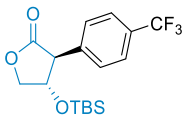
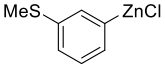
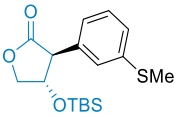
Table 2. Stereoselective cobalt-Catalyzed cross-couplings of arylzinc reagents of type **76** with *α*-bromolactone **75**.

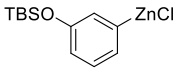
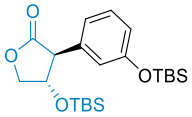
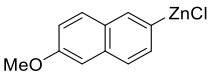
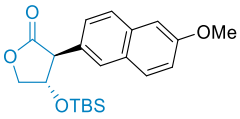
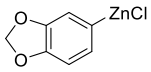
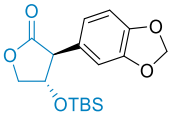
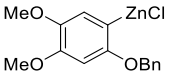
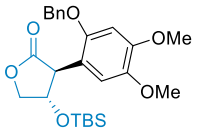


75 (1.0 equiv)
dr = 99:1, 99% *ee*

76 (1.2 equiv)

77, 62-94%
dr = 99:1, 99% *ee*

entry	arylzinc reagent	product	yield[a]
1	 **76b**	 **77b**	63%
2	 **76c**	 **77c**	62%
3	 **76d**	 **77d**	63%

entry	arylzinc reagent	product	yield[a]
4	 **76e**	 **77e**	77%
5	 **76f**	 **77f**	61%
6	 **76g**	 **77g**	84%
7	 **76h**	 **77h**	94%

[a] Isolated yield of analytically pure lactones of type **77**.

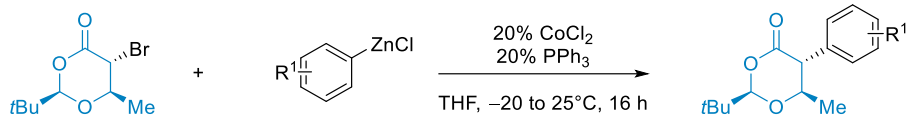
The arylation of **75** with (6-methoxynaphthalen-2-yl)zinc chloride (**76f**) and the benzodioxolylzinc reagent **76g** gave the lactone derivatives **77f** and **77g** in 61-84% yield (dr = 99:1, 99% *ee*, entries 5-6). Interestingly, the sterically hindered organozinc chloride **76h**, having a benzyloxy substituent in the *ortho*-position, was efficiently coupled with *α*-bromolactone **75**. The arylated lactone **77h** was obtained in 94% yield; dr = 99:1; 99% *ee* (entry 7).

1.4 Stereoselective Cobalt-Catalyzed Cross-Coupling Reactions of Arylzinc Chlorides with *α*-Bromolactone 78

Starting from *L*-threonine and pivalaldehyde, the chiral *α*-bromolactone **78** was prepared, bearing a smaller methyl substituent in the *β*-position.[8] The cross-coupling of **78** with various arylzinc reagents of type **76** was performed (Table 3). Thus, *p*-anisylzinc chloride **76a** led to the desired product **79a** in 81% yield (dr = 99:1, 99% *ee*). Similarly, *p*-trifluoromethoxyphenylzinc chloride **76b** and the electron-poor trifluoromethylsubstituted arylzinc reagent **76c** underwent the coupling reaction affording the protected *β*-hydroxy ester derivatives **79b** and **79c** (dr = 99:1, 99% *ee*) in 61-63% yield (entries 2-3). This arylation also proceeded well with *meta*-substituted zinc organometallics, such as the TBS-protected phenol (**76e**) and thioanisylzinc chloride (**76d**). The corresponding arylated esters **79d** and **79e** were obtained in 61-69% yield (dr = 99:1, 99% *ee*, entries 4-5). Methoxynaphthylzinc chloride **76f** and benzodioxolylzinc chloride **76g**

stereoselectively arylated the *α*-bromolactone **78**, leading to the protected *β*-hydroxy esters **79f** and **79g** in 73-82% yield (dr = 99:1, 99% *ee*, entries 6-7). Also, the zinc organometallics **76i** and **76j** bearing an ester function in the *meta*- and *para*-position were satisfactory coupling partners, leading to **79h** and **79i** in 52-76% yield (entries 8-9). The *meta*-carbethoxyphenylzinc chloride **76j** gave the product in excellent diastereomeric ratio (dr = 99:1). However, an ester substituent in the *para*-position resulted in epimerization in the course of the reaction (dr = 50:50). This can be explained by a subsequent base-catalyzed epimerization of the very acidic proton in the *α*-position to the aryl substituent in **79h**.

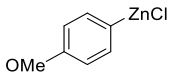
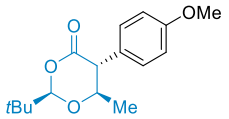
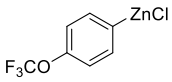
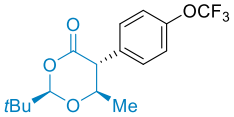
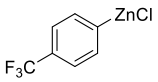
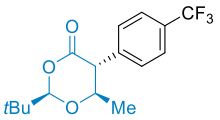
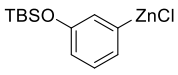
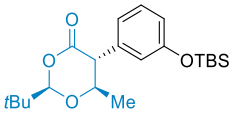
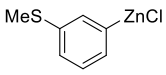
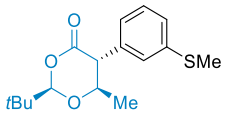
Table 3. Stereoselective cobalt-catalyzed cross-couplings of arylzinc reagents of type **76** with *α*-bromolactone **78** leading to protected *β*-hydroxy esters of type **79**.

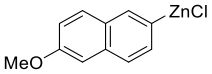
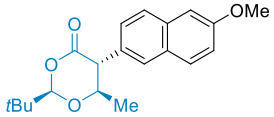
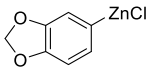
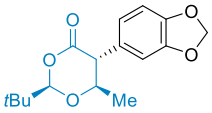
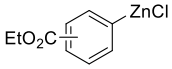
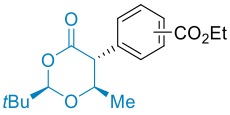


78 (1.0 equiv)
dr = 99:1, 99% *ee*

76 (1.5 equiv)

79, 52-82%
dr = 99:1, 99% *ee*

entry	arylzinc reagent	product	yield[a]
1	 **76a**	 **79a**	81%
2	 **76b**	 **79b**	63%
3	 **76c**	 **79c**	61%
4	 **76e**	 **79d**	69%
5	 **76d**	 **79e**	61%

entry	arylzinc reagent	product	yield[a]
6	 **76f**	 **79f**	82%
7	 **76g**	 **79g**	73%
			
8	**76i**: *para*	**79h**: *para*	*para*: 76%[b]
9	**76j**: *meta*	**79i**: *meta*	*meta*: 52%

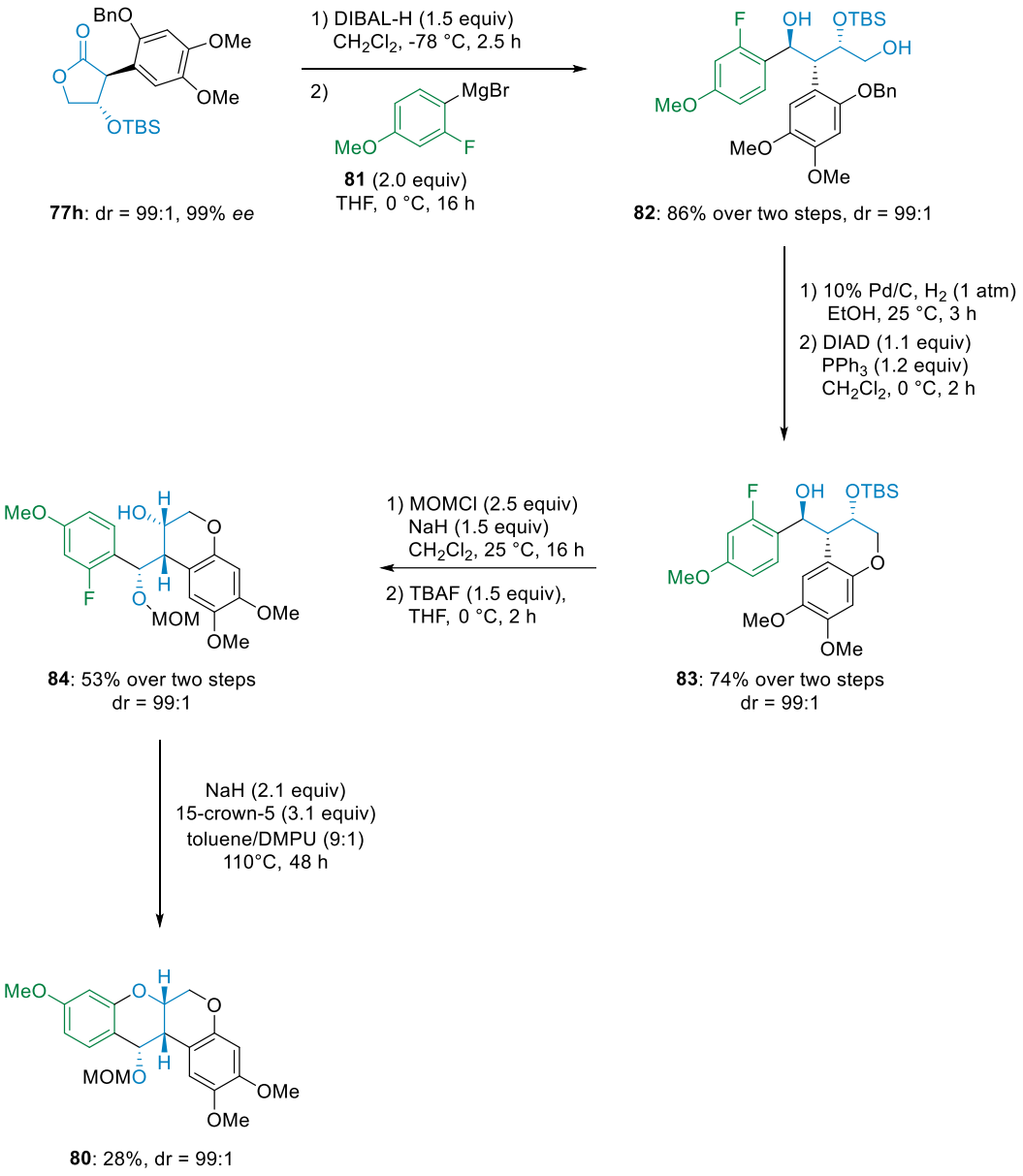
[a] Isolated yield of analytically pure lactones of type **79**. [b] dr = 50:50.

1.5 Synthesis of an Artificial Rotenoid Derivative MOM-Protected Munduserol

Many naturally occurring rotenoids and their structurally closely related unnatural derivatives show considerable antiplasmodial or cytotoxic activities.[67] These bioactive compounds were the target of several total syntheses.[68] Using this new Co-catalyzed arylation, we have prepared MOM-protected munduserol **80**, an artificial rotenoid derivative starting from the *α*-arylated lactone **77h** (Scheme 28). Thus, **77h** was reduced to the lactol with DIBAL-H and trapped with 2-fluoro-4-methoxyphenylmagnesium chloride (**81**). Interestingly, the diol **82** was obtained as a single diastereomer in 86% yield over two steps (dr = 99:1).[69] Next, the benzyl protecting group of **82** was removed via a palladium-catalyzed hydrogenolysis.[70] A selective Mitsunobu reaction allowed the first ring closure, affording the desired product **83** in 74% yield over two steps (dr = 99:1). Protection of **83** with MOMCl and deprotection of the silyl group with TBAF furnished **84** in 53% yield over two steps (dr = 99:1). Deprotonation of the secondary alcohol under forcing reaction conditions allowed the second ring closure *via* an intramolecular

[67] (a) N. Fang, J. E. Casida, *Proc. Natl. Acad. Sci. U. S. A.* **1998**, *95*, 3380; (b) N. Fang, J. E. Casida, *J. Agric. Food Chem.* **1999**, *47*, 2130-2136; (c) A. Yenesew, S. Derese, J. O. Midiwo, H. A. Oketch-Rabah, J. Lisgarten, R. Palmer, M. Heydenreich, M. G. Peter, H. Akala, J. Wangui, P. Liyala, N. C. Waters, *Phytochemistry* **2003**, *64*, 773-779; (d) A. Ahmed-Belkacem, S. Macalou, F. Borrelli, R. Capasso, E. Fattorusso, O. Taglialatela-Scafati, A. Di Pietro, *J. Med. Chem.* **2007**, *50*, 1933-1938; (e) R. S. Varughese, W. S.-T. Lam, A. A. b. H. Marican, S. H. Viganeshwari, A. S. Bhave, N. L. Syn, J. Wang, A. L.-A. Wong, A. P. Kumar, P. E. Lobie, S. C. Lee, G. Sethi, B. C. Goh, L. Wang, *Cancer* **2019**, *125*, 1789-1798.
[68] (a) N. Nakatani, M. Matsui, *Agric. Biol. Chem.* **1968**, *32*, 769-772; (b) E. H. Granados-Covarrubias, L. A. Maldonado, *J. Org. Chem.* **2009**, *74*, 5097-5099; (c) M. Nayak, I. Kim, *J. Org. Chem.* **2015**, *80*, 11460-11467; (d) K. H. Georgiou, S. C. Pelly, C. B. de Koning, *Tetrahedron* **2017**, *73*, 853-858; (e) K. Nakamura, K. Ohmori, K. Suzuki, *Angew. Chem. Int. Ed.* **2017**, *56*, 182-187; (f) S. Matsuoka, K. Nakamura, K. Ohmori, K. Suzuki, *Synthesis* **2019**, *51*, 1139-1156; (g) S. Perveen, S. Yang, M. Meng, W. Xu, G. Zhang, X. Fang, *Commun. Chem.* **2019**, *2*, 8.
[69] (a) A. Mengel, O. Reiser, *Chem. Rev.* **1999**, *99*, 1191-1224; (b) D. A. Evans, V. J. Cee, S. J. Siska, *J. Am. Chem. Soc.* **2006**, *128*, 9433-9441.
[70] W. H. Hartung, R. Simonoff in *Organic Reactions*, John Wiley and Sons, **1953**, pp. 263-326.

nucleophilic aromatic substitution. The MOM-protected munduserol **80** was obtained in 28% yield (dr = 99:1).



Scheme 28. Total synthesis of the artificial rotenoid derivative MOM-protected munduserol (**80**).

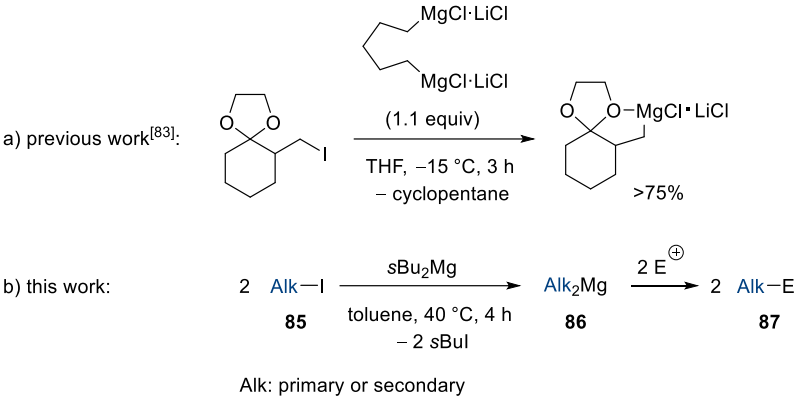
2 Preparation of Primary and Secondary Dialkylmagnesiums by A Radical I/Mg-exchange Reaction Using *s*Bu_2Mg in Toluene[71]

2.1 Introduction

Organomagnesium reagents are indispensable organometallic reagents with numerous synthetic applications.[2a,c,4,72] They combine the inherent high reactivity of the carbon-magnesium bond with a good functional group tolerance[2d,3] and an excellent compatibility with Lewis acid catalysts.[73] Magnesium organometallics are prepared by a direct insertion of magnesium turnings into organic halides[2d] or by a directed magnesiation of aromatic and heterocyclic derivatives[74] triggered by magnesium bases such as TMPMgCl·LiCl[21,75] or TMP_2Mg·2LiCl[22] (TMP = 2,2,6,6-tetramethylpiperidyl). Recently, *s*Bu_2Mg in toluene was used for directed magnesiations[76] allowing the preparation of various diaryl- and diheteroaryl-magnesium reagents in toluene, an industrially friendly solvent.[77] A further preparation of organomagnesium reagents involves a halogen/magnesium exchange of aryl iodides or bromides.[78] In contrast to the insertion of magnesium turnings, this reaction is of high industrial relevance and more practical for many synthetic applications due to its homogenous nature. *i*PrMgCl·LiCl[16a,79] or *s*Bu_2Mg·2LiOR[80] are highly efficient exchange reagents broadly used for the preparation of unsaturated aryl-, heteroaryl- and alkenylmagnesium reagents. However, the preparation of alkylmagnesium derivatives using an I/Mg-exchange is scarcely described in literature and suffers from a highly narrow substrate scope limited to primary alkyl iodides bearing a remote oxygen-coordinating group on the alkyl iodide (Scheme

[71] Adapted with permission from (A. S. Sunagatullina, F. H. Lutter, P. Knochel, *Angew. Chem. Int. Ed.* ***2022****, e202116625*). Copyright (2022) Wiley-VCH GmbH.
[72] a) A. Boudier, L. O. Bromm, M. Lotz, P. Knochel, *Angew. Chem. Int. Ed*. **2000**, *39*, 4415-4435; *Angew. Chem.* **2000**, *112*, 4584-4606; b) 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; *Angew. Chem.* **2003**, 115, 4438-4456.
[73] a) A. Frischmuth, M. Fernandez, N. M. Barl, F. Achrainer, H. Zipse, G. Berionni, H. Mayr, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2014**, *53*, 7928-7932; *Angew. Chem.* **2014**, *126*, 8062-8066; b) L. Klier, E. Aranzamendi, D. Ziegler, J. Nickel, K. Karaghiosoff, T. Carell, P. Knochel, *Org. Lett.* **2016**, *18,* 1068-1071; c) A. Kremsmair, A. Hess, B. Heinz, P. Knochel, *Chem. Eur. J.* **2021**, *27*, DOI: 10.1002/chem.202103269
[74] a) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794-9824; *Angew. Chem.* **2011**, *123*, 9968-9999; b) M. Balkenhohl, P. Knochel, *SynOpen* **2018**, *2*, 0078-0095; c) S. D. Robertson, M. Uzelac, R. E. Mulvey, *Chem. Rev*. **2019**, *119*, 8332-8405.
[75] a) A. Unsinn, C. J. Rohbogner, P. Knochel, *Adv. Synth. Catal.* **2013**, *355*, 1553-1560; b) K. Schwärzer, C. P. Tüllmann, S. Graβl, B. Górski, C. E. Brocklehurst, P. Knochel, *Org. Lett.* **2020**, *22*, 1899-1902.
[76] a) A. Hess, J. P. Prohaska, S. B. Doerrich, F. Trauner, F. H. Lutter, S. Lemaire, S. Wagschal, K. Karaghiosoff, P. Knochel, *Chem. Sci*. **2021**, *12*, 8424-8429; b) F. H. Lutter, L. Grokenberger, L. A. Perego, D. Broggini, S. Lemaire, S. Wagschal, P. Knochel, *Nat Commun* **2020**, *11*, 4443.
[77] a) *Solvent Recovery Book* (Ed.: I. M. Smallwood), Blackwell Science Ltd., Oxford, **2002**; b) L. Delhaye, A. Ceccato, P. Jacobs, C. Köttgen, A. Merschaert, *Org. Process Res. Dev.* **2007**, *11*, 160-164.
[78] a) D. S. Ziegler, B. Wei, P. Knochel, *Chem. Eur. J.* **2019**, *25*, 2695-2703; b) M. Balkenhohl, P. Knochel, *Chem. Eur. J.* **2020**, *26*, 3688-3697.
[79] a) L. Shi, Y. Chu, P. Knochel, H. Mayr, *J. Org. Chem.* **2009**, *74*, 2760-2764; b) P. Knochel, A. Gavryushin in *Encyclopedia of Reagents for Organic Synthesis*, **2010**, John Wiley & Sons, New York.
[80] a) D. S. Ziegler, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 6701-6704; *Angew. Chem.* **2018**, *130*, 6811-6815; b) A. Desaintjean, T. Haupt, L. J. Bole, N. R. Judge, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2021**, *60*, 1513-1518; *Angew. Chem.* **2021**, *133*, 1536-1541.

29a).[81] A more general protocol for preparing alkylmagnesium reagents was therefore highly desirable. Herein, we wish to report a *s*Bu_2Mg mediated I/Mg-exchange reaction of various primary or secondary alkyl iodides of type **85** in toluene providing dialkylmagnesiums of type **86** under mild reaction conditions. Trapping with various electrophiles (E^+) provided a range of polyfunctional products of type **87** (Scheme 29). Furthermore, we have found that this new exchange reaction proceeded *via* a radical mechanism.[82] Applied to secondary alkyl iodides, the new method allowed the stereoconvergent preparation of diastereomerically and enantiomerically enriched secondary dialkylmagnesiums.



Scheme 29. Preparation of dialkylmagnesium reagents **86** from primary or secondary alkyl iodides **85** *via* an I/Mg-exchange in toluene using *s*Bu_2Mg leading after quenching reactions with electrophiles to products of type **87**.

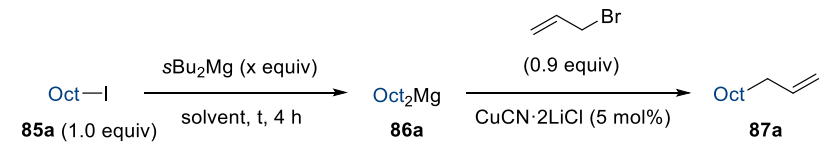
2.2 Optimization of Reaction Conditions

Thus, in preliminary experiments, we have examined the reaction of octyl iodide (**85a**) with *i*PrMgCl·LiCl in THF and have obtained mostly the corresponding substitution product (2-methyldecane in 71% yield) with little amount of desired Oct_2Mg **86a** (<5%).[83] Quenching **86a** with allyl bromide in the presence of 5 mol% CuCN·2LiCl[84] furnished 1-undecene (**87a**) which yield was easily determined by GC-analysis. Furthermore, switching from THF to toluene as solvent provided **86a** in 21% GC-yield.[85] These results led us to look for alternative exchange reagents and we found that *s*Bu_2Mg gave the best results.[85] *s*Bu_2Mg was conveniently prepared by treating *s*BuMgCl with *s*BuLi in a cyclohexane:ether mixture. Evaporation of the solvent and replacement with toluene

[81] C. B. Rauhut, V. A. Vu, F. F. Fleming, P. Knochel, *Org. Lett*. **2008**, *10*, 1187-1189.
[82] a) R. M. Peltzer, J. Gauss, O. Eisenstein, M. Cascella, *J. Am. Chem. Soc*. **2020**, *142*, 2984-2994; b) R. M. Peltzer, O. Eisenstein, A. Nova, M. Cascella, *J. Phys. Chem. Soc*. *B* **2017**, *121*, 4226-4237.
[83] See Experimental part.
[84] P. Knochel, M. C. P. Yeh, S. C. Berk, J. Talbert, *J. Org. Chem*. **1988**, *53*, 2390-2392.

produced 0.43-0.48 M homogenous solutions of *s*Bu_2Mg.[78a] Furthermore, variation of the solvent at 25 °C showed that running the reaction in pure toluene without any coordinating co-solvent led to superior yields of **87a** (entries 1-3 of Table 4).[85] Performing the reaction at 40 °C further increased the yield of **87a** to 65% (entry 4). By using 0.7 equiv of the exchange reagent *s*Bu_2Mg, **87a** was formed in 81% yield (entry 5).

Table 4. Optimization of the reaction of octyl iodide (**85a**) with *s*Bu_2Mg leading after allylation to undecene (**87a**).



entry	equiv of *s*Bu_2Mg	solvent	t [°C]	yield of **87a** [%][a]
1	0.6	THF	25	3
2	0.6	Bu_2O	25	traces
3	0.6	toluene	25	55
4	0.6	toluene	40	65
5	0.7	toluene	40	81

[a] All reactions were performed on a 0.5 mmol scale. Yields were determined by GC-analysis using undecane as internal standard.

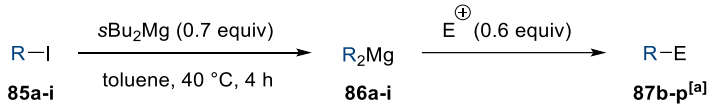
2.3 Preparation of Primary Dialkylmagnesiums by A Radical I/Mg-exchange Reaction Using *s*Bu_2Mg in Toluene

With these optimized results in hand, we treated magnesium reagent **86a** with various electrophiles and investigated the reaction scope (Table 5). Thus, acylation of the copper derivative of **86a** obtained by adding CuCN·2LiCl (as 1 M solution in THF; 1 equiv)[71] and further reaction with benzoyl chloride or cyclopropanecarbonyl chloride (0.6 equiv, −40 °C, 3 h) furnished the corresponding ketones **87b-c** in 70-86% isolated yield. Addition of **86a** to 3-iodo-2-cyclohexanone (0.6 equiv, 0 °C, 1 h) provided the tertiary alcohol **87d** in 50% yield. Fe-catalyzed cross-coupling (5% $Fe(acac)_3$, 20% TMEDA)[86] with (*E*)-3-styryl bromide (0.6 equiv, 0 °C, 0.5 h) gave (*E*)-1-phenyl-1-undecene (**87e**) in 71% yield (*E*:*Z* = 99:1). Unsaturated 1-iodo-4-pentene (**85b**) gave after I/Mg-exchange di(4-pentenyl)magnesium (**86b**). After transmetalation with CuCN·2LiCl and reaction with benzoyl chloride, ketone **87f** was obtained in 75% yield. (*Z*)-4-Phenyl-4-hexenyl

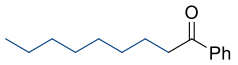
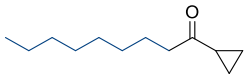
[85] We suspect that THF or Bu_2O interfered with the radical chain reaction and quenched the desired chain reaction.
[86] a) R. Martin, A. Fürstner, *Angew. Chem. Int. Ed.* **2004**, *43*, 3955-3957; b) M. Nakamura, K. Matsuo, S. Ito, E. Nakamura, *J. Am. Chem. Soc.* **2004**, *126*, 3686-3687; c) C. Bolm, J. Legros, J. L. Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217-6254 ; d) G. Cahiez, V. Habiak, C. Duplais, A. Moyeux, *Angew. Chem. Int. Ed.* **2007**, *46*, 4364-4366; *Angew. Chem.* **2007**, *119*, 4442-4444; e) W. M. Czaplik, M. Mayer, A. J. von Wangelin, *ChemCatChem* **2011**, *3*, 135-138.

iodide (**85c**)[87] reacted similarly and the corresponding dialkylmagnesium **86c** was benzoylated with 3,4,5-trimethoxybenzoyl chloride (−40 °C, 3 h) giving the ketone **87g** (*Z*:*E* = 99:1) in 79% yield. A diastereoselective addition of **86c** to (*S*)-carvone in toluene gave the tertiary alcohol **87h** in 54% yield (*Z*:*E* = 99:1; dr = 95:5).[88] The terpenic iodide derived from (*R*)-nopol (**85d**) gave the expected diorganomagnesium species **86d** which after a Cu-transmetalation underwent a smooth acylation with benzoyl chloride as well as an addition-elimination with 3-iodo-2-cyclohexen-1-one[89] leading to the corresponding ketones **87i-j** in 82-84% yield. Homopropargylic iodide **85e**[85] and the chloro-substituted iodide **85f** were selectively converted with *s*Bu_2Mg under the standard conditions to the dialkylmagnesiums **86e** and **86f** which afforded after addition of furfural the corresponding alcohols **87k** and **87l** in 80-86% yield. 2-(4-Fluorophenyl)ethyl iodide (**85g**)[85] furnished after I/Mg-exchange, transmetalation with CuCN·2LiCl and acylation with 3-(chloromethyl)benzoyl chloride ketone **87m** in 72% yield. Silyl-substituted iodides such as 6-*tert*-butyldimethylsilyloxychlorohexane (**85h**)[85] gave after I/Mg-exchange the corresponding dialkylmagnesium **86h** which was added to a functionalized benzaldehyde leading to alcohol **87n** in 77% yield. Heterocyclic iodides such as 3-(2-iodoethyl)thiophene (**85i**)[85] underwent cleanly the I/Mg-exchange with *s*Bu_2Mg and after transmetalation and acylation with 4-chlorobutyroyl chloride or 3-fluorobenzoyl chloride gave the ketones **87o-p** in 81-85% yield.

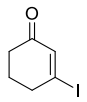
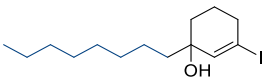
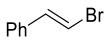
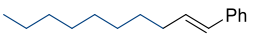
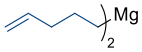
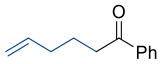
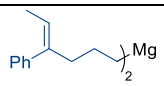
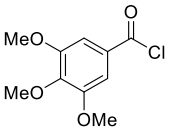
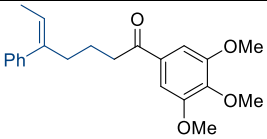
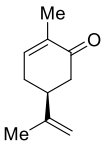
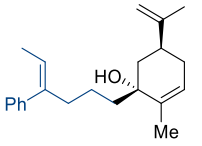
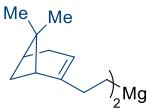
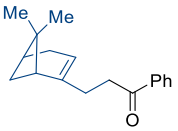
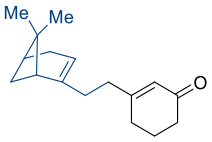
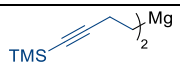
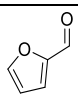
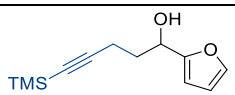
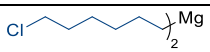
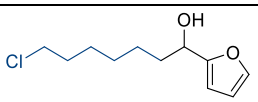
Table 5. Preparation of various primary dialkylmagnesiums (**86a-86i**) from the corresponding iodides (**85a-85i**) using *s*Bu_2Mg in toluene and quenching with various electrophiles leading to products **87b-87p**.

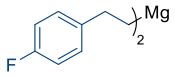
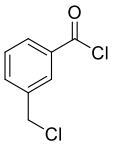
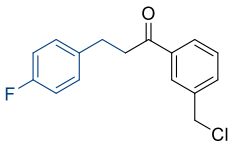
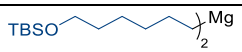
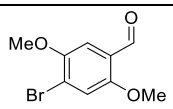
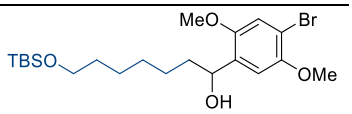
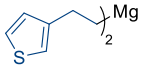
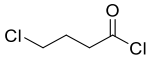
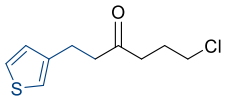
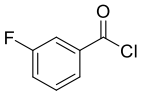
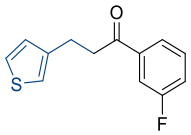


85a-i **86a-i** **87b-p**[a]

R_2Mg	electrophile	product, yield
Oct_2Mg **86a**		 **87b**, 86%
86a		 **87c**, 70%

[87] S. E. Denmark, J. Y. Choi, D. Wehrli, Z. Wu, L. Neuville, W. Pan, R. F. Sweis, Z. Wang, S.-M. Yang (University of Illinois), US 6867323, **2005**.
[88] a) T. P. Truong, S. J. Bailey, A. E. Golliher, E. Y. Monroy, U. K. Shrestha, W. A. Maio, *J. Chem. Educ.* **2018**, *95*, 438-444; b) A. A. Verstegen-Haaksma, H. J. Swarts, B. J. M. Jansen, A. De Groot, *Tetrahedron* **1994**, *50*, 10073-10082.
[89] P. Knochel, N. Millot, A. Rodriguez, C. E. Tucker in *Organic Reactions, Vol. 58* (Ed.: L. E. Overman), Wiley, New York, **2001**, pp. 417-731.

R_2Mg	electrophile	product, yield
86a		 **87d,** 50%
86a		 **87e,** 71%, *E/Z* = 99:1
 **86b**		 **87f**, 75%
 **86c**		 **87g**, 79%, *Z/E* = 99:1
86c		 **87h**, 54%, *Z/E* = 99:1 dr = 95:5
 **86d**		 **87i**, 82%[b]
		 **87j**, 84%
 **86e**		 **87k**, 80%
 **86f**		 **87l**, 86%

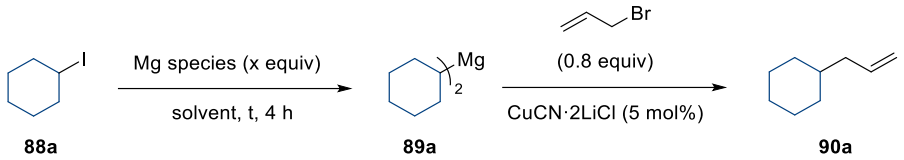
R_2Mg	electrophile	product, yield
 **86g**		 **87m**, 72%
 **86h**		 **87n**, 77%
 **86i**		 **87o**, 85%
86i		 **87p**, 81%

[a] Isolated yield of analytically pure products. [b] This experiment was performed on 5 mmol scale.

2.4 Preparation of Secondary Substituted Dicyclohexylmagnesiums by A Radical I/Mg-exchange Reaction Using *s*Bu_2Mg in Toluene

Then we turned our attention to secondary alkyl iodides and chose cyclohexyl iodide (**88a**) as a model substrate (Table 6). A treatment of **88a** with different exchange reagents as *i*PrMgCl·LiCl and *n*Bu_2Mg gave moderate yields (entry 1-2). Performing exchange reaction in THF led to only 5% GC-yield (entry 3). In contrast, in toluene in 4 hours 44% GC-yield was observed (entry 4). In contrast to primary alkyl iodides, no heating was required (entry 5). Different amounts of *s*Bu_2Mg were tested (entries 6-7). We have found again that the best exchange was obtained at 25 °C in toluene using *s*Bu_2Mg (0.6 equiv) affording dicyclohexylmagnesium (**89a**) after only 2 h reaction time in 42% GC-yield (entry 8). Quenching with allyl bromide gave 2-propenyl cyclohexane **90a** in 48% isolated yield.

Table 6. Optimization of the reaction of cyclohexyl iodide (**88a**) with *s*Bu_2Mg leading after allylation to 2-propenyl cyclohexane (**90a**).



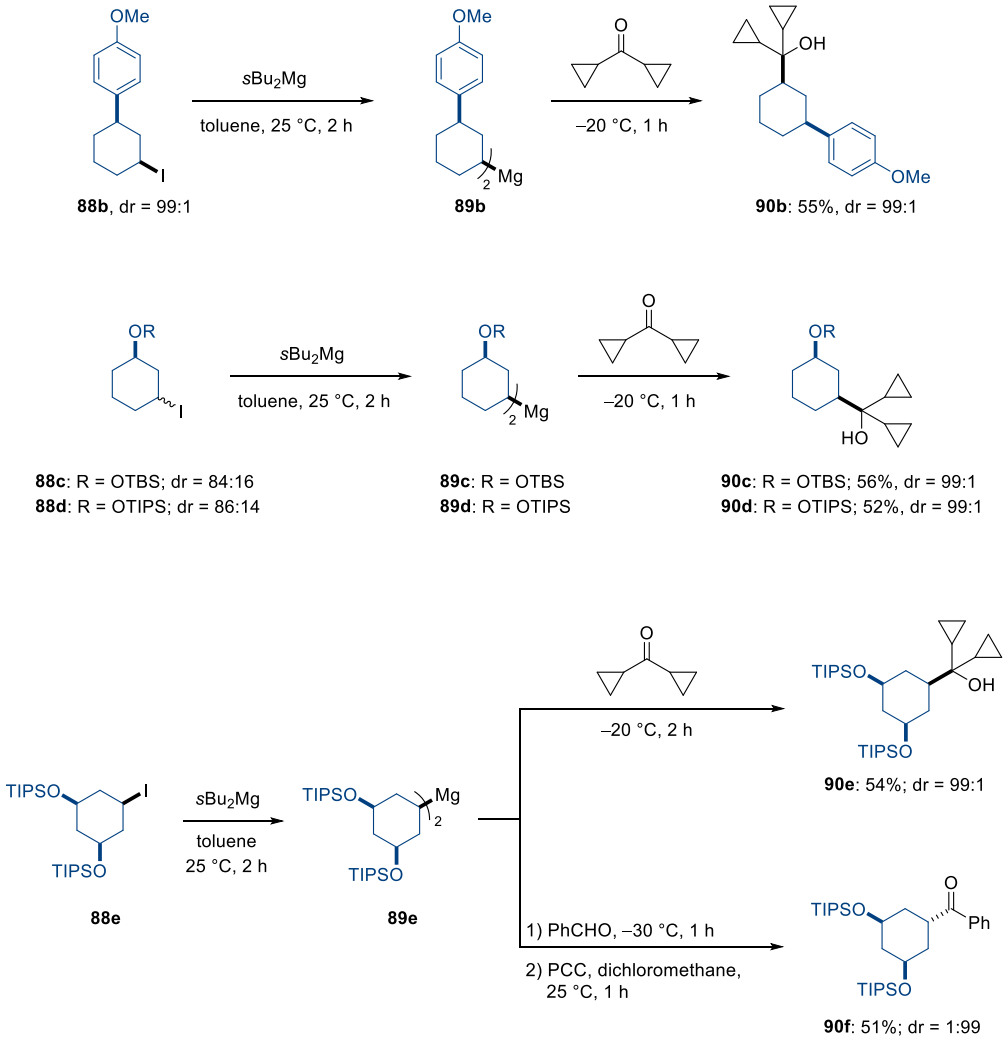
88a **89a** **90a**

entry	Mg species	equiv of Mg species	solvent	t [°C]	yield of **90a** [%][a]
1	*i*PrMgCl·LiCl	1.2	THF	25	26
2	*n*Bu_2Mg	0.6	toluene	25	32
3	*s*Bu_2Mg[b]	0.6	THF	25	5
4	*s*Bu_2Mg	0.6	toluene	25	44
5	*s*Bu_2Mg	0.6	toluene	40	39
6	*s*Bu_2Mg	0.7	toluene	25	42
7	*s*Bu_2Mg	1.2	toluene	25	traces
8	*s*Bu_2Mg	0.6	toluene	25	42[c] (48)[d]

[a] Reactions were performed on a 0.5 mmol scale. Yields were determined by GC-analysis using undecane ($C_{11}H_{24}$) as an internal standard. [b] Relevant formula is *s*$Bu_2Mg·0.5Et_2O$. [c] Exchange reaction time was 2 h. [d] Isolated yield of analytically pure compound.

Although a higher conversion could not be reached, these promising results led us to examine some substituted iodocyclohexane derivatives such as **88b**-**88e**. Although, we realize that this radical reaction may result in an absolute stereochemistry loss of the carbon-iodine bond, a good relative stereoselectivity may still be reached in favourable equilibration processes. Therefore, we have chosen the secondary alkyl iodides **88b-88e** bearing a bulky substituent in position 3.[90] These cyclohexyl iodides used as *cis-trans* mixtures reacted with *s*Bu_2Mg (0.6 equiv) at 25 °C within 2 h and provided the corresponding dicyclohexylmagnesium species **89b**-**89e** (optimum conversion of 75%) tentatively written as *cis*-isomers. Accordingly, quenching reactions of **89b**-**89e** with dicyclopropyl ketone provided only the diastereomerically pure *cis*-tertiary alcohols **90b**-**90e** in 52-56% yield showing that the exchange reaction proceeded in a stereoconvergent way (Scheme 30). In the case of the TIPSO-substituted dicyclohexylmagnesium **89e**, quenching with benzaldehyde followed by PCC-oxidation (PCC = pyridinium chlorochromate)[91] led to an epimerization and provided the diastereomerically pure *trans*-ketone **90f** in 51% yield (dr = 1:99).

[90] In contrast to the previously reported I/Li-exchange which is not a radical reaction, this new radical exchange does not allow an absolute stereocontrol but relies on favourable equilibration processes producing the most stable diastereoisomer. See: A. Kremsmair, H. R. Wilke, M. M. Simon, Q. Schmidt, K. Karaghiosoff, P. Knochel, *Chem. Sci.* **2022**, *13*, 44-49.
[91] G. Piancatelli, A. Scettri, M. D'Auria, *Synthesis* **1982**, 245-258.



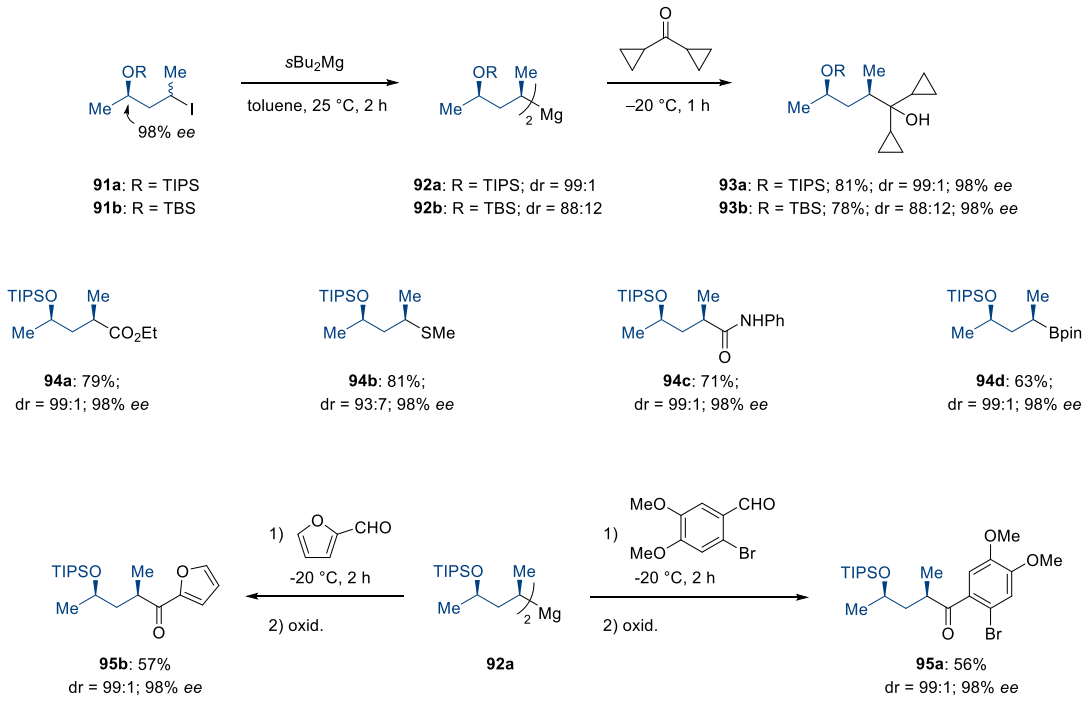
Scheme 30. Stereoconvergent I/Mg-exchange on cyclohexyl iodides **88b**-**88e** leading to dialkylmagnesium reagents **89b**-**89e** and subsequent addition to dicyclopropyl ketone providing the diastereomerically pure *cis*-alcohols **90b**-**90e** and the *trans*-ketone **90f**.

2.5 Preparation of Chiral Secondary Dialkylmagnesiums by A Radical I/Mg-exchange Reaction Using *s*Bu$_2$Mg in Toluene

With these results in hand, we turned our attention to silylated oxygenated derivatives of commercially available optically enriched (*R*,*R*)-pentanediol (98% *ee*).[92] We anticipated that the presence of a closely located silyl-ether function would improve the conversion of these I/Mg-exchanges. Thus, epimeric mixtures of iodides **91a** or **91b** were submitted to the usual I/Mg-exchange protocol using *s*Bu$_2$Mg (0.6 equiv) in toluene (25 °C, 2 h). As expected a stereoconvergent I/Mg-exchange[79] provided diastereomerically enriched

[92] a) 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; *Angew. Chem.* **2015**, *127*, 2793-2796; b) V. Morozova, J. Skotnitzki, K. Moriya, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 5516-5519; *Angew. Chem.* **2018**, *130*, 5614-5617.

Grignard reagents **92a** and **92b** as shown by subsequent quenching reactions with dicyclopropyl ketone affording the tertiary alcohol **93a** (dr = 99:1) and **93b** (dr = 88:12). These results indicated that the stereoconvergence of the Grignard formation **92** is highest with the TIPS-protected substrate (**91a**). Thus, we have treated **92a** with various electrophiles such as ethyl cyanoformate, *S*-methyl benzenethiosulfonate, phenyl isocyanate and methyl pinacolyl borate leading to the corresponding products **94a**-**94d** with high enantiomeric and diastereomeric purity (98% *ee* and dr up to 99:1; Scheme 31).



Scheme 31. Preparation of enantiomerically and diastereomerically enriched dialkylmagnesium reagents **92a** and **92b** followed by trapping with various electrophiles.

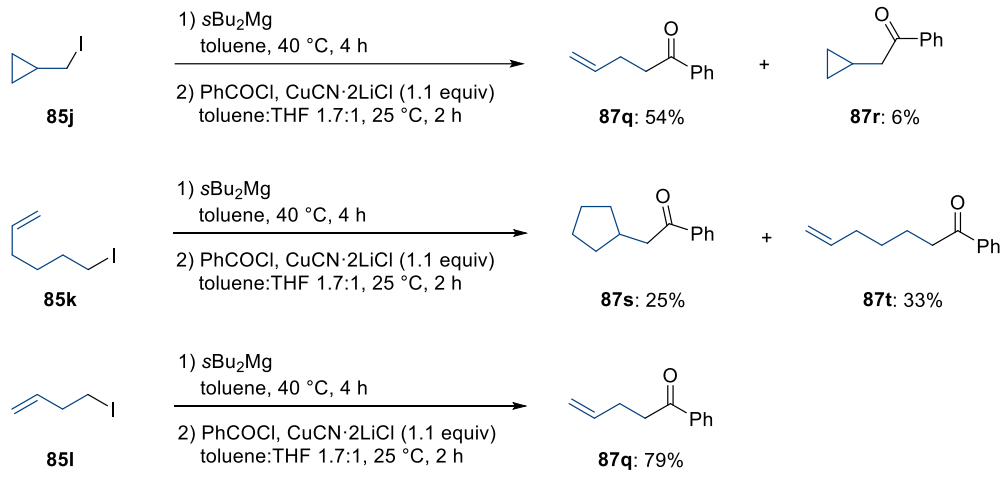
The relative stereochemistry of products of type **94** was confirmed by treating **94a** with CF_3SO_3H in dichloromethane, 25 °C, 2 h affording the corresponding *trans*-2,4-dimethylbutyrolactone in 79% yield.[79,85] Additionally, we have reacted **92a** with 3,4-dimethoxybenzaldehyde or furfural (−20 °C, 2 h) producing intermediate alcohols which were oxidized using the Dess-Martin periodinane[93] affording the valuable homo-aldol products **95a** and **95b** in 56-57% overall yields (dr = 99:1; 98% *ee*).

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

2.6 Mechanistic Probes

2.6.1 Radical clocks

Preliminary mechanistic studies were undertaken to demonstrate the radical nature of this I/Mg-exchange. Thus, the treatment of radical clock probes[94] such as alkyl iodides **85j**, **85k** and **85l** provided evidence of a radical pathway, since cyclopropylmethyl iodide **85j** gave, after quenching with PhCOCl, mostly the open-chain product **87q** with less than 10% of the non-rearranged ketone **87r**. On another hand, treatment of 5-hexenyl iodide (**85k**) under the I/Mg-exchange conditions afforded after benzoylation a significant amount of ring closure product cyclopentylmethyl phenyl ketone (**87s**) as well as open-chain product **87t**. As expected 3-butenyl iodide (**85l**) furnished under the same conditions only the open-chain ketone **87q** in 79% yield (Scheme 32).



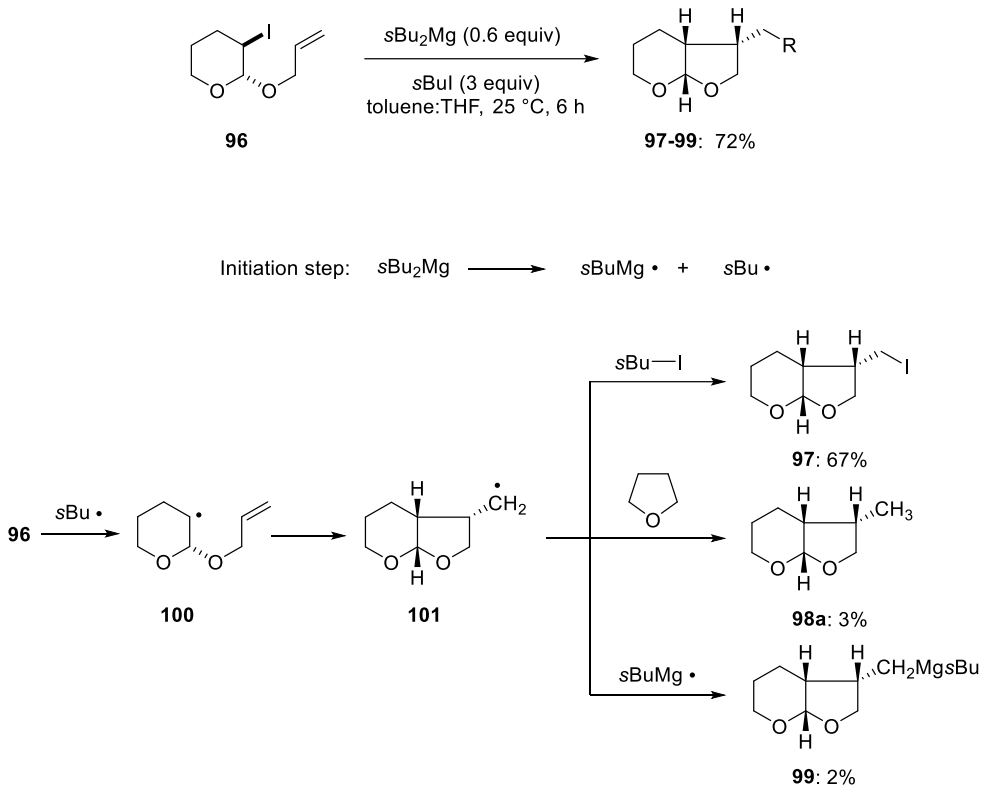
Scheme 32. Radical clock experiments using alkyl iodides **85j**, **85k** and **85l** for I/Mg-exchanges and subsequent benzoylations.

2.6.2 An Atom-Transfer Cyclization of the Cyclic Iodo-Acetale 96

The cyclic iodo-acetal **96**[95] was subjected to the I/Mg-exchange under various conditions. We have observed the formation of products **97**, **98a** and **99** in various proportions[85] but could optimize the reaction to produce the cyclic iodide **97** in 67% yield (dr = 95:5) by using commercial *n*Bu_2Mg or *s*Bu_2Mg in THF in the presence of *s*BuI (3 equiv). Interestingly, the addition of styrene inhibited the reaction completely showing the radical character of this reaction.[85] This cyclization may be rationalized by an atom-transfer

[94] M. Newcomb in *Encyclopedia of Radicals in Chemistry, Biology and Materials, Vol. 1* (Eds.: C. Chatgilialoglu, A. Studer), Wiley-Interscience, Hoboken, **2012**, pp. 107-124.
[95] a) A. Inoue, H. Shinokubo, K. Oshima, *Org. Lett.* **2000**, *2*, 651-653; b) J. L. Kuo, C. Lorenc, J. M. Abuyuan, J. R. Norton, *J. Am. Chem. Soc.* **2018**, *140*, 4512-4516.

mechanism[96] (Scheme 33). Thus, we assumed that the initiation step was a homolytic cleavage of *s*Bu_2Mg,[72b] followed by a radical chain reaction induced by a *s*-butyl radical producing the radical **100** from the iodide **96**. After cyclization, the new radical **101** was produced and trapped by *s*BuI affording the major product **97** in 67% yield. Reaction of **101** with THF gave the bicyclic acetal **98a**. Recombination of **101** with the *s*BuMg radical will provide **99**, which was detected in 2% yield. These observations supported an atom-transfer mechanism for the I/Mg-exchange.



Scheme 33. Atom-transfer cyclization of **96** triggered by *s*Bu_2Mg providing selectively the bicyclic iodide **97**.

[96] a) D. P. Curran, *Synthesis* **1988**, 489-513; b) A. Studer, D. P. Curran, *Angew. Chem. Int. Ed.* **2016**, *55,* 58-102; *Angew. Chem.* **2015**, *128*, 58-106.

3 Iron-Catalyzed Radical Zincations of Alkyl Iodides

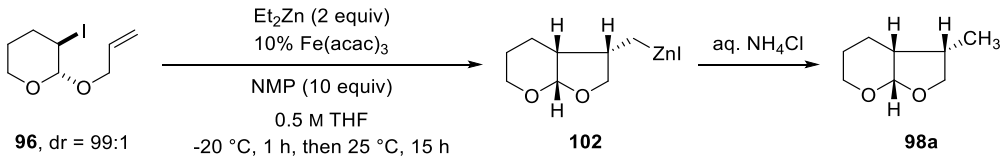
The halogen-metal exchange is an important method for the preparation of organometallic reagents.[78,97] The rate of such an exchange reaction strongly depends on the nature of the metal. The more electropositive, the faster is the exchange reaction[98] demonstrated by the I/Li-exchange as one of the fastest reactions in organic synthesis.[99] However, the I/Mg-exchange, in comparison, is usually much slower[100] and the I/Zn-exchange even requires polar solvents[101] or tailored organozinc exchange reagents such as the zincate *s*$Bu_2Zn \cdot 2LiOR$.[50] Also, I/Zn-exchange reactions under transition metal catalysis were reported.[102] Thus, Pd(II) and Ni(II) salts proved to catalyze the I/Zn-exchange under mild conditions.[105] In the search of a less expensive catalyst, we have examined an iron-catalyzed reaction.[103] Indeed, iron salts were reported to catalyze a range of radical cyclizations,[106,104] using organomagnesium[105] or organozinc reagents followed by various cross-couplings.[106] Furthermore, Bertrand has described a non-transition metal catalyzed generation of radicals from alkyl iodides promoted by air.[107] Herein, we wish to report a new iron-catalyzed I/Zn-exchange reaction allowing the

[97] a) 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; *Angew. Chem.* **2003**, *115*, 4438-4456; b) A. Kremsmair, J. H. Harenberg, K. Schwärzer, A. Hess, P. Knochel, *Chem. Sci.* **2021**, *12*, 6011-6019; c) B. Wei, P. Knochel, *Synthesis* **2022**, *54*, 246-254.
[98] a) A. Krasovskiy, B. F. Straub, P. Knochel, *Angew. Chem. Int. Ed.*, **2006**, *45*, 159-162; *Angew. Chem.* **2005**, *118*, 165-169; b) A. D. Benischke, L. Anthore-Dalion, G. Berionni, P. Knochel, *Angew. Chem. Int. Ed.* **2017**, *56*, 16390-16394; *Angew. Chem.* **2017**, *129*, 16608-16612; c) A. D. Benischke, L. Anthore-Dalion, F. Kohl, P. Knochel, *Chem. Eur. J.* **2018**, *24*, 11103-11109; d) L. Anthore-Dalion, A. D. Benischke, B. Wei, G. Berionni, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58,* 4046-4050; *Angew. Chem.* **2019**, *131*, 4086-4090; e) J. H. Harenberg, N. Weidmann, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2021**, *60*, 731-735; *Angew. Chem.* **2021**, *133*, 742-746.
[99] W. F. Bailey, J. J. Patricia, T. T. Nurmi, W. Wang, *Tetrahedron Lett.* **1986**, *27*, 1861-1864.
[100] a) L. Shi, Y. Chu, P. Knochel, H. Mayr, *Angew. Chem. Int. Ed.* **2008**, *47*, 202-204; *Angew. Chem.* **2007**, *120*, 208-210; b) L. Shi,Y. Chu, P. Knochel, H. Mayr, *Org. Lett.* **2009**, *11*, 3502-3505; c) L. Shi, Y. Chu, P. Knochel, H. Mayr, *Org. Lett.* **2012**, *14*, 2602-2605.
[101] F. F. Kneisel, M. Dochnahl, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 1017-1021; *Angew. Chem.* **2004**, *116*, 1032-1036.
[102] a) H. Stadtmüller, R. Lentz, C. E. Tucker, T. Stüdemann, W. Dörner, P. Knochel, *J. Am. Chem. Soc.* **1993**, *115*, 7027-7028; b) H. Stadtmüller, A. Vaupel, C. E. Tucker, T. Stüdemann, P. Knochel, *Chem. Eur. J.* **1996**, *2*, 1204-1220; c) A. Vaupel, P. Knochel, *J. Org. Chem.* **1996**, *61*, 5743-5753.
[103] a) G. Cahiez, H. Avedissian, *Synthesis* **1998**, *1998*, 1199-1205; b) C. Bolm, J. Legros, J. Le Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217-6254; c) F. Vallée, J. J. Mousseau, A. B. Charette, *J. Am. Chem. Soc.* **2010**, *132*, 1514-1516; d) *Iron catalysis. Fundamentals and Applications*, B. Plietker (Ed.), Springer, Heidelberg, **2011**; e) *The Chemistry of Organoiron Compounds*, I. Marek, Z. Rappoport (Eds.), Wiley, Chichester, **2014**; f) G. Cahiez, A. Moyeux, J. Cossy, *Adv. Synth. Catal.* **2015**, *357*, 1983-1989; g) R. B. Bedford, *Acc. Chem. Res.* **2015**, *48*, 1485-1493; h) I. Bauer, H.-J. Knölker, *Chem. Rev.* **2015**, *115*, 3170-3387; i) A. Fürstner, *ACS Cent. Sci.* **2016**, *2*, 778-789; j) G. Pototschnig, N. Maulide, M. Schnürch, *Chem. Eur. J.* **2017**, *23*, 9206-9232.
[104] a) J. Y. Hwang, J. H. Baek, T. I. Shin, J. H. Shin, J. W. Oh, K. P. Kim, Y. You, E. J. Kang, *Org. Lett.* **2016**, *18*, 4900-4903; b) S. H. Kyne, M. Clémancey, G. Blondin, E. Derat, L. Fensterbank, A. Jutand, G. Lefèvre, C. Ollivier, *Organometallics* **2018**, *37*, 761-771; c) F. T. Pulikottil, R. Pilli, V. Murugesan, C. G. Krishnan, R. Rasappan, *ChemCatChem* **2019**, *11*, 2438-2442.
[105] a) Y. Hayashi, H. Shinokubo, K. Oshima, *Tetrahedron Lett.* **1998**, *39*, 63-66; b) J. G. Kim, Y. H. Son, J. W. Seo, E. J. Kang, *Eur. J. Org. Chem.* **2015**, 1781-1789.
[106] T. Hatakeyama, Y. Kondo, Y.-i. Fujiwara, H. Takaya, S. Ito, E. Nakamura, M. Nakamura, *Chem. Commun.* **2009**, 1216-1218.
[107] a) J. Maury, D. Mouysset, L. Feray, S. R. A. Marque, D. Siri, M. P. Bertrand, *Chem. Eur. J.* **2012**, *18*, 3241-3247; b) J. Maury, S. Jammi, F. Vibert, S. R. A. Marque, D. Siri, L. Feray, M. Betrand, *J. Org. Chem.* **2012**, *77*, 9081-9086; c) S. Jammi, D. Mouysset, D. Siri, M. P. Bertrand, L. Feray, *J. Org. Chem.* **2013**, *78*, 1589-1603; d) K. Aikawa, Y. Nakamura, Y. Yokota, W. Toya, K. Mikami, *Chem. Eur. J.* **2015**, *21*, 96-100; e) H. Kato, K. Hirano, D. Kurauchi, N. Toriumi, M. Uchiyama, *Chem. Eur. J.* **2015**, *21*, 3895-3900.

preparation of various alkylzinc organometallics from the corresponding alkyl iodides under mild conditions.

Thus, we have initiated our studies with the cyclic iodohydrin **96**.[104c] Treatment of iodide **96** with a 1 M solution of diethylzinc in toluene in the presence of catalytic amounts of $Fe(acac)_3$ and *N*-methylpyrrolidone (NMP; 10 equiv) in THF at −20 °C for 1 h and subsequent aging of the mixture for 15 h at 25 °C provided the bicyclic alkylzinc iodide **102**. After aqueous work-up, the bicyclic acetal **98a** was obtained in 80% isolated yield and high diastereoselectivity (dr = 95:5; entry 1 of Table 1). In the absence of iron salts, a low GC-yield of 18% with a decreased dr of 90:10 was obtained (entry 2). Furthermore, using $FeCl_3 \cdot 6H_2O$ as an iron source gave only 5% yield of **96** (entry 3). Lowering the amount of catalyst to 2% $Fe(acac)_3$ led to 60% GC-yield of **96** (entry 4). Exchanging NMP for *N*, *N'*-dimethylpropyleneurea (DMPU) decreased the GC-yield of **96** to 54% (entry 5). When acetonitrile was used as a solvent, 39% of acetal **96** was obtained (dr = 92:8; entry 6).[108] Notably, performing the zincation at 25 °C resulted in 75% GC-yield but lower diastereoselectivity (dr = 92:8; entry 7).

Table 7. Optimization of the reaction conditions for the iron-catalyzed radical zincation of cyclic iodohydrin **96** leading to the bicyclic acetal **98a**.



96, dr = 99:1 **102** **98a**

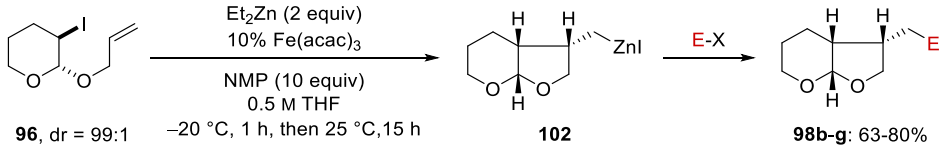
entry	deviation from standard conditions	GC-yield of **98a** (%)[a]	dr (**98a**)[a]
1	None	80[b]	95:5
2	No $Fe(acac)_3$	18	90:10
3	10% $FeCl_3 \cdot 6H_2O$	5	-
4	2% $Fe(acac)_3$	60	95:5
5	DMPU instead of NMP as additive	54	95:5
6	MeCN instead of THF	39	92:8
7	Performing reaction at 25 °C	75	92:8

[a] The reactions were performed on 0.5 mmol scale. Yields and dr (diastereomeric ratio) were determined by GC-analysis using $C_{11}H_{24}$ as internal standard. [b] Isolated yield of analytically pure products.

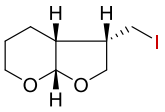
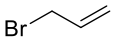
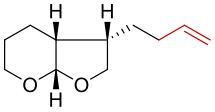
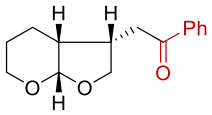
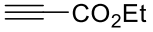
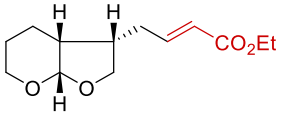
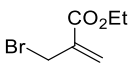
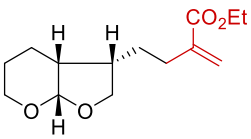
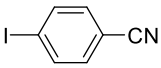
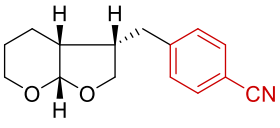
[108] a) H. Fillon, C. Gosmini, J. Périchon, *J. Am. Chem. Soc.* **2003**, *125*, 3867-3870; b) I. Kazmierski, C. Gosmini, J. M. Paris, J. Périchon, *Tetrahedron Lett.* **2003**, *44*, 6417-6420; c) J.-M. Bégouin, C. Gosmini, *J. Org. Chem.* **2009**, *74*, 3221-3224.

With these optimized conditions in hand, we have treated the zinc reagent **102** with various electrophiles (Table 8). Thus, iodolysis of **102** furnished the corresponding cyclic iodide **98b** in 79% isolated yield and dr = 95:5. Transmetalation of **102** using CuCN·2LiCl (as 1 M solution in THF; 1 equiv) and further reaction with benzoyl chloride (3 equiv, −40 °C, 3 h) gave the ketone **98c** in 76% yield (dr = 95:5). Allylation of **102** with ethyl (2-bromomethyl)acrylate or allyl bromide (2.1-3.0 equiv, −20 °C, 2 h) in the presence of 5 mol% CuCN·2LiCl furnished the corresponding allylated products **98d-e** in 72-80% (dr = 95:5). Trapping of **102**, after transmetalation with CuCN·2LiCl (1.0 equiv), with ethyl propiolate led to ester derivative **98f** in 63% yield (*E*/*Z* = 99:1; dr = 94:6). Furthermore, Pd-catalyzed cross-coupling (5% $Pd(OAc)_2$, 10% CPhos)[109] with 4-iodobenzonitrile (25 °C, 16 h) gave the arylated acetal **98g** in 75% yield (dr = 95:5).

Table 8. Products of type **98**, obtained after iron-catalyzed I/Zn-exchange of **96** followed by trapping reactions with electrophiles.



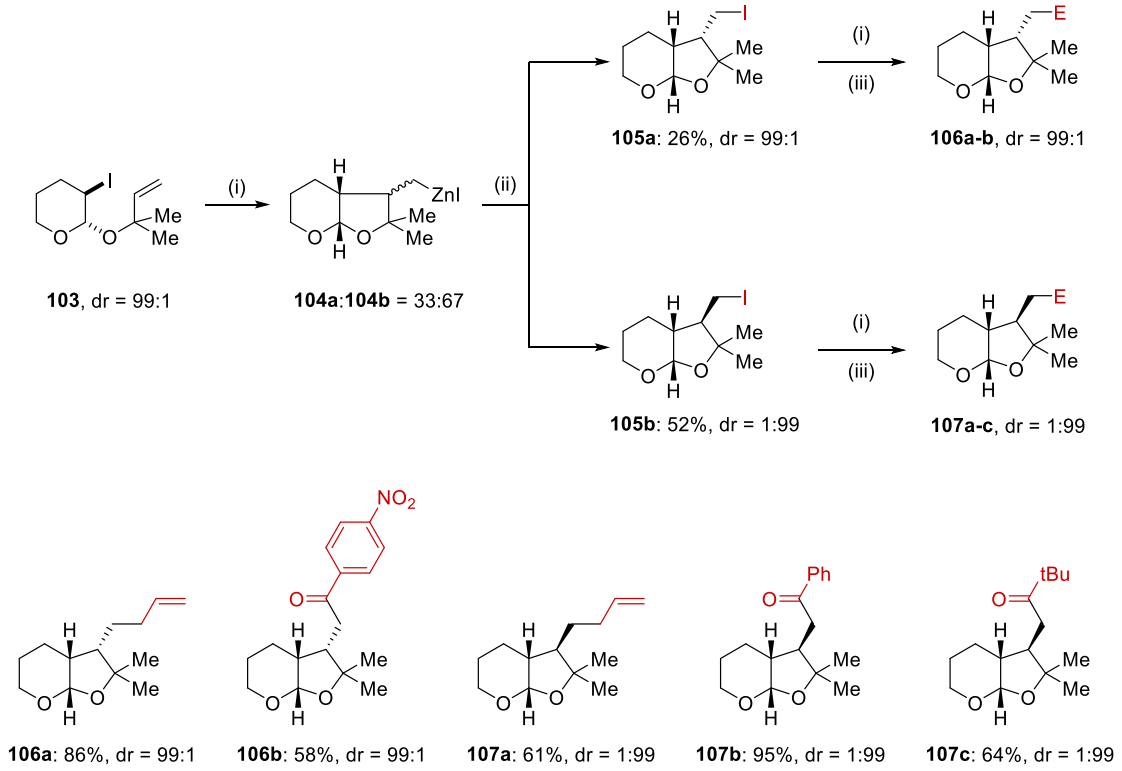
96, dr = 99:1 — **102** — **98b-g**: 63-80%

electrophile	product of type **98**, yield[a]	electrophile	product of type **98**, yield[a]
I_2	 **98b**: 79%, dr = 95:5		 **98e**: 72%, dr = 95:5[c]
PhCOCl	 **98c**: 76%, dr = 95:5[b]		 **98f**: 63%, *E*/*Z* = 99:1, dr = 94:6[b]
	 **98d**: 80%, dr = 95:5[c]		 **98g**: 75%, dr = 95:5[d]

Reaction conditions: [a] isolated yield of analytically pure products; [b] CuCN·2LiCl (1.0 equiv), electrophile (3.0 equiv), −40 °C to 25 °C, 2 h; [c] allyl bromide (2.1-3.0 equiv), CuCN·2LiCl (5 mol%), −20 °C to 25 °C, 2 h; [d] 5% $Pd(OAc)_2$, 10% CPhos, 25 °C, 16 h.

[109] C. Han, S. L. Buchwald, *J. Am. Chem. Soc.* **2009**, *131*, 7532-7533.

Similarly, the sterically hindered dimethyl-substituted iodooxanyl acetal **103**[107a] underwent the iron-catalyzed zincation at 50 °C giving the diastereomeric zinc species *syn*-**104a** and *anti*-**104b**. Iodolysis gave two separable diastereomers *syn*-**105a** (26%) and *anti*-**105b** (52%) after column chromatographical purification (Scheme 34).



Scheme 34. Diastereomerically enriched products **106a-b** and **107a-c** obtained after an iron-catalyzed zincation of **103** followed by different trapping reactions. Reaction conditions: (i) Et_2Zn (2 equiv), 10% $Fe(acac)_3$, NMP (10 equiv), THF, 50 °C, 8 h. (ii) I_2, 25 °C, 1 h, separation of diastereomers. (iii) Electrophile (3 equiv).

The relative stereochemistry of *syn*-**105a** and *anti*-**105b** was proved by NOE-NMR and X-Ray analyses[110,111] (Figure 1). Subsequent Fe-catalyzed iodine-zinc exchange reaction of *syn*-**105a** and *anti*-**105b** under the same conditions, followed by various trapping reactions led to functionalized dimethyltetrahydrofurans **106a-b** and **107a-c**. Thus, allylation of **104a** or **104b** with allyl bromide in the presence of 5 mol% of CuCN·2LiCl gave alkenes **106a** and **107a** in 61-86% yield (dr = 99:1). Transmetalation of **104a** or **104b** with stoichiometric amounts of CuCN·2LiCl followed by the addition of benzoyl chloride, *tert*-butylacetyl chloride or 4-nitrobenzoyl chloride gave the ketones **106b** and **107b-c** in 58-95% yield (dr = 99:1).

[110] See Experimental Part.
[111] CCDC-2201809 (*anti*-**105b**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/structures.

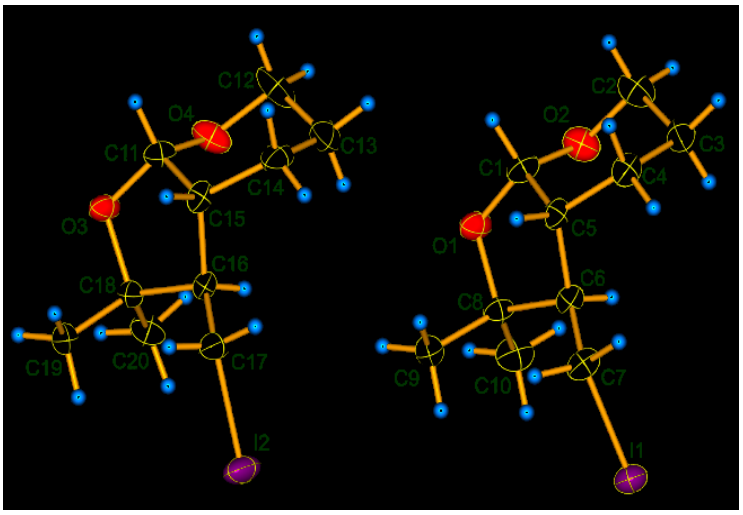
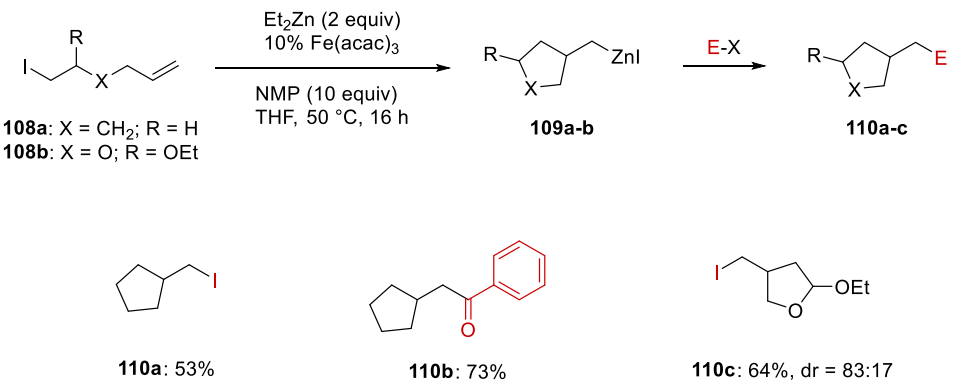


Figure 1. Molecular structure of the alkyl iodide *anti*-**105b** in the crystal. View of the two crystallographically independent molecules.[112,113]

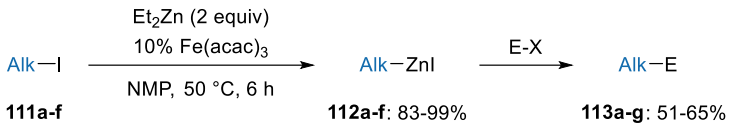
We have extended this I/Zn-exchange to alkenyl iodides **108a** and **108b**[102c] (Scheme 35). Thus, 6-iodohex-1-ene (**108a**) underwent the I/Zn-exchange at 50 °C instead of −20 °C in the case of the diastereoselective ring closure (Table 7 and Scheme 34) leading to the corresponding zinc species **109a** which after iodolysis afforded cyclopentylmethyl iodide **110a** in 53% yield. These harsher conditions may be due to the generation of an intermediate primary alkyl radical which is less stable than a secondary alkyl radical. The copper-derivative of **109a** obtained by adding CuCN·2LiCl (as 1 M solution in THF; 1 equiv) was acylated with benzoyl chloride (3 equiv, −40 °C, 3 h) and gave ketone **110b** in 73% yield. Iodoacetal **108b** provided after an iron-catalyzed I/Zn-exchange the zinc species **109b** which after iodolysis furnished the iodide **110c** in 64% yield (dr = 83:17).

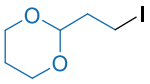
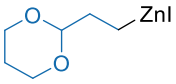
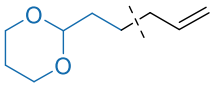
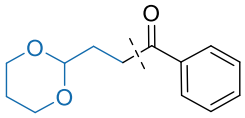
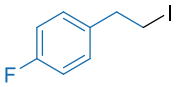
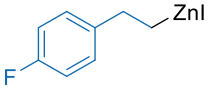
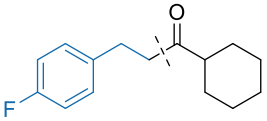
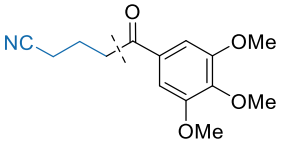
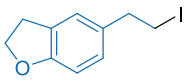
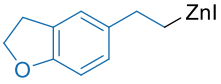
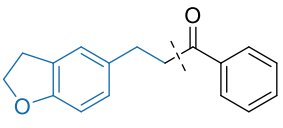


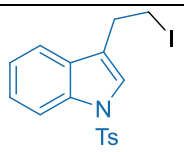
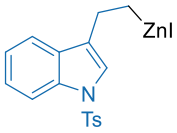
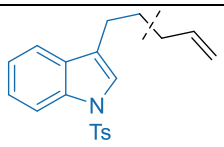
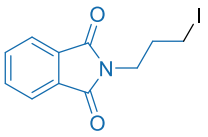
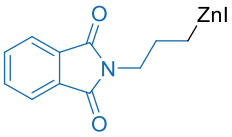
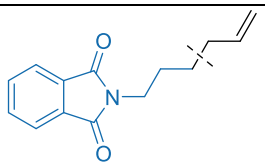
Scheme 35. Iron-catalyzed I/Zn-exchange of alkenyl iodides of type **108**.

Additionally, a range of functionalized primary alkyl iodides **111a-f** underwent an iron-catalyzed zincation within 6 h at 50 °C in NMP as solvent leading to alkylzinc iodides **112a-f** in 83-99% yield.[110] After various trapping reactions with typical electrophiles, we have obtained the expected products **113a-g** in 51-65% yield (Table 9). Thus, (2-(1,3-dioxan-2-yl)ethyl)zinc iodide **112a** was trapped with allyl bromide in the presence of 5 mol% of CuCN·2LiCl giving the allylated product **113a** in 55% yield. Acylation of copper derivatives of **112a-d**, obtained by addition of CuCN·2LiCl (1 M solution in THF; 1 equiv), with various acyl chlorides gave ketones **113b-e** in 51-62% yield. Interestingly, alkyl iodides containing heteroaryl moieties (**111e-f**) readily underwent the I/Zn-exchange and after allylations with allyl bromide in the presence of 5 mol% of CuCN·2LiCl gave the expected alkenes **113f-g** in 61-65% yield.

Table 9. Iron-catalyzed zincation of primary alkyl iodides (**111a-f**) followed by quenching reactions with electrophiles leading to products **113a-g**.

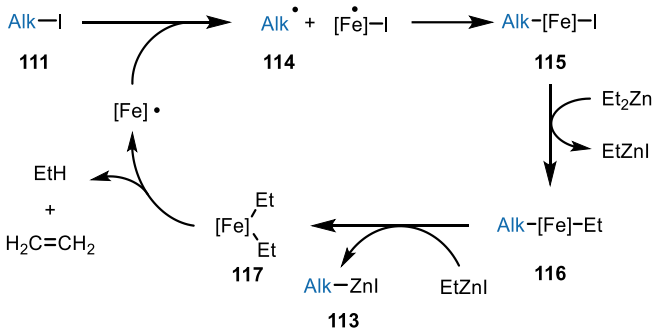


entry	alkyl iodide of type **111**	zinc reagents of type **112**	product of type **113**, yield[a]
1	 **111a**	 **112a**	 **113a**: 55%[b]
2	**111a**	**112a**	 **113b**: 54%[c]
3	 **111b**	 **112b**	 **113c**: 61%[c]
4	 **111c**	 **112c**	 **113d**: 51%[c]
5	 **111d**	 **112d**	 **113e**: 62%[c]

entry	alkyl iodide of type **111**	zinc reagents of type **112**	product of type **113**, yield[a]
6	 **111e**	 **112e**	 **113f**: 65%[b]
7	 **111f**	 **112f**	 **113g**: 61%[b]

Reaction conditions: [a] isolated yield of analytically pure products; [b] allyl bromide (1.5 equiv), CuCN·2LiCl (5 mol%), −20 °C to 25 °C, 2 h; [c] CuCN·2LiCl (1.0 equiv), acyl chlorides (1.2-3.0 equiv), −40 °C to 25 °C, 3 h.

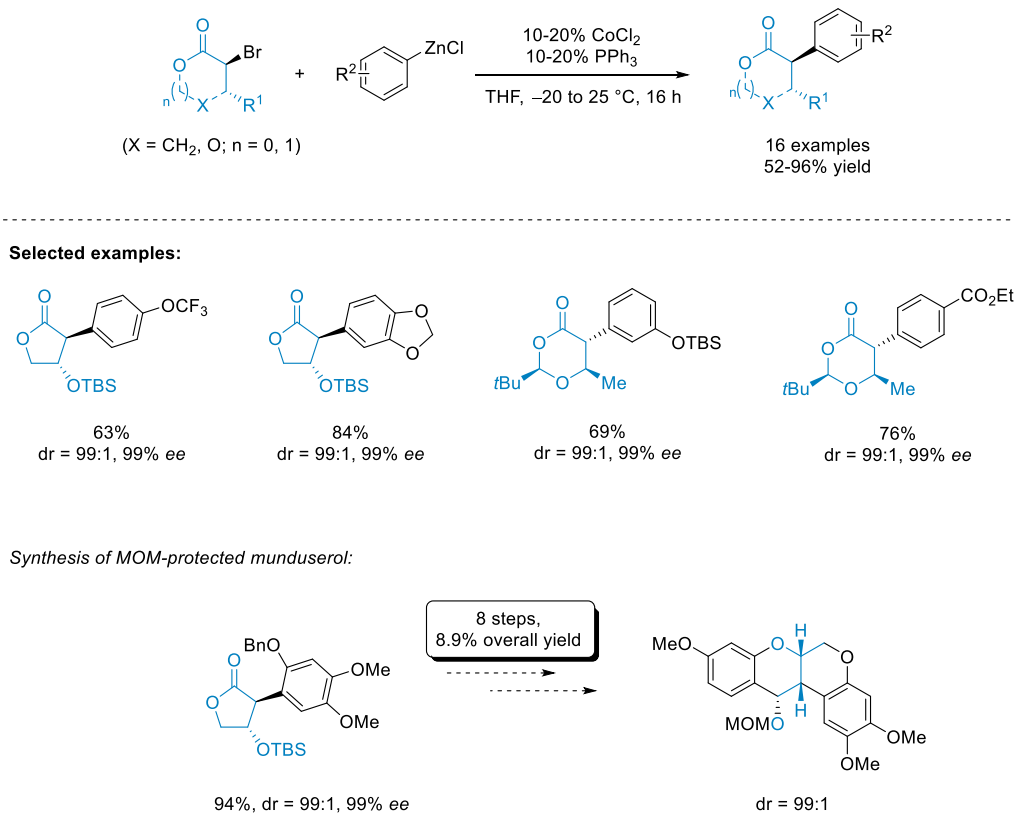
Although no detailed mechanistic studies have been performed, we propose the following mechanism in which the iron-catalyst converts the alkyl iodide **111** into an alkyl radical **114** which by recombination afforded alkyl-iron intermediate **115**. Subsequently, iron species **116** was produced *via* ligand exchange with Et_2Zn which after transmetalation generated the diethyl iron intermediate **117** (which decomposed to ethane and ethylene) and alkylzinc iodide **113** (Scheme 36).



Scheme 36. Tentative radical mechanism for the iron-catalyzed preparation of alkylzinc iodides (**113**) from alkyl iodides (**111**).

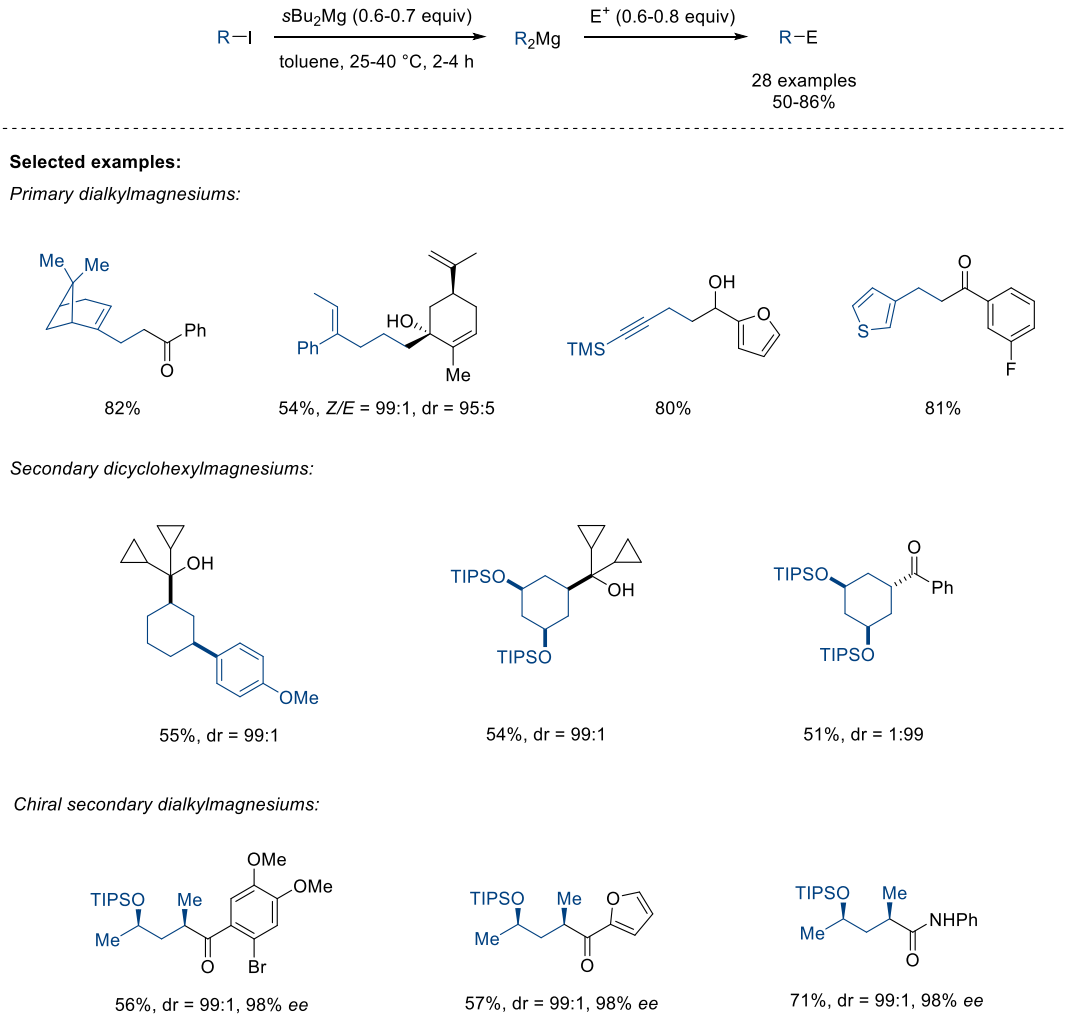
IV Summary

The first part of this thesis focused on the development of new cobalt-catalyzed reactions of functionalized arylzinc reagents. A highly *trans*-diastereoselective Co-catalyzed cross-coupling of arylzinc reagents with *α*-bromolactones bearing a substituent in the *β*-position was developed. *α*-Arylated butyrolactones and *α*-arylated protected *β*-hydroxyesters were obtained in the presence of 10-20% $CoCl_2$ and 10-20% PPh_3 in THF under mild conditions (25 °C, 16 h) in 52-96% yield (dr = 99:1, 99% *ee*). A stereoselective synthesis of an artificial rotenoid derivative MOM-protected munduserol was performed in 8.9% overall yield (dr = 99:1) (Scheme 37).



Scheme 37. Stereoselective cobalt-catalyzed cross-coupling reactions of arylzinc chlorides with *α*-bromolactones and related derivatives.

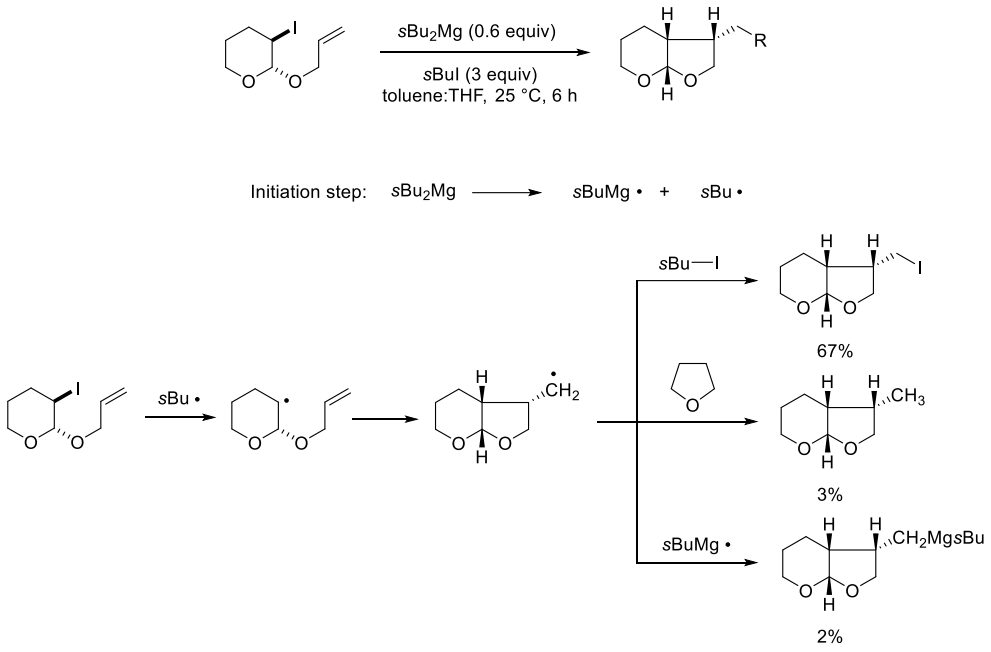
The second part of this thesis was devoted to a new preparation of various primary and secondary dialkylmagnesiums in toluene using *s*Bu_2Mg as an exchange reagent. This exchange reaction allows the preparation of various primary dialkylmagnesiums in toluene and is extended to several secondary cyclohexyl iodides providing the thermodynamically most favored Grignard reagents. The diastereomeric ratio of these I/Mg-exchanges on secondary iodides could be further improved by using secondary alkyl iodides bearing a TIPSO-group at the 3-position. Thus, chiral secondary dialkylmagnesiums are prepared from 3-substituted silyl ethers and gave after various quenching reactions with electrophiles, highly enantiomerically and diastereomerically enriched products (up to dr = 99:1 and 98% *ee*) (Scheme 38).



Scheme 38. Preparation of primary and secondary dialkylmagnesiums using *s*Bu_2Mg in toluene.

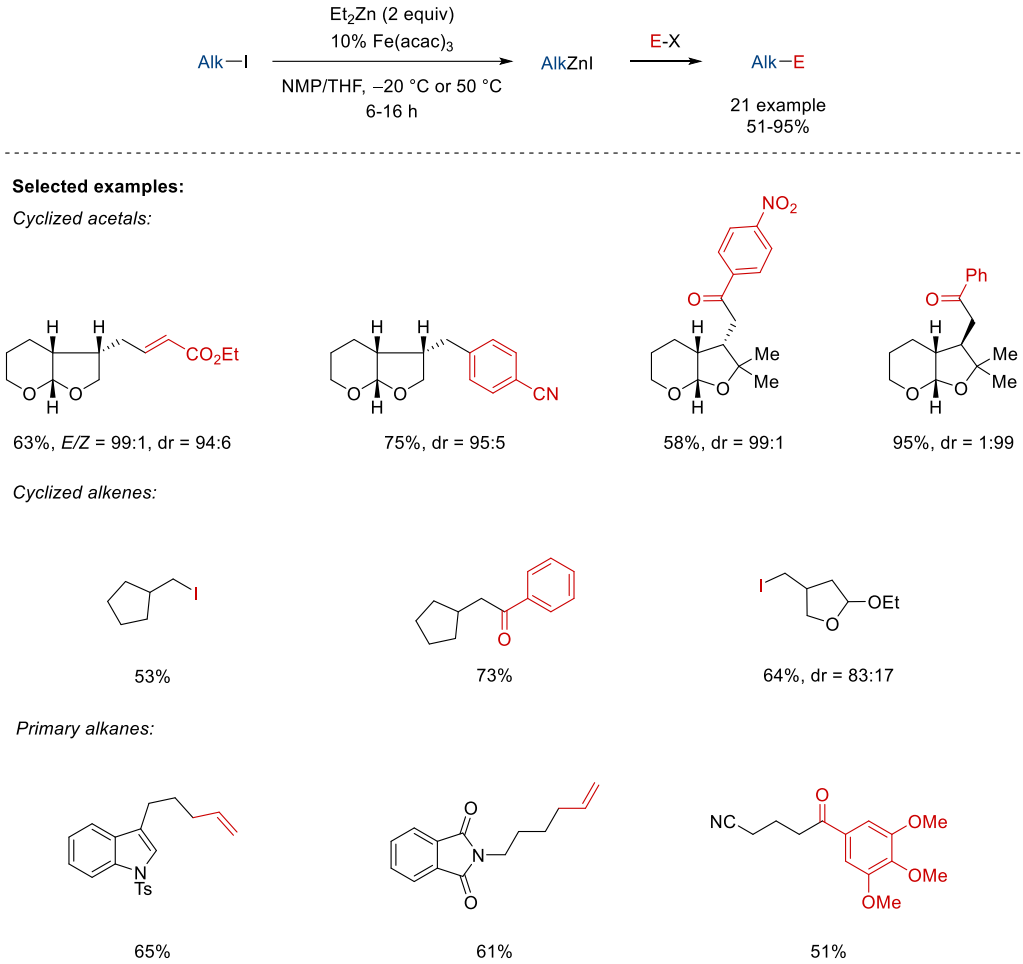
Mechanistic investigations using different radical clocks showed radical nature of the I/Mg-exchange reaction. *s*Bu_2Mg-mediated cyclization of the cyclic iodo-acetal gave

different products which brightly supports an atom-transfer mechanism. Using *s*BuI as an additive led to the cyclic iodide as a main product (Scheme 39).



Scheme 39. Atom-transfer cyclization of cyclic iodo-acetale triggered by *s*Bu_2Mg providing selectively the bicyclic iodide.

Also, a new practical iron-catalyzed I/Zn-exchange reaction allowing the conversion of primary and tailored secondary alkyl iodides to the corresponding alkylzinc reagents was developed. In the presence of a remote double bond at position 5, a highly diastereoselective cyclization took place. All the prepared organozinc reagents were trapped with allylic bromides, acid chlorides or aryl iodides in the presence of copper- or palladium catalysts (Scheme 40).



Scheme 40. Iron-catalyzed I/Zn-exchange of alkyl iodides.

V Experimental Part

1 General Information

All reactions were performed in flame dried glassware under argon with magnetic stirring under argon atmosphere using *Schlenk* techniques. Syringes used to transfer solvents and reagents were purged with argon prior to use. Starting materials were purchased from Sigma Aldrich, TCI, Acros, Alfa Aesar or Fluorochem and used without further purification.

1.1 Solvents

THF was purchased from Acros (99.5% extra dry, stored over molecular sieve, stabilized).
CH_2Cl_2 was predried over $CaCl_2$ and distilled from CaH_2.
Toluene was continuously refluxed and distilled over sodium.
DMPU was predried over CaH_2 (4 h) and distilled (bp = 247 °C).
MeCN was purchased from Acros (99.9+% extra dry).
Solvents for reaction workups and column chromatography separations were distilled prior to use

1.2 Purification

Thin layer chromatography (TLC) was performed using aluminum plates covered with SiO_2 (Merck 60, F-254) and visualized either by UV detection or by staining with $KMnO_4$ solution (1.5 g $KMnO_4$, 10 g K_2CO_3, 1.25 mL 10% NaOH solution in 200 mL H_2O) or molybdatophosphoric acid stain (10 g PMA in 100 mL absolute ethanol).
Flash column chromatography was performed using silica gel 60 (40-63 µm 230-400 mesh ASTM) from Merck.

1.3 Analytical Data

NMR spectra were recorded on Varian VXR 400S, Bruker Avance III HD 400 MHz and Bruker AMX 600 instruments. Chemical shifts (δ) are reported in parts per million (ppm) relative to the residual solvent peak of $CHCl_3$ (δ_H = 7.26, δ_C = 77.0) or benzene (δ_H = 7.16, δ_C = 128.1) respectively. For the characterization of the observed signal multiplicities the following abbreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), m (multiplet), br (broad signal).

Mass spectra and **high resolution mass spectra** (HRMS) were recorded on a Finnigan MAT 95Q (EI) or a ThermoFinnigan LTQ FT instrument (ESI). Electron impact ionization (EI) was conducted with an electron energy of 70 eV. Electrospray ionization (ESI) was conducted with an IonMax ion-source equipped with an ESI head. It was performed with a voltage of 4 kV at the spray capillary tube, a heating filament temperature of 250 °C and a nitrogen flow of 25 units.

Gas Chromatography (GC, GC/MS) was performed with machines of the types Hewlett-Packard 6890 or 5890 Series II (Hewlett Packard, 5% phenylmethylpolysiloxane; column length: 15 m, diameter: 0.25 mm; film thickness: 0.25 *µ*m). For the combination of gas chromatography with mass spectroscopic detection, a GC-MS from Hewlett Packard of type 6890/MSD 5973 was used.

Chiral HPLC (cHPLC) was measured on a Shimazu HPLC Prominence with Daicel Chiracel columns.

Enantiomeric excess (*ee*). The enantiomeric excess of optical enriched compounds was determined *via* chiral HPLC analysis on a Shimadzu Prominence 20A HPLC system. For developing a chiral resolution method, different chiral normal phase columns were tested with *n*-heptane and *i*PrOH as mobile phase (isocratic) using a racemic mixture of the compound.

Optical Rotation values were recorded on an Anton Paar MCP 500 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.

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 DuraSample IR II Diamond ATR sensor was used. The absorption bands ($\tilde{\nu}$) are reported in wave numbers (cm^{-1}).

Melting points (m.p.) were measured using a Büchi B-540 apparatus and are uncorrected.

Determination of diastereomeric ratios: The selectivity of every reaction was evaluated *via* GC/MS of crude reaction mixtures prior to purification. Only a single diastereomer was detected in all the diastereoselective cases. After purification, the reported dr was determined *via* NMR.

Reactions were monitored by gas chromatography (GC and GC-MS) using an internal standard (undecane) or thin layer chromatography (TLC). Yields refer to isolated yields of compounds estimated to be >95% pure as determined by ^{1}H NMR (25 °C) and capillary GC analysis.

1.4 Reagents

Preparation of *s*Bu$_2$Mg solution in toluene[112]

A dry and argon flushed 250mL Schlenk-tube, equipped with a magnetic stirrer and a septum, was charged with *s*BuMgCl (2 M in diethyl ether, 10 mL, 20 mmol). Then *s*BuLi (1.7 M in cyclohexane, 12 mL, 20 mmol) was added dropwise at room temperature. After the addition was complete, the reaction mixture was stirred for 1 h. The solvents were then removed under vacuum affording a greyish solid. Dry toluene was then slowly added under stirring. Then salts were allowed to precipitate (*ca.* 24 h) and the solution was filtered *via* syringe filter (30 mm with 0.45 µm glass fiber membrane) and transferred to a dry argon flushed *Schlenk*-tube. The concentration of the *s*Bu$_2$Mg was determined *via* titration with benzoic acid (70 mg in 2 mL THF) and 4-(phenylazo)diphenylamine as indicator.

CuCN·2LiCl solution in tetrahydrofurane (THF) (1 M)[113]

LiCl (8.40 g, 200 mmol) and CuCN (8.96 g, 100 mmol) were dried in a Schlenk-flask under high vacuum at 150 °C for 4 h. After cooling to 25 °C, dry THF was added until a total volume of 100 mL was reached. The suspension was left stirring overnight at rt until all salts had completely dissolved. The solution was stored under argon upon use.

*s*BuLi solution in cyclohexane was purchased from Albemarle and titrated against *i*PrOH in THF using 1,10-phenantroline (2 mL, 0.5 M).[114] *s*BuMgCl was purchased from Sigma

[112] A. Hess, J.P. Prohaska, S.B. Doerrich, F. Trauner, F.H. Lutter, S. Lemaire, S. Wagschal, K. Karaghiosoff, P. Knochel, *Chem. Sci*. **2021**, *12*, 8424-8429.
[113] P. Knochel, C.P.M. Yeh, S.C. Berk, J. Talbert, *J. Org. Chem.* **1988**, *53*, 2390-2392.
[114] J. Skotnitzki, A. Kremsmair, D. Keefer, Y. Gong, R. de Vivie-Riedle, P. Knochel, *Angew. Chem. Int. Ed.* **2020**, *59*, 320-324.

Aldrich and titrated against iodide in THF solution (2 mL, 0.5 M).[115] *n*Bu_2Mg was used from Albemarle and titrated against iodide in LiCl THF solution (2 mL, 0.5 M). $Fe(acac)_3$ (99.9% purity) was purchased from Sigma Aldrich.

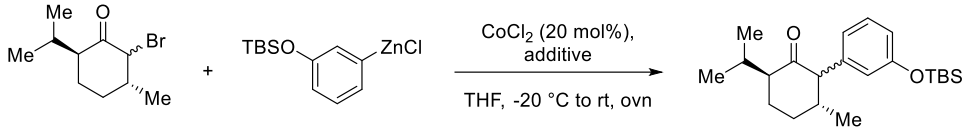
[115] A. Krasovskiy, P. Knochel, *Synthesis* **2006**, 890-891.

2 Stereoselective Cobalt-Catalyzed Cross-Coupling Reactions of Arylzinc Chlorides with *α*-Bromolactones and Related Derivatives

2.1 Optimization of Reaction Conditions

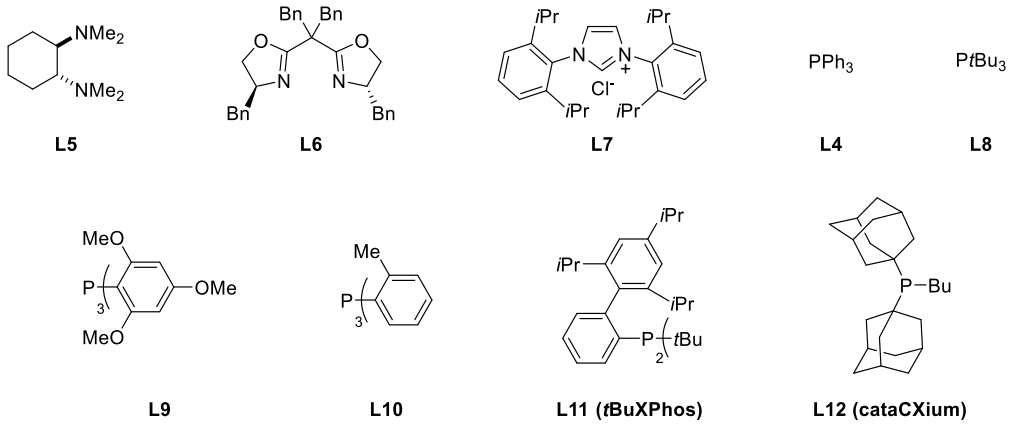
Extended Ligand Screening: The ligand effect on the arylation of the more challenging *α*-bromomenthone **S1** was determined in more detail (Table S1). Using *N,N,N',N'*-cyclohexyl-1,2-diamine (**L5**), the bisoxazoline ligand **L6**, and the NHC-ligand **L7** did not lead to significant enhancements of the diastereomeric ratio for product **S2** (entries 1-4). In contrast, 40 mol% of triphenylphosphine (**L4**) afforded **S2** in 83% yield (dr = 85:15, entry 5). Reducing the amount of PPh_3 (**L4**) to 20 mol% led to similar results (entry 6). Various trialkyl- or triarylphosphines, such as **L8-12** as additives gave the arylated menthone **S2** in lower yields or decreased diastereoselectivity (entries 7-11).

Table S1. Extended ligand screening using the *α*-bromomenthone **S1**.



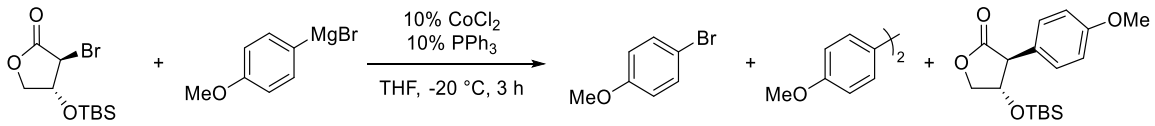
S1 (dr = 80:20) (1.0 equiv) | **76e** (1.5 equiv) | **S2**

entry	additive	yield[a]	dr
1	-	76%	70:30
2	**L5** (20 mol%)	60%	70:30
3	**L6** (20 mol%)	77%	75:25
4	**L7** (20 mol%)	76%	71:29
5	**L4** (40 mol%)	83%	85:15
6	**L4** (20 mol%)	82%	85:15
7	**L8** (40 mol%)	67%	69:31
8	**L9** (40 mol%)	27%	65:35
9	**L10** (40 mol%)	85%	72:28
10	**L11** (40 mol%)	73%	72:28
11	**L12** (40 mol%)	52%	68:32



[a] Calibrated GC-yield using undecane as internal standard.

Reaction of 75 with 4-anisylmagnesium bromide. The coupling of 4-anisylmagnesium bromide with *α*-bromolactone **75** mainly led to the formation of bromoanisole and extensive homocoupling (Scheme S1). The arylation product **77a** was only formed in 3%.

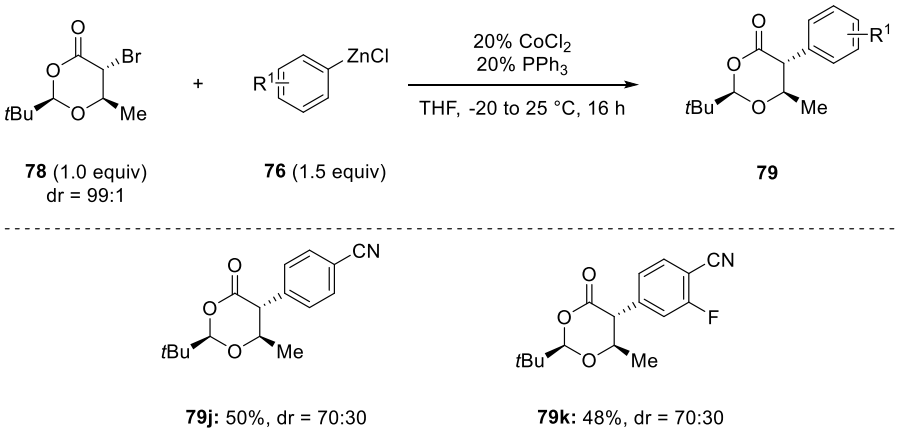


75 (1.0 equiv) (1.2 equiv) **77a**, 3%

Scheme S1. Reaction of **75** with 4-anisylmagnesium bromide.

2.2 Limitations of Method

Some *para*-substituted electron-poor organozinc chlorides **76** led to the arylation of **78** with decreasing diastereoselectivity (Scheme S2).



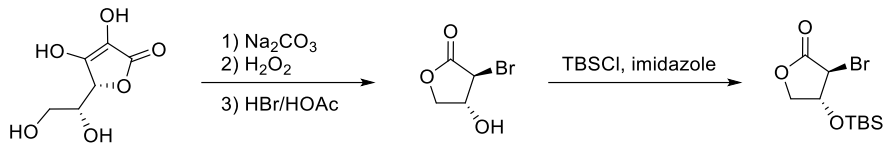
78 (1.0 equiv) dr = 99:1 **76** (1.5 equiv) **79**

79j: 50%, dr = 70:30 **79k:** 48%, dr = 70:30

Scheme S2. Arylation of **78** with electron-poor organozinc chlorides **76**.

2.3 Preparation of the *α*-Bromolactones

(3*S*,4*R*)-3-Bromo-4-((*tert*-butyldimethylsilyl)oxy)dihydrofuran-2(3*H*)-one (75a)



D-isoascorbic acid **S3** | **S4** | **75a**

D-Isoascorbic acid (**S3**, 200 g, 1.14 mol, 1.00 equiv) was dissolved in water (1.5 L). The solution was cooled to 0 °C and Na_2CO_3 (168 g, 1.59 mol, 1.40 equiv) was added in portions. The reaction mixture was allowed to warm to rt, stirred for 30 min and cooled to 0 °C again. Hydrogen peroxide (33% in water, 400 mL, 3.98 mol, 3.50 equiv) was added very slowly in small portions. The mixture was slowly heated to 55 °C and stirred for 40 min. After cooling to 0 °C, activated charcoal (25.0 g) was added, the mixture was heated to 70 °C for 1 h and the hot suspension was filtered over celite. The filtrate was acidified to pH = 1 with concentrated hydrochloric acid (*ca.* 170 mL) and the water was removed on a rotatory evaporator. The resulting residue was extracted by refluxing in EtOAc (6 x 900 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue containing the crude chiral dihydroxylactone (128 g, 1.09 mol, 96% yield) as a yellowish oil was used in the next step without further purification.[116]

Hydrobromic acid (33% in glacial acetic acid, 420 mL) was cooled to 0 °C and added to the residue containing the dihydroxylactone. The mixture was allowed to warm to rt and was stirred for 2 h. Methanol (500 mL) was added over 3 h using a dropping funnel and the mixture was stirred at rt overnight. The volatiles were removed under reduced pressure and the resulting suspension was extracted with EtOAc (3 x 250 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 6:4) to afford the *α*-bromo-*β*-hydroxylactone **S4** as brownish oil (54.0 g, 300 mmol, 26% yield over two steps).[117]

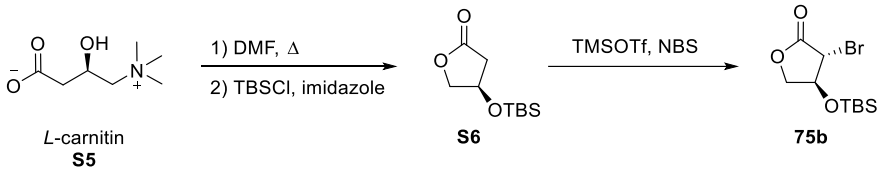
The *α*-bromo-*β*-hydroxylactone **S4** (54.0 g, 300 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (500 mL) and cooled to 0 °C. Imidazole (26.6 g, 390 mmol, 1.30 equiv) and

[116] a) N. Cohen, B. L. Banner, A. J. Laurenzano, L. Carozza *Org. Synth.* **1985**, *63*, 127. b) L. L. Wong, R. L. Wong, G. Loh, P. E. W. Tan, S. K. Teoh, S. M. Shaik, P. N. Sharratt, W. Chew, S. T. Tan, D. Wang *Org. Process Res. Dev.* **2012**, *16*, 1003-1012. c) S. R. Borkar, N. Bokolia, I. S. Aidhen, I. A. Khan *Tetrahedron: Asymmetry* **2017**, *28*, 186-195.
[117] a) M. Bols, I. Lundt *Acta Chem. Scand. Ser. B* **1988**, *42*, 67-74. b) C. Falentin, D. Beaupère, G. Demailly, I. Stasik *Tetrahedron* **2008**, *64*, 9989-9991.

DMAP (367 mg, 3 mmol, 1 mol%) were added and TBSCl (58.8 g, 390 mmol, 1.30 equiv) dissolved in CH_2Cl_2 (200 mL) was added dropwise over 30 min. The mixture was allowed to warm to rt and was stirred overnight, was washed with sat. aq. $NaHCO_3$ (300 mL) and water (300 mL). The organic layer was dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 100:2.5) to afford the *α*-bromolactone **75a** as colorless solid (52.0 g, 176 mmol, 59% yield, dr = 99:1, 99% *ee*).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.60 (dd, *J* = 9.7, 2.4 Hz, 1H), 4.51 (td, *J* = 4.3, 2.3 Hz, 1H), 4.19 (dd, *J* = 9.7, 2.2 Hz, 1H), 4.04 (d, *J* = 2.5 Hz, 1H), 0.88 (s, 9H), 0.12 (d, *J* = 5.7 Hz, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 171.8, 75.4, 74.1, 41.8, 25.7, 18.0, -4.6, -4.8.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2953, 2928, 2893, 2884, 2857, 1781, 1747, 1470, 1462, 1373, 1367, 1360, 1346, 1259, 1251, 1231, 1193, 1170, 1103, 1057, 997, 987, 937, 906, 875, 838, 824, 807, 780, 765, 713, 671, 663.
MS (EI, 70 eV): *m/z* (%) = 159 (12), 158 (12), 119 (13), 118 (32), 117 (100), 103 (10), 89 (23), 75 (30), 73 (24), 59 (16), 57 (35), 45 (12), 41 (20).
HR-MS (EI, 70 eV): $[C_6H_{10}BrO_3Si] = [M - C(CH_3)_3]^+$, calcd.: 236.9589; found: 236.9575.
cHPLC: Chiracel OD-H; heptane:*i*-PrOH = 99.5:0.5; 1 mL·min^{-1}; 209 nm; R_f(3*S*,4*R*) = 9.2 min; R_f(3*R*-4*S*) = 9.9 min.
Optical Rotation: $[\alpha]_D^{20}$ = −35.2 (c = 1.0, $CHCl_3$).
m.p.: 39 – 40 °C.

(3*R*,4*S*)-3-Bromo-4-((*tert*-butyldimethylsilyl)oxy)dihydrofuran-2(3*H*)-one (75b)



L-carnitin **S5** — **S6** — **75b**

L-carnitine (**S5**, 3.22 g, 20.0 mmol, 1.0 equiv) was dissolved in DMF (32 mL). The mixture was heated to 150 °C for 16 h, cooled to room temperature and DMF was evaporated under reduced pressure. Sat. aq. NH_4Cl (10 mL) was added and extracted with EtOAc (3 x 25 mL). The combined organic layers were washed with 10% aq. LiCl (25 mL) and brine (25 mL), dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 7:3) to afford the chiral *β*-hydroxylactone (561 mg, 5.50 mmol, 28% yield).

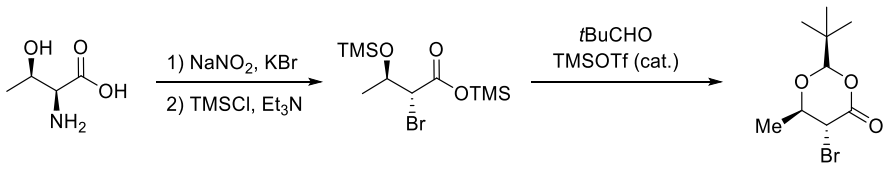
The *β*-hydroxylactone (561 mg, 5.50 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (11 mL), DMF (8 µL) and NEt_3 (0.92 mL, 6.60 mmol, 1.20 equiv) were added. The mixture was cooled to 0 °C. TBSCl (995 mg, 6.60 mmol, 1.20 equiv) was added and allowed to warm to rt overnight. Sat. aq. NH_4Cl (10 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 7:3) to afford the *β*-OTBS-substituted lactone **S6** (1.18 g, 5.47 mmol, 99% yield).

Lactone **S6** (1.18 g, 5.47 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (30 mL) and NEt_3 (4.67 mL, 32.8 mmol, 6.00 equiv) was added. The mixture was cooled to 0 °C and TMSOTf (3.0 mL, 16.4 mmol, 3.0 equiv) was added and stirring was continued for 30 min. *N*-Bromosuccinimide (1.49 g, 8.20 mmol, 1.50 equiv) was dissolved in CH_2Cl_2 (15 mL) and the solution was added to the reaction mixture dropwise. Stirring was continued for 1 h, sat. aq. Na_2CO_3 (20 mL) and water (20 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 100:3) to afford the *α*-bromolactone **75b** as colorless solid (983 mg, 3.34 mmol, 61% yield, dr = 99:1, 99% *ee*).

The analytical data is identical to the (3*S*,4*R*)-enantiomer **75a.**

Optical Rotation: $[\alpha]_D^{20}$ = +35.4 (c = 1.0, $CHCl_3$).

(2*R*,5*R*,6*R*)-5-Bromo-2-(*tert*-butyl)-6-methyl-1,3-dioxan-4-one (78a)[118]



L-threonine **S7** — **S8** — **78a**

L-threonine (**S7**, 20.0 g, 168 mmol, 1.00 equiv) and KBr (31.0 g, 260 mmol, 1.50 equiv) were dissolved in water (300 mL) and conc. H_2SO_4 (50 mL) was added. The solution was cooled to −12 °C and $NaNO_2$ (18.8 g, 272 mmol, 1.60 equiv) dissolved in water

[118] J. Zimmermann, D. Seebach *Helv. Chim. Acta* **1987**, *70*, 1104-1114.

(60 mL) was added dropwise over 2 h. The mixture was allowed to warm to rt, stirred overnight and extracted with EtOAc (3 x 200 mL). The combined organic layers were dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The crude viscous oil containing the *α*-bromo acid (22.0 g, 120 mmol) was dissolved in CH_2Cl_2 (150 mL), cooled to 0 °C, and NEt_3 (36.8 mL, 264 mmol, 2.20 equiv) and TMSCl (33.5 mL, 264 mmol, 2.20 equiv) were added. The mixture was allowed to warm to rt and was stirred for 3 d. Pentane (100 mL) was added, the salts were removed by filtration and the filtrate was evaporated to dryness. Pentane (150 mL) was added again, the salts were removed by filtration and the filtrate was evaporated to dryness. The crude product **S8** (32.8 g, 100 mmol, 60% yield over two steps) was clean enough for the following transformation.

The TMS-protected compound **S8** (32.8 g, 100 mmol, 1.0 equiv) and pivalaldehyde (8.44 g, 98.0 mmol, 0.98 equiv) were dissolved in CH_2Cl_2 (220 mL) and the solution was cooled to −78 °C. TMSOTf (0.54 mL, 3 mol%) was added and stirring at −78 °C was continued overnight. Pyridine (0.8 mL, 10.0 mmol, 0.10 equiv) was added, the mixture was allowed to warm to rt and washed with sat. aq. $NaHCO_3$ (30 mL). The organic layer was dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 9:1) to afford the chiral (*R*)-*α*-bromolactone **78a** (6.87 g, 27.4 mmol, 27% yield) as colorless solid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.00 (s, 1H), 4.31 (d, *J* = 2.2 Hz), 3.88 (qd, *J* = 6.1, 2.2 Hz, 1H), 1.40 (d, *J* = 6.1 Hz, 3H), 1.01 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 165.4, 110.0, 72.1, 46.1, 35.7, 24.0, 19.1.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2979, 2938, 2878, 1716, 1706, 1701, 1685, 1670, 1654, 1647, 1636, 1458, 1374, 1281, 1168, 1126, 1084, 1028, 941, 853.

cHPLC: Chiracel OJ-H; heptane:*i*-PrOH = 95:5; 1 mL·min^{-1}; 230 nm; R_f(*R**) = 7.4 min; R_f(*S**) = 16.3 min.

Optical Rotation: $[\alpha]_D^{20}$ = −14.2 (c = 1.0, $CHCl_3$).

m.p.: 49 – 51 °C.

(2*S*,5*S*,6*S*)-5-Bromo-2-(*tert*-butyl)-6-methyl-1,3-dioxan-4-one (78b)

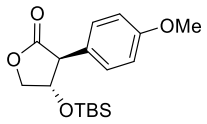
The (*S*)-enantiomer was synthesized by using *D*-threonine as starting material.

The analytical data is identical to the other (*R*)-enantiomer **78a**.

Optical Rotation: $[\alpha]_D^{20}$ = +15.8° (c = 1.0, $CHCl_3$).

2.4 Stereoselective Cobalt-Catalyzed Cross-Coupling Reactions of Arylzinc Reagents with *α*-Bromolactones

Typical Procedure 1 (TP1) for the cobalt-catalyzed cross-couplings of arylzinc reagents with *α*-bromolactones. Synthesis of (3*S*,4*S*)-4-((*tert*-butyldimethylsilyl)oxy)-3-(4-methoxyphenyl)-dihydrofuran-2(3*H*)-one (77a)



A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum, was charged with magnesium turnings (291 mg, 12.0 mmol, 1.20 equiv), dry LiCl (508 mg, 12.0 mmol, 1.20 equiv) and dry THF (1 M solution relating to the aryl halide, 10 mL). 4-Bromoanisole (1.87 g, 10.0 mmol, 1.00 equiv) was added dropwise at 0 °C. The progress of the magnesium insertion was monitored by GC-analysis of reaction aliquots quenched with I_2. Upon completion of the insertion (2 h), the concentration of the Grignard reagent was determined by titration[4] of I_2 in THF (c = 0.82 M).

Solid $ZnCl_2$ (681 mg, 5.00 mmol, 1.00 equiv) was placed in a dry and argon flushed *Schlenk*-tube equipped with a magnetic stirring bar and a septum and dried under vacuum at 250 °C for 5 min. After cooling to rt under vacuum, an argon atmosphere was applied and THF (1 M according to $ZnCl_2$, 5 mL) was added. The Grignard reagent (6.1 mL, 5.00 mmol, 1.00 equiv) was added at 0 °C, the solution was allowed to warm to rt and stirred for 15 min. The concentration of 4-anisylzinc chloride was determined by titration[119] of I_2 (c = 0.43 M).

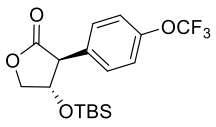
A dry and argon-flushed 20 mL *Schlenk*-tube, equipped with a stirring bar and a septum, was charged with $CoCl_2$ (6.5 mg, 0.05 mmol, 10 mol%). The solid was flame dried under high vacuum for 5 min. After cooling to rt, PPh_3 (13 mg, 0.05 mmol, 10 mol%) and the *α*-bromolactone **75a** (148 mg, 0.50 mmol, 1.00 equiv) was added. The mixture was dissolved in THF (1 mL) and cooled to −20 °C. 4-Anisylzinc chloride (1.4 mL, 0.60 mmol, 1.20 equiv) was added and the mixture was allowed to warm to rt overnight. The reaction was monitored by GC-analysis ($C_{11}H_{24}$ was used as an internal standard) and TLC. Upon complete consumption of the starting material (conversion 100%), sat. aq. NH_4Cl (5 mL) and ethyl acetate (5 mL) were added, the phases were separated and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were

[119] A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006,** *45*, 6040-6044.

dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **77a** as colorless solid (131 mg, 0.41 mmol, 81% yield, dr = 99:1, 99% *ee*).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.16 – 7.02 (m, 2H), 6.97 – 6.73 (m, 2H), 4.44 (dd, *J* = 5.9, 2.4 Hz, 2H), 4.11 – 3.97 (m, 1H), 3.80 (s, 3H), 3.64 (d, *J* = 6.1 Hz, 1H), 0.83 (s, 9H), -0.07 (s, 3H), -0.12 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 175.8, 159.4, 129.5, 126.6, 114.6, 76.3, 72.6, 55.4, 55.0, 25.7, 18.0, -4.8, -4.9.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2997, 2953, 2930, 2856, 1785, 1613, 1515, 1473, 1465, 1345, 1249, 1221, 1177, 1144, 1122, 1109, 1091, 1072, 1023, 1011, 942, 915, 838, 826, 816, 778, 675.
MS (EI, 70 eV): *m/z* (%) = 237 (13), 190 (26), 162 (20), 133 (68), 121 (40), 117 (14), 89 (10), 77 (11), 75 (100), 45 (10), 44 (11), 43 (66).
HR-MS (EI, 70 eV): [$C_{17}H_{26}O_4Si$], calcd.: 322.1600; found: 322.1607.
cHPLC: Chiracel OD-H; heptane:*i*-PrOH = 98:2; 1 mL·min^{-1}; 227 nm; R_f(*S**) = 13.3 min; R_f(*R**) = 16.8 min.
Optical Rotation: $[\alpha]_D^{20}$ = −36.6 (c = 1.0, $CHCl_3$).
m.p.: 56 – 58 °C.

(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(4-(trifluoromethoxy)phenyl)dihydro-furan-2(3*H*)-one (77b)



According to **TP1**, *α*-bromolactone **75a** (148 mg, 0.50 mmol, 1.00 equiv) was treated with 4-trifluoromethoxyphenylzinc chloride **76b** (0.60 mmol, 1.20 equiv). The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **77b** as colorless solid (63% yield, dr = 99:1, 99% *ee*, 119 mg, 0.32 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.25 (d, *J* = 2.2 Hz, 4H), 4.56 – 4.31 (m, 2H), 4.21 – 3.97 (m, 1H), 3.79 – 3.57 (m, 1H), 0.82 (s, 9H), -0.08 (s, 3H), -0.15 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 174.7, 149.0, 133.4, 130.1, 121.7, 120.8 (q, *J* = 257.5 Hz), 76.2, 72.4, 54.9, 25.6, 18.0, -4.9.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2956, 2932, 2860, 1786, 1510, 1472, 1464, 1390, 1254, 1214, 1154, 1126, 1070, 1028, 1004, 922, 836, 778, 674.

MS (EI, 70 eV): *m/z* (%) = 290 (31), 244 (38), 216 (18), 188 (14), 187 (97), 174 (31), 118 (14), 117 (100), 101 (11), 89 (11), 75 (84), 73 (11), 61 (16), 43 (52).

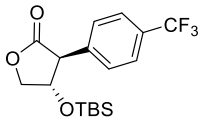
HR-MS (EI, 70 eV): [$C_{17}H_{23}O_4F_3Si$], calcd.: 376.1318; found: 376.1311.

cHPLC: Chiracel OD-H; heptane:*i*-PrOH = 98:2; 1 mL·min^{-1}; 210 nm; R_f(*S**) = 11.1 min; R_f(*R**) = 17.6 min.

Optical Rotation: $[\alpha]_D^{20}$ = −11.0 (c = 1.0, $CHCl_3$).

m.p.: 57 – 58 °C.

(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(4-(trifluoromethyl)phenyl)dihydrofuran-2(3*H*)-one (77c)



According to **TP1**, *α*-bromolactone **75a** (148 mg, 0.50 mmol, 1.00 equiv) was coupled with 4-trifluoromethylphenylzinc chloride **76c** (0.60 mmol, 1.20 equiv). The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (100:8) as an eluent to afford **77c** as yellowish solid (62% yield, dr = 99:1, 99% *ee*, 112 mg, 0.31 mmol).

^{1}H-NMR (400 MHz, benzene-D_6, ppm): *δ* = 7.32 (d, *J* = 8.1 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 3.93 – 3.70 (m, 2H), 3.47 (dd, *J* = 8.6, 7.0 Hz, 1H), 3.15 (d, *J* = 8.1 Hz, 1H), 0.74 (s, 9H), -0.36 (s, 3H), -0.45 (s, 3H).

^{13}C-NMR (101 MHz, benzene-D_6, ppm): *δ* = 173.0, 139.5, 130.1 (q, *J* = 32.4 Hz), 129.4, 125.8 (q, *J* = 3.9 Hz), 124.8 (q, *J* = 272.1 Hz), 75.7, 71.4, 54.8, 25.6, 17.8, -5.1, -5.2.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2952, 2932, 2858, 1795, 1621, 1469, 1325, 1257, 1224, 1155, 1136, 1125, 1111, 1068, 1012, 923, 836, 784, 765, 702, 674.

MS (EI, 70 eV): *m/z* (%) = 245 (8), 228 (5), 171 (15), 151 (5), 118 (7), 117 (100), 89 (6), 75 (28), 73 (7), 43 (18).

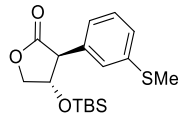
HR-MS (EI, 70 eV): [$C_{17}H_{23}F_3O_3Si$], calcd.: 360.1369; found: 360.1344.

cHPLC: Chiracel AD-H; heptane:*i*-PrOH = 98:2; 1 mL·min^{-1}; 216 nm; R_f(*S**) = 9.3 min; R_f(*R**) = 7.4 min.

Optical Rotation: $[\alpha]_D^{20}$ = −24 (c = 1.0, $CHCl_3$).

m.p.: 61 – 63 °C.

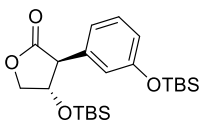
(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(3-(methylthio)phenyl)dihydrofuran-2(3*H*)-one (77d)



According to **TP1**, *α*-bromolactone **75a** (148 mg, 0.50 mmol, 1.00 equiv) was coupled with 3-thioanisylzinc chloride **76d** (0.60 mmol, 1.20 equiv). The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **77d** as colorless solid (63% yield, dr = 99:1, 99% *ee*, 107 mg, 0.32 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.29 (t, *J* = 7.7 Hz, 1H), 7.20 (ddd, *J* = 7.9, 1.9, 1.1 Hz, 1H), 7.08 (t, *J* = 1.9 Hz, 1H), 6.97 (dt, *J* = 7.5, 1.5 Hz, 1H), 4.49 – 4.35 (m, 2H), 4.15 – 4.01 (m, 1H), 3.70 – 3.62 (m, 1H), 2.47 (s, 3H), 0.84 (s, 9H), -0.07 (s, 3H), -0.12 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 175.1, 139.6, 135.3, 129.5, 126.6, 126.1, 124.9, 76.1, 72.7, 55.5, 25.7, 18.0, 15.9, -4.8, -4.9.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2954, 2928, 2858, 1792, 1592, 1574, 1468, 1416, 1350, 1262, 1252, 1226, 1180, 1152, 1126, 1086, 1070, 1014, 928, 868, 860, 836, 794, 780, 744, 696, 682, 674.
MS (EI, 70 eV): *m/z* (%) = 207 (13), 206 (100), 150 (14), 149 (74), 134 (17), 117 (29), 115 (11), 102 (21), 75 (78).
HR-MS (EI, 70 eV): [$C_{17}H_{26}O_3SSi$], calcd.: 338.1372; found: 338.1376.
cHPLC: Chiracel AD-H; heptane:*i*-PrOH = 99.5:0.5; 1 mL·min^{-1}; 213 nm; R_f(*S**) = 31.1 min; R_f(*R**) = 40.0 min.
Optical Rotation: $[\alpha]_D^{20}$ = −23.6 (c = 1.0, $CHCl_3$).
m.p.: 109 – 110 °C.

(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(3-((*tert*-butyldimethylsilyl)oxy)phenyl)-dihydrofuran-2(3*H*)-one (77e)

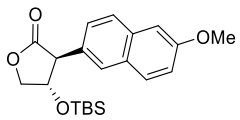


According to **TP1**, *α*-bromolactone **75a** (148 mg, 0.50 mmol, 1.00 equiv) was coupled

with arylzinc reagent **76e** (0.60 mmol, 1.20 equiv). The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **77e** as yellow oil (77% yield, dr = 99:1, 99% *ee*, 163 mg, 0.386 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.22 (t, *J* = 7.9 Hz, 1H), 6.83 – 6.75 (m, 2H), 6.68 (t, *J* = 2.1 Hz, 1H), 4.52 – 4.40 (m, 2H), 4.14 – 4.03 (m, 1H), 3.64 (d, *J* = 5.7 Hz, 1H), 0.98 (s, 9H), 0.84 (s, 9H), 0.19 (s, 6H), -0.06 (s, 3H), -0.09 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 175.4, 156.3, 136.0, 130.1, 121.3, 120.3, 119.7, 76.3, 72.8, 55.6, 25.8, 25.7, 18.3, 18.0, -4.3, -4.8, -4.9.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2955, 2930, 2891, 2858, 1786, 1774, 1603, 1586, 1487, 1472, 1464, 1438, 1279, 1253, 1237, 1160, 1121, 1028, 1002, 908, 870, 837, 808, 779, 722, 694.
MS (EI, 70 eV): *m/z* (%) = 365 (39), 337 (60), 278 (25), 277 (62), 233 (100), 159 (63), 117 (88).
HR-MS (EI, 70 eV): [$C_{22}H_{38}O_4Si_2$], calcd.: 422.2309; found: 422,2313.
cHPLC: Chiracel OD-H; heptane:*i*-PrOH = 98:2; 1 mL·min^{-1}; 270 nm; R_f(*S**) = 5.6 min; R_f(*R**) = 7.8 min.
Optical Rotation: $[\alpha]_D^{20}$ = −13.4 (c = 1.0, $CHCl_3$).

(3S,4S)-4-((tert-Butyldimethylsilyl)oxy)-3-(6-methoxynaphthalen-2-yl)dihydro-furan-2(3H)-one (77f)



According to **TP1**, *α*-bromolactone **75a** (148 mg, 0.50 mmol, 1.00 equiv) was coupled with (6-methoxynaphthalen-2-yl)zinc chloride **76f** (0.60 mmol, 1.20 equiv). The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **77f** as colorless solid (61% yield, dr = 99:1, 99% *ee*, 113 mg, 0.30 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.76 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 8.9 Hz, 1H), 7.60 (d, *J* = 1.9 Hz, 1H), 7.30 – 7.24 (m, 1H), 7.20 – 7.09 (m, 2H), 4.61 – 4.44 (m, 2H), 4.13 (dd, *J* = 8.9, 5.7 Hz, 1H), 3.92 (s, 3H), 3.84 (d, *J* = 6.4 Hz, 1H), 0.84 (s, 9H), -0.08 (s, 3H), -0.14 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 175.7, 158.0, 134.1, 129.5, 129.4, 129.0, 127.9,

127.5, 126.3, 119.5, 105.7, 76.2, 72.9, 55.7, 55.4, 25.7, 18.0, -4.7, -4.9.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2954, 2928, 2856, 1792, 1608, 1508, 1488, 1468, 1422, 1402, 1392, 1346, 1274, 1262, 1252, 1238, 1228, 1192, 1182, 1154, 1134, 1086, 1072, 1028, 1018, 1002, 974, 928, 906, 888, 860, 848, 834, 814, 782, 738, 704, 686, 670.

MS (EI, 70 eV): *m/z* (%) = 372 (17), 316 (2), 315 (7), 314 (23), 288 (4), 287 (18), 240 (24), 171 (100).

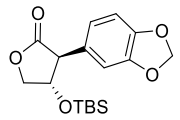
HR-MS (EI, 70 eV): [$C_{21}H_{28}O_4Si$], calcd.: 372.1757; found: 372.1747.

cHPLC: Chiracel OJ-H; heptane:*i*-PrOH = 98:2; 1 mL·min^{-1}; 233 nm; R_f(*S**) = 36.6 min; R_f(*R**) = 25.7 min.

Optical Rotation: $[\alpha]_D^{20}$ = −39.9 (c = 1.0, EtOAc).

m.p.: 136 – 137 °C.

(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(benzo[*d*][1,3]dioxol-5-yl)dihydrofuran-2(3*H*)-one (77g)



According to **TP1**, *α*-bromolactone **75a** (148 mg, 0.50 mmol, 1.00 equiv) was coupled with benzodioxolylzinc chloride **76g** (0.60 mmol, 1.20 equiv). The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (100:8) as an eluent to afford **77g** as colorless solid (84% yield, dr = 99:1, 99% *ee*, 141 mg, 0.42 mmol).

^{1}H-NMR (400 MHz, benzene-D$_6$, ppm): *δ* = 6.71 – 6.54 (m, 2H), 6.47 (dd, *J* = 8.0, 1.8 Hz, 1H), 5.35 – 5.18 (m, 2H), 3.96 (dt, *J* = 7.6, 6.6 Hz, 1H), 3.84 (dd, *J* = 8.8, 6.4 Hz, 1H), 3.51 (dd, *J* = 8.8, 6.8 Hz, 1H), 3.19 (d, *J* = 7.8 Hz, 1H), 0.77 (s, 9H), -0.29 (s, 3H), -0.31 (s, 3H).

^{13}C-NMR (101 MHz, benzene-D$_6$, ppm): *δ* = 174.0, 148.6, 147.7, 129.1, 122.5, 109.1, 108.6, 101.2, 76.0, 71.5, 55.0, 25.7, 17.9, -5.0, -5.1.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2955, 2927, 2857, 2359, 2332, 1760, 1605, 1508, 1471, 1444, 1379, 1359, 1269, 1252, 1237, 1164, 1095, 1063, 1044, 996, 932, 913, 888, 826, 775, 723, 681, 666.

MS (EI, 70 eV): *m/z* (%) = 251 (30), 204 (12), 162 (21), 147 (25), 135 (100), 117 (41), 89 (14), 75 (48), 73 (13), 43 (19).

HR-MS (EI, 70 eV): [$C_{17}H_{24}O_5Si$], calcd.: 336.1393; found: 336.1388.

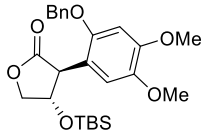
cHPLC: Chiracel OD-H; heptane:*i*-PrOH = 99:1; 1 mL·min^{-1}; 289 nm; R_f(*S**) = 18.9 min;

R_f(*R**) = 27.4 min.

Optical Rotation: $[\alpha]_D^{20}$ = −28.9 (c = 1.0, $CHCl_3$).

m.p.: 75 – 77 °C.

(3*S*,4*S*)-3-(2-(Benzyloxy)-4,5-dimethoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)dihydrofuran-2(3*H*)- one (77h)



According to **TP1**, *α*-bromolactone **75a** (2.50 g, 8.46 mmol, 1.00 equiv) was coupled with arylzinc reagent **76h** (10.2 mmol, 1.20 equiv). The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (8:2) as an eluent to afford **77h** as yellow solid (94% yield, dr = 99:1, 99% *ee*, 3.65 g, 7.96 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): *δ* = 7.47 – 7.32 (m, 5H), 6.71 (s, 1H), 6.63 (s, 1H), 5.06 (q, *J* = 11.4 Hz, 2H), 4.68 (td, *J* = 6.8, 6.3 Hz, 1H), 4.29 (dd, *J* = 9.0, 6.9 Hz, 1H), 3.97 (dd, *J* = 9.0, 6.3 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.60(d, *J* = 6.8 Hz, 1H), 0.81 (s, 9H), -0.12 (s, 3H), -0.17 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm): *δ* = 176.1, 150.5, 149.6, 143.3, 136.6, 128.7, 128.2, 127.8, 115.3, 115.3, 99.3, 74.2, 73.2, 71.6, 56.7, 56.3, 53.1, 25.7, 18.0, -4.8, -5.0.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2952, 2929, 2897, 2886, 2855, 1779, 1612, 1511, 1463, 1450, 1400, 1388, 1338, 1251, 1223, 1195, 1152, 1117, 1071, 1021, 933, 882, 836, 815, 780, 758, 733, 697, 683, 672.

MS (EI, 70 eV): *m/z* (%) = 326 (28), 235 (51), 207 (13), 179 (11), 91 (100), 75 (42), 73 (17).

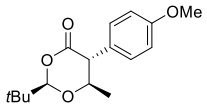
HR-MS (EI, 70 eV): [$C_{25}H_{34}O_6Si$], calcd.: 458.2125; found: 458.2116.

cHPLC: Chiracel AD-H; heptane:*i*-PrOH = 95:5; 1 mL·min^{-1}; 220 nm; R_f(*S**) = 11.7 min; R_f(*R**) = 18.5 min.

Optical Rotation: $[\alpha]_D^{20}$ = −44.7 (c = 1.0, $CHCl_3$).

m.p.: 83 – 85 °C.

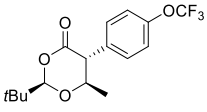
(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-5-(4-methoxyphenyl)-6-methyl-1,3-dioxan-4-one (79a)



According to **TP1**, *α*-bromolactone **78a** (126 mg, 0.50 mmol, 1.00 equiv) was coupled with 4-anisylzinc chloride **76a** (0.75 mmol, 1.50 equiv) using $CoCl_2$ (13 mg, 0.10 mmol, 20 mol%) and PPh_3 (26 mg, 0.10 mmol, 20 mol%) as catalytic system. The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **79a** as colorless solid (81% yield, dr = 99:1, 97% *ee*, 113 mg, 0.41 mmol).

^{1}H-NMR (400 MHz, benzene-D_6, ppm): δ = 6.88 – 6.78 (m, 2H), 6.78 – 6.69 (m, 2H), 4.78 (s, 1H), 3.53 (dq, *J* = 10.5, 6.0 Hz, 1H), 3.30 (s, 3H), 3.12 (d, *J* = 10.7 Hz, 1H), 1.04 (s, 9H), 0.90 (d, *J* = 6.0 Hz, 3H).
^{13}C-NMR (101 MHz, benzene-D_6, ppm): δ = 168.5, 159.6, 130.7, 114.5, 108.2, 77.3, 55.5, 54.8, 35.5, 24.1, 19.3.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2961, 2907, 2838, 1736, 1616, 1519, 1484, 1461, 1409, 1345, 1271, 1209, 1177, 1152, 1120, 1081, 1026, 992, 970, 924, 881, 830, 762.
MS (EI, 70 eV): *m/z* (%) = 193 (47), 165 (32), 149 (28), 148 (100), 147 (45), 133 (17), 121 (14), 91 (15), 77 (16), 57 (17), 43 (13), 41 (15).
HR-MS (EI, 70 eV): [$C_{16}H_{22}O_4$], calcd.: 278.1518; found: 278.1514.
cHPLC: Chiracel OJ-H; heptane:*i*-PrOH = 9:1; 1 mL·min^{-1}; 222 nm; R_f(*R**) = 13.3 min; R_f(*S**) = 9.4 min.
Optical Rotation: $[\alpha]_D^{20}$ = +29.4 (c = 1.0, EtOAc).
m.p.: 68 – 70 °C.

(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-6-methyl-5-(4-(trifluoromethoxy)phenyl)-1,3-dioxan-4-one (79b)

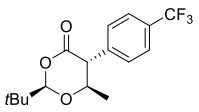


According to **TP1**, *α*-bromolactone **78a** (126 mg, 0.50 mmol, 1.00 equiv) was coupled with 4-trifluoromethoxyphenylzinc chloride **76b** (0.75 mmol, 1.50 equiv) using $CoCl_2$ (13 mg, 0.10 mmol, 20 mol%) and PPh_3 (26 mg, 0.10 mmol, 20 mol%) as catalytic system.

The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **79b** as colorless solid (63% yield, dr = 99:1, 99% *ee*, 105 mg, 0.32 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.21 (s, 4H), 5.15 (s, 1H), 3.99 (dq, *J* = 10.5, 6.0 Hz, 1H), 3.50 (d, *J* = 10.6 Hz, 1H), 1.23 (d, *J* = 6.1 Hz, 3H), 1.03 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 169.6, 148.9 (q, *J* = 1.9 Hz), 134.2, 130.8, 121.6, 120.5 (q, *J* = 257.5 Hz), 109.1, 77.0, 55.5, 35.5, 24.0, 19.6.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2974, 2966, 2876, 1738, 1512, 1486, 1366, 1344, 1258, 1208, 1150, 1114, 1088, 1030, 1020, 992, 966, 938, 922, 884, 844, 804, 762.
HR-MS: Fragmentation: $[C_{10}H_{10}O_2F_3]$ = M – $[C_6H_9O_2]$, calcd.: 219.0633; found: 219.0625.
cHPLC: Chiracel OD-H; heptane:*i*-PrOH = 98:2; 1 mL·min^{-1}; 210 nm; R_f(*R**) = 7.9 min; R_f(*S**) = 8.7 min.
Optical Rotation: $[\alpha]_D^{20}$ = −3.3 (c = 1.0, $CHCl_3$).
m.p.: 64 – 67 °C.

(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-6-methyl-5-(4-(trifluoromethyl)phenyl)-1,3-dioxan-4-one (79c)



According to **TP1**, *α*-bromolactone **78a** (126 mg, 0.50 mmol, 1.00 equiv) was coupled with 4-trifluoromethylphenylzinc chloride **76c** (0.75 mmol, 1.50 equiv) using $CoCl_2$ (13 mg, 0.10 mmol, 20 mol%) and PPh_3 (26 mg, 0.10 mmol, 20 mol%) as catalytic system. The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **79c** as colorless crystals (61% yield, dr = 99:1, 99% *ee*, 97 mg, 0.31 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.83 – 7.55 (m, 2H), 7.51 – 7.14 (m, 2H), 5.17 (s, 1H), 4.03 (dq, *J* = 10.6, 6.0 Hz, 1H), 3.56 (d, *J* = 10.6 Hz, 1H), 1.23 (d, *J* = 6.0 Hz, 3H), 1.03 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 169.3, 139.4 (d, *J* = 1.5 Hz), 130.3 (q, *J* = 32.6 Hz), 129.8, 126.1 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 272.1 Hz), 109.2, 76.8, 55.9, 35.5, 24.0, 19.5.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2967, 2919, 2875, 2359, 2341, 1733, 1619, 1484, 1452, 1366,

1322, 1283, 1214, 1165, 1128, 1117, 1066, 1020, 992, 964, 884, 830, 760, 685.

MS (EI, 70 eV): *m/z* (%) = 214 (3), 213 (31), 203 (31), 187 (11), 186 (100), 185 (22), 158 (13), 117 (52), 115 (11).

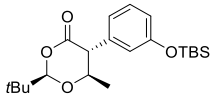
HR-MS (EI, 70 eV): Fragmentation: $[C_{10}H_{10}OF_3]$ = M – $[C_6H_9O_2]$, calcd.: 203.0684; found: 203.0677.

cHPLC: Chiracel AD-H; heptane:*i*-PrOH = 70:30; 1 mL·min^{-1}; 215 nm; R_f(*R**) = 7.9 min; R_f(*S**) = 17.5 min.

Optical Rotation: $[\alpha]_D^{20}$ = +24.0 (c = 1.0, $CHCl_3$).

m.p.: 90 – 94 °C.

(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-5-(3-((*tert*-butyldimethylsilyl)oxy)phenyl)-6-methyl-1,3-dioxan-4-one (79d)



According to **TP1**, *α*-bromolactone **78a** (126 mg, 0.50 mmol, 1.00 equiv) was coupled with arylzinc reagent **76e** (0.75 mmol, 1.50 equiv) using $CoCl_2$ (13 mg, 0.10 mmol, 20 mol%) and PPh_3 (26 mg, 0.10 mmol, 20 mol%) as catalytic system. The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (95:5) as an eluent to afford **79d** as colorless solid (69% yield, dr = 99:1, 99% *ee*, 131 mg, 0.35 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): *δ* = 7.20 (t, *J* = 7.9 Hz, 1H), 6.85 – 6.69 (m, 2H), 6.64 (t, *J* = 2.1 Hz, 1H), 5.14 (s, 1H), 3.98 (dq, *J* = 10.4, 6.0 Hz, 1H), 3.41 (d, *J* = 10.6 Hz, 1H), 1.23 (d, *J* = 6.0 Hz, 3H), 1.03 (s, 9H), 0.98 (s, 9H), 0.19(s, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm): *δ* = 169.9, 156.1, 136.9, 130.1, 122.2, 121.2, 119.5, 108.9, 77.2, 56.1, 35.5, 25.8, 24.1, 19.6, 18.3, -4.2, -4.3.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2959, 2931, 2859, 1732, 1602, 1585, 1485, 1473, 1458, 1446, 1342, 1274, 1253, 1236, 1217, 1151, 1114, 1030, 1002, 993, 982, 961, 939, 926, 874, 860, 837, 804, 783, 758, 728, 699.

MS (EI, 70 eV): *m/z* (%) = 378 (5), 293 (8), 248 (18), 192 (24), 191 (100), 73 (8).

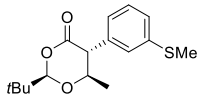
HR-MS (EI, 70 eV): $[C_{21}H_{34}O_4Si]$, calcd.: 378.2226; found: 378.2212.

cHPLC: Chiracel OD-H; heptane:*i*-PrOH = 99.5:0.5; 1 mL·min^{-1}; 218 nm; R_f(*R**) = 7.2 min; R_f(*S**) = 12.3 min.

Optical Rotation: $[\alpha]_D^{20}$ = −0.9 (c = 1.0, $CHCl_3$).

m.p.: 62 – 63 °C.

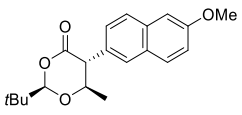
(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-6-methyl-5-(3-(methylthio)phenyl)-1,3-dioxan-4-one (79e)



According to **TP1**, *α*-bromolactone **78a** (126 mg, 0.50 mmol, 1.00 equiv) was coupled with 3-thioanisylzinc chloride **76d** (0.75 mmol, 1.50 equiv) using $CoCl_2$ (13 mg, 0.10 mmol, 20 mol%) and PPh_3 (26 mg, 0.10 mmol, 20 mol%) as catalytic system. The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **79e** as colorless solid (61% yield, dr = 99:1, 99% *ee*, 90 mg, 0.31 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.28 (t, *J* = 7.7 Hz, 1H), 7.19 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.05 (t, *J* = 1.8 Hz, 1H), 6.94 (dt, *J* = 7.6, 1.4 Hz, 1H), 5.15 (s, 1H), 4.01 (dq, *J* = 10.6, 6.1 Hz, 1H), 3.44 (d, *J* = 10.6 Hz, 1H), 2.47 (s, 3H), 1.23 (d, *J* = 6.1 Hz, 3H), 1.03 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 169.7, 139.6, 136.2, 129.5, 127.4, 126.0, 125.9, 109.0, 77.1, 56.1, 35.5, 24.1, 19.6, 15.9.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2978, 2962, 2872, 1738, 1592, 1574, 1482, 1440, 1422, 1410, 1378, 1366, 1342, 1278, 1234, 1212, 1150, 1112, 1086, 1030, 992, 968, 938, 926, 914, 780, 760, 738, 696.
MS (EI, 70 eV): *m/z* (%) = 294 (6), 181 (19), 165 (11), 164 (100), 163 (13), 117 (60), 115 (15).
HR-MS (EI, 70 eV): [$C_{16}H_{22}O_3S$], calcd.: 294.1290; found: 294.1281.
cHPLC: Chiracel OJ-H; heptane:*i*-PrOH = 98:2; 1 mL·min^{-1}; 211 nm; R_f(*S**) = 12.29 min; R_f(*R**) = 20.01 min.
Optical Rotation: $[\alpha]_D^{20}$ = +4.3 (c = 1.0, $CHCl_3$).
m.p.: 56 – 57 °C.

(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-5-(6-methoxynaphthalen-2-yl)-6-methyl-1,3-dioxan-4-one (79f)

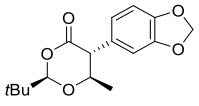


According to **TP1**, *α*-bromolactone **78a** (126 mg, 0.50 mmol, 1.00 equiv) was coupled

with (6-methoxynaphthalen-2-yl)zinc chloride **76f** (0.75 mmol, 1.50 equiv) using $CoCl_2$ (13 mg, 0.10 mmol, 20 mol%) and PPh_3 (26 mg, 0.10 mmol, 20 mol%) as catalytic system. The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **79f** as colorless solid (82% yield, dr = 99:1, 99% *ee*, 134 mg, 0.41 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.74 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 8.9 Hz, 1H), 7.60 (d, *J* = 1.8 Hz, 1H), 7.23 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.16 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.12 (d, *J* = 2.5 Hz, 1H), 5.22 (s, 1H), 4.26 – 4.02 (m, 1H), 3.91 (s, 3H), 3.62 (d, *J* = 10.6 Hz, 1H), 1.26 (d, *J* = 6.1 Hz, 3H), 1.06 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 170.2, 158.0, 134.1, 130.6, 129.3, 129.0, 128.6, 127.8, 126.9, 119.4, 109.0, 105.7, 77.2, 56.2, 55.4, 35.5, 24.1, 19.6.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2962, 2906, 2874, 1730, 1630, 1606, 1484, 1462, 1394, 1378, 1364, 1342, 1266, 1234, 1218, 1204, 1176, 1162, 1142, 1110, 1080, 1026, 992, 980, 960, 946, 936, 922, 900, 882, 846, 826, 812, 756, 736, 718, 668.
MS (EI, 70 eV): *m/z* (%) = 328 (37), 243 (47), 215 (27), 199 (56), 198 (100), 155 (24).
HR-MS (EI, 70 eV): [$C_{20}H_{24}O_4$], calcd.: 328.1675; found: 328.1668.
cHPLC: Chiracel OJ-H; heptane:*i*-PrOH = 98:2; 1 mL·min^{-1}; 232 nm; R_f(*R**) = 39.7 min; R_f(*S**) = 45.9 min.
Optical Rotation: $[\alpha]_D^{20}$ = +64.2 (c = 1.0, EtOAc).
m.p.: 199 – 200 °C.

(2*R*,5*R*,6*R*)-5-(Benzo[*d*][1,3]dioxol-5-yl)-2-(*tert*-butyl)-6-methyl-1,3-dioxan-4-one (79g)



According to **TP1**, *α*-bromolactone **78a** (126 mg, 0.50 mmol, 1.0 equiv) was coupled with benzodioxolylzinc chloride **76g** (0.75 mmol, 1.5 equiv) using $CoCl_2$ (13 mg, 0.10 mmol, 20 mol%) and PPh_3 (26 mg, 0.10 mmol, 20 mol%) as catalytic system. The crude product was purified by column chromatography on silica using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **79g** as colorless oil (73% yield, dr = 99:1, 99% *ee*, 107 mg, 0.37 mmol).

^{1}H-NMR (400 MHz, benzene-D_6, ppm): δ = 6.58 (d, *J* = 7.9 Hz, 1H), 6.48 (d, *J* = 1.8 Hz, 1H), 6.29 (dd, *J* = 7.9, 1.8 Hz, 1H), 5.29 (dd, *J* = 13.0, 1.4 Hz, 2H), 4.71 (s, 1H), 3.44

(dq, *J* = 10.5, 6.0 Hz, 1H), 3.00 (d, *J* = 10.7 Hz, 1H), 1.02 (s, 9H), 0.86 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR (101 MHz, benzene-D$_6$, ppm): δ = 168.2, 148.4, 147.6, 129.9, 123.2, 109.8, 108.6, 108.1, 101.2, 77.1, 55.9, 35.4, 24.1, 19.3.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2978, 2962, 2906, 2874, 1738, 1506, 1486, 1464, 1444, 1410, 1378, 1366, 1340, 1278, 1246, 1228, 1212, 1152, 1112, 1084, 1030, 992, 968, 930, 806, 762, 734.

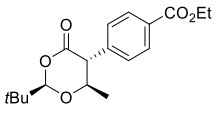
MS (EI, 70 eV): *m/z* (%) = 292 (7), 207 (17), 163 (11), 162 (100), 43 (32).

HR-MS (EI, 70 eV): [$C_{16}H_{20}O_5$], calcd.: 292.1311; found: 292.1298.

cHPLC: Chiracel OJ-H; heptane:*i*-PrOH = 9:1; 1 mL·min^{-1}; 234 nm; R_f(*R**) = 10.4 min; R_f(*S**) = 7.9 min.

Optical Rotation: $[\alpha]_D^{20}$ = +13.4 (c = 1.0, $CHCl_3$).

Ethyl 4-((2*R*,4*R*,5*R*)-2-(*tert*-butyl)-4-methyl-6-oxo-1,3-dioxan-5-yl)benzoate (79h)



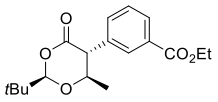
A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum, was charged with ethyl 4-iodobenzoate (207 mg, 0.75 mmol, 1.00 equiv) and dry THF (1.5 mL). The mixture was cooled to −20 °C, *i*PrMgCl·LiCl (0.50 mL, 0.83 mmol, 1.10 equiv) was added dropwise and stirred for 30 min. Solid $ZnCl_2$ (0.75 mmol, 1.00 equiv) was placed in a dry and argon flushed *Schlenk*-tube equipped with a magnetic stirring bar and a septum and dried under vacuum at 250 °C for 5 min. After cooling to rt under vacuum, an argon atmosphere was applied and THF (1.5 mL) was added. The solution was added to the Grignard reagent at −20 °C. The mixture containing arylzinc reagent **76i** was allowed to warm to rt and stirred for 15 min.

A dry and argon-flushed 20 mL *Schlenk*-tube, equipped with a stirring bar and a septum, was charged with $CoCl_2$ (13 mg, 0.10 mmol, 20 mol%). The solid was flame dried under high vacuum for 5 min. After cooling to rt, PPh_3 (26 mg, 0.10 mmol, 20 mol%) and the *α*-bromolactone **79a** (126 mg, 0.50 mmol, 1.00 equiv) was added. The mixture was dissolved in THF (1 mL) and cooled to −20 °C. The freshly prepared organozinc chloride **76i** was added and the mixture was allowed to warm to rt overnight. Sat. aq. NH_4Cl (5 mL) and ethyl acetate (5 mL) were added, the phases were separated and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to

column chromatography purification on using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **79h** as a mixture of diastereomers (76% yield, dr = 50:50, 121 mg, 0.38 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 8.09 – 8.00 (m, 2H), 7.31 – 7.22 (m, 2H), 5.17 (s, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 4.03 (dq, *J* = 10.5, 6.1 Hz, 1H), 3.55 (d, *J* = 10.6 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.27 – 1.19 (m, 3H), 1.03 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 169.3, 166.2, 140.4, 130.3, 130.3, 129.4, 109.1, 61.2, 56.1, 35.5, 29.8, 24.1, 19.6, 14.5.
HR-MS (EI, 70 eV): [$C_{18}H_{24}O_5$], calcd.: 320.1624; found: 320.1632.

Ethyl 3-((2*R*,4*R*,5*R*)-2-(*tert*-butyl)-4-methyl-6-oxo-1,3-dioxan-5-yl)benzoate (79i)



A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum, was charged with ethyl 3-iodobenzoate (207 mg, 0.75 mmol, 1.00 equiv) and dry THF (1.5 mL). The mixture was cooled to −20°C, *i*PrMgCl·LiCl (0.50 mL, 0.83 mmol, 1.10 equiv) was added dropwise and stirred for 30 min. Solid $ZnCl_2$ (0.75 mmol, 1.00 equiv) was placed in a dry and argon flushed *Schlenk*-tube equipped with a magnetic stirring bar and a septum and dried under vacuum at 250 °C for 5 min. After cooling to rt under vacuum, an argon atmosphere was applied and THF (1.5 mL) was added. The solution was added to the Grignard reagent at −20 °C. The mixture containing arylzinc reagent **76j** was allowed to warm to rt and stirred for 15 min.
A dry and argon-flushed 20 mL *Schlenk*-tube, equipped with a stirring bar and a septum, was charged with $CoCl_2$ (13 mg, 0.10 mmol, 20 mol%). The solid was flame dried under high vacuum for 5 min. After cooling to rt, PPh_3 (26 mg, 0.10 mmol, 20 mol%) and the *α*-bromolactone **78a** (126 mg, 0.50 mmol, 1.00 equiv) was added. The mixture was dissolved in THF (1 mL) and cooled to −20 °C. The freshly prepared organozinc chloride **76j** was added and the mixture was allowed to warm to rt overnight. Sat. aq. NH_4Cl (5 mL) and ethyl acetate (5 mL) were added, the phases were separated and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification on using *i*-hexane/ethyl acetate (9:1) as an eluent to afford **79i** as colorless oil (52% yield, dr = 99:1, 83 mg, 0.26 mmol).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.99 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.86 (t, *J* = 1.8 Hz,

1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.37 (dt, *J* = 7.7, 1.6 Hz, 1H), 5.18 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 4.06 (dq, *J* = 10.6, 6.1 Hz, 1H), 3.53 (d, *J* = 10.7 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.22 (d, *J* = 6.0 Hz, 3H), 1.03 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 169.6, 166.2, 135.8, 133.8, 131.3, 130.2, 129.2, 129.2, 109.0, 76.9, 61.3, 55.9, 35.5, 24.0, 19.5, 14.4.

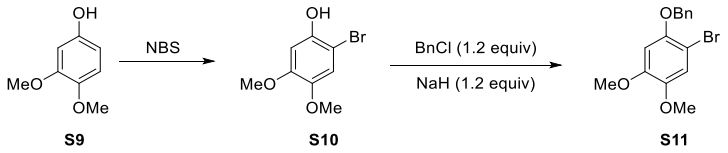
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2980, 2964, 2938, 2906, 2874, 1734, 1716, 1367, 1343, 1283, 1236, 1213, 1189, 1150, 1107, 1084, 1029, 993, 970, 912, 764, 751, 729, 705, 695.

MS (EI, 70 eV): *m/z* (%) = 275 (20), 235 (24), 217 (18), 191 (32), 190 (100), 162 (17), 161 (46), 145 (87), 117 (41), 115 (30), 91 (23), 57 (21).

HR-MS (EI, 70 eV): $[C_{18}H_{23}O_5] = [M-H]^+$, calcd.: 319.1545; found: 319.1547.

2.5 Total Synthesis of the Rotenoid Derivative MOM-Protected Munduserol (80)

1-(Benzyloxy)-2-bromo-4,5-dimethoxybenzene (S11)



3,4-Dimethoxyphenol (**S9**, 5.00 g, 32.4 mmol, 1.00 equiv) was dissolved in freshly distilled CH_2Cl_2 (60 mL) and cooled to 0 °C. *N*-Bromosuccinimide (5.77 g, 32.4 mmol, 1.00 equiv) was added slowly, the reaction mixture was allowed to warm to rt and stirred for 16 h. The reaction was stopped by adding sodium thiosulfate (15 mL), a sat. solution of NH_4Cl (15 mL) and water (15 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 8:2). 2-Bromo-4,5-dimethoxyphenol (**S10**) was isolated as a brown solid (4.78 g, 20.5 mmol, 63% yield).

2-Bromo-4,5-dimethoxyphenol (**S10**, 4.78 g, 20.5 mmol, 1.00 equiv) was dissolved in THF (40 mL). The solution was cooled to 0 °C and sodium hydride (60% in paraffin oil, 1.07 g, 26.7 mmol, 1.30 equiv) was added slowly. The reaction mixture was allowed to warm to rt and stirred for 30 min. Benzyl bromide (3.65 mL, 30.8 mmol, 1.50 equiv) was added and the mixture was refluxed at 80 °C overnight. Water (100 mL) was added and the mixture was extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 9:1). 1-(Benzyloxy)-2-bromo-4,5-dimethoxybenzene (**S11**) was isolated as a as yellowish solid (5.51 g, 17.1

mmol, 83% yield).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.56 – 7.44 (m, 2H), 7.44 – 7.36 (m, 2H), 7.36 – 7.30 (m, 1H), 7.04 (s, 1H), 6.56 (s, 1H), 5.10 (s, 2H), 3.83 (s, 3H), 3.80 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 149.4, 148.9, 144.4, 136.8, 128.7, 128.2, 127.5, 116.1, 102.6, 101.6, 72.7, 56.6, 56.3.

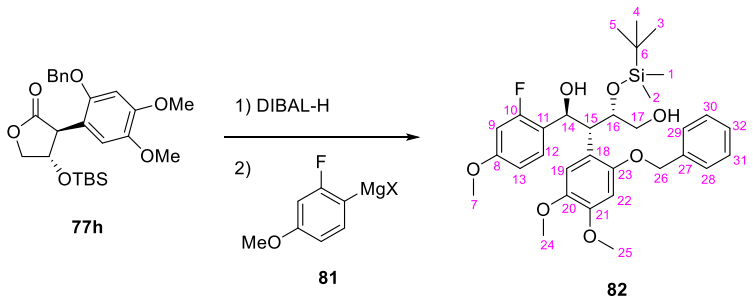
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3084, 2998, 2969, 2952, 2934, 2920, 2909, 2899, 2877, 2845, 1580, 1503, 1462, 1455, 1445, 1437, 1392, 1373, 1331, 1276, 1264, 1247, 1211, 1199, 1186, 1168, 1164, 1119, 1083, 1045, 1033, 1027, 1011, 997, 975, 966, 922, 843, 817, 804, 759, 727, 700.

MS (EI, 70 eV): *m/z* (%) = 324 (16), 322 (17), 244 (11), 243 (71), 233 (44), 231 (43), 211 (10), 205 (42), 203 (41), 190 (17), 188 (17), 175 (11), 173 (11), 91 (100).

HR-MS (EI, 70 eV): [$C_{15}H_{15}BrO_3$], calcd.: 322.0205; found: 322.0197.

m.p.: 80 – 81 °C.

(1*S*,2*R*,3*S*)-2-(2-(Benzyloxy)-4,5-dimethoxyphenyl)-3-((*tert*-butyldimethylsilyl)oxy)-1-(2-fluoro-4- methoxyphenyl)butane-1,4-diol (82)



A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with the chiral arylated lactone **77h** (3.45 g, 7.52 mmol, 1.00 equiv) and dry CH_2Cl_2 (40 mL) was added. The solution was cooled to -78 °C and a solution of diisobutylaluminum hydride (1.0 M in CH_2Cl_2, 11.3 mL, 11.3 mmol, 1.50 equiv) was added dropwise to the reaction. Upon disappearance of the starting material (TLC, after 2.5 h) the reaction was quenched with sat. aq. Rochelle's salt (10 mL) and EtOAc (10 mL) and allowed to warm to rt and stirred for another 30 min. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (5 x 20 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue containing the corresponding lactol was used without further purification for the next step.

The crude lactol was dissolved in THF (8 mL) and slowly added to the arylmagnesium reagent **81** (19.5 mL, 15.0 mmol, 2.00 equiv) at 0 °C. The mixture was allowed to warm to rt and stirred for 16 h. Sat. aq. NH_4Cl (15 mL) and EtOAc (15 mL) was added. The

layers were separated, and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 7:3) to afford the alcohol **82** as a foamy solid (3.80 g, 6.49 mmol, 86% yield over two steps).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.39 – 7.33 (m, 2H, H-12, H-19), 7.30 (d, *J* = 7.6 Hz, 2H, H-27-28), 7.20 (dd, *J* = 7.5 Hz, 2H, H-29-30), 7.11 (t, *J* = 7.4 Hz, 1H, H-31), 6.50 (dd, *J* = 8.6, 2.4 Hz, 1H, H-13), 6.25 (dd, *J* = 12.1, 2.5 Hz, 1H, H-9), 6.15 (s, 1H, H-22), 5.66 (d, *J* = 10.6 Hz, 1H, H-14), 4.81 (dd, *J* = 5.7, 2.8 Hz, 1H, H-16), 4.62 (d, *J* = 11.7 Hz, 1H, H-26'), 4.51 (d, *J* = 11.8 Hz, 1H, H-26), 4.15 (dd, *J* = 10.5, 2.6 Hz, 1H, H-15), 3.82 (s, 3H, H-25), 3.68 (dd, *J* = 11.1, 5.6 Hz, 1H, H-17'), 3.46 (dd, *J* = 11.2, 7.9 Hz, 1H, H-17), 3.23 (s, 3H, H-24), 3.00 (s, 3H, H-7), 2.54 (s, 1H, OH), 1.04 (s, 9H, H-3-4), 0.32 (s, 3H, H-1/2), 0.16 (s, 3H, H-1/2).

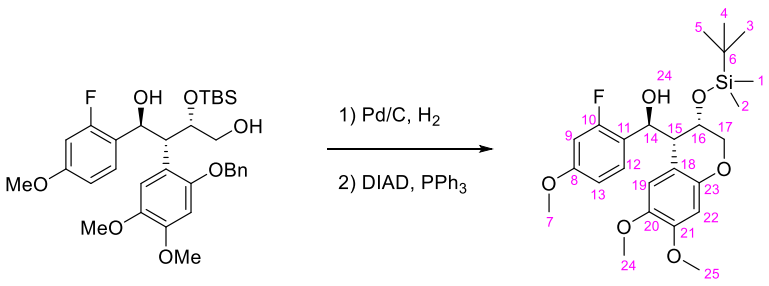
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 161.2 (d, *J* = 244.5 Hz, C-10), 160.4 (d, *J* = 11.0 Hz, C-8), 150.9 (C-23), 149.1 (C-20), 144.5 (C-21), 137.6 (C-27), 129.4 (d, *J* = 6.4 Hz, C-12), 129.0 (C-30-31), 127.8 (C-32), 127.6 (C-28-29), 123.7 (d, *J* = 13.9 Hz, C-11), 118.5 (C-18), 116.1 (C-19), 111.0 (d, *J* = 2.9 Hz, C-13), 100.7 (d, *J* = 26.9 Hz, C-9), 100.0 (C-22), 73.0 (C-16), 72.1 (C-26), 66.9 (C-14), 65.6 (C-17), 56.5 (C-25), 55.5 (C-24), 54.8 (C-7), 45.3 (C-15), 26.3 (C-3-5), 18.5 (C-6), -4.4 (d, *J* = 38.2 Hz, C-1-2).

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3489, 2953, 2932, 2855, 1737, 1624, 1613, 1587, 1507, 1484, 1464, 1444, 1401, 1374, 1360, 1313, 1248, 1214, 1191, 1153, 1106, 1092, 1033, 1025, 973, 948, 920, 889, 859, 830, 812, 775, 735, 696, 667.

HR-MS (EI, 70 eV): [$C_{32}H_{43}FO_7Si$], calcd.: 586.2762; found: 586.2760.

Optical Rotation: $[\alpha]_D^{20}$ = +13.4 (c = 1.0, $CHCl_3$).

(*S*)-((3*S*,4*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-6,7-dimethoxychroman-4-yl)(2-fluoro-4-methoxyphenyl)methanol (83)



82 **83**

A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with the benzyl protected alcohol **82** (2.76 g, 4.70 mmol, 1.00 equiv). Pd/C (10 mol%) and dry ethanol (30 mL) was added. H_2 was bubbled through the mixture for 1 min at rt. The reaction was stirred under H_2 (1 atm.) for 3 h until full consumption of the starting material was observed *via* TLC. The reaction was filtered over celite and rinsed with EtOAc (100 mL). The solution was dried over Na_2SO_4, the solvents were evaporated under reduced pressure and the residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 1:1) to afford the deprotected product as a colorless solid.

A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum, was charged with the aromatic alcohol (2.00 g, 4.04 mmol, 1.00 equiv) and PPh_3 (1.27 g, 4.85 mmol, 1.20 equiv). The mixture was dissolved in CH_2Cl_2 (16 mL) and cooled to 0 °C. Diisopropyl azodicarboxylate (2.34 mL, 4.45 mmol, 1.10 equiv) was added and stirring was continued for 2 h until full consumption of the starting material was observed *via* TLC. The reaction was warmed to rt and sat. aq. NH_4Cl (5 mL) and CH_2Cl_2 (5 mL) were added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3x20 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 7:3) to afford product **83** as a yellowish oil (1.67 g, 3.49 mmol, 74% yield over two steps).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.46 (t, *J* = 8.6 Hz, 1H, H-12), 6.97 (s, 1H, H-24), 6.67 (dd, *J* = 8.9, 2.6 Hz, 1H, H-13), 6.66 (s, 1H, H-19), 6.53 (dd, *J* = 12.4, 2.5 Hz, 1H, H-9), 6.47 (s, 1H, H-22), 5.51 (d, *J* = 10.1 Hz, 1H, H-14), 4.51 (dt, *J* = 8.0, 6.7 Hz, 1H, H-16), 4.21 (dd, *J* = 8.8, 6.9 Hz, 1H, H-17'), 3.93 (dd, *J* = 8.7, 6.3 Hz, 1H, H-17), 3.78 (s, 3H, H-24), 3.77 (s, 3H, H-25), 3.74 (s, 3H, H-7), 3.64 (dd, *J* = 10.1, 8.0 Hz, 1H, H-15), 0.89 (s, 9H, H-3-5), 0.02 (d, *J* = 15.9 Hz, 6H, H-1-2).

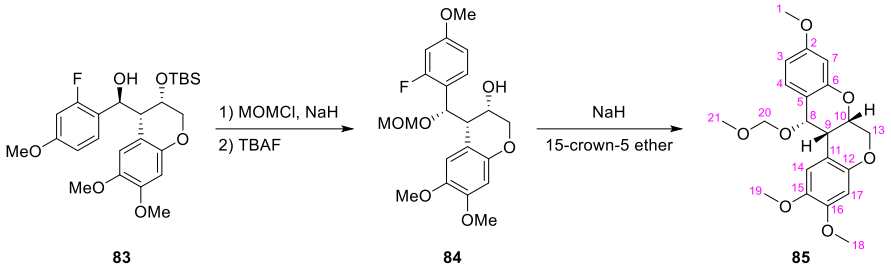
^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 161.3 (d, *J* = 246.1 Hz, C-10), 160.9 (d, *J* = 11.4 Hz, C-8), 149.7 (C-23), 148.8 (C-21), 142.8 (C-20), 129.1 (d, *J* = 5.7 Hz, C-12), 118.5 (d, *J* = 13.0 Hz, C-11), 114.4 (C-15), 110.7 (d, *J* = 2.9 Hz, C-13), 110.3 (C-19), 101.8 (C-22), 101.3 (d, *J* = 26.2 Hz, C-9), 80.4 (C-16), 74.8 (C-14), 73.5 (C-17), 56.5 (C-24), 55.9 (C-25), 55.6 (C-7), 54.3 (C-15), 25.8 (C-3-5), 18.0 (C-6), -4.8 (d, *J* = 40.4 Hz, C-1-2).

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3323, 2980, 2969, 2954, 2934, 2883, 2856, 1709, 1626, 1588, 1510, 1465, 1451, 1417, 1374, 1311, 1229, 1203, 1180, 1153, 1106, 1076, 1043, 1029, 1006, 948, 933, 897, 833, 812, 775, 729, 671.

HR-MS (EI, 70 eV): [$C_{25}H_{35}FO_6Si$], calcd.: 478.2187; found: 478.2181.

Optical Rotation: $[\alpha]_D^{20}$ = +28 (c = 1.0, $CHCl_3$).

MOM-Protected Munduserol (80)



83 **84** **85**

The benzylic alcohol **83** (1.10 g, 2.30 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (5 mL) and the mixture was cooled to 0 °C. NaH (184 mg, 7.67 mmol, 2.00 equiv) was added, stirring at 0 °C was continued for 30 min and chloromethyl methyl ether (0.44 mL, 5.78 mmol, 2.50 equiv) was added. The reaction was allowed to warm to 25 °C and stirred overnight. Sat. aq. NH_4Cl (15 mL) and CH_2Cl_2 (20 mL) were added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 8:2) to afford the MOM- and TBS-protected compound.

This intermediate was dissolved in THF (8 mL) and cooled to 0 °C. TBAF (1.0 M in THF, 2.88 mL, 2.88 mmol, 1.50 equiv) was added, and the mixture was stirred for 2 h. Sat. aq. NH_4Cl (20 mL) and EtOAc (20 mL) was added, the layers were separated, and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to column chromatography purification (silica, *i*-hexane/EtOAc 3:7) to afford **84** as a yellowish oil (502 mg, 1.23 mmol, 53% yield over two steps).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.46 (t, J = 8.5 Hz, 1H), 6.72 (d, J = 4.5 Hz, 2H), 6.68 (ddd, J = 8.6, 2.5, 0.8 Hz, 1H), 6.50 (dd, J = 12.2, 2.5 Hz, 1H), 5.26 (d, J = 9.1 Hz, 1H), 5.05 (d, J = 6.7 Hz, 1H), 4.99 (d, J = 6.7 Hz, 1H), 4.58 (td, J = 5.8, 3.8 Hz, 1H), 4.31 – 4.22 (m, 1H), 4.08 (dd, J = 9.5, 3.8 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.74 (s, 3H), 3.59 (dd, J = 9.2, 5.5 Hz, 1H), 3.41 (s, 3H), 2.58 (s, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 161.1 (d, J = 246.6 Hz), 160.5 (d, J = 11.1 Hz), 149.8, 148.5, 144.3, 128.7 (d, J = 6.0 Hz), 119.5 (d, J = 13.3 Hz), 118.9, 111.5, 110.3 (d, J = 2.9 Hz), 101.4 (d, J = 25.8 Hz), 101.1, 96.0, 79.4, 78.9, 74.9, 56.6, 56.6, 56.2, 56.1, 55.6.

HR-MS (EI, 70 eV): [$C_{21}H_{25}FO_7$], calcd.: 408.1584; found: 408.1572.

A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum, was charged with the alcohol **84** (37 mg, 0.091 mmol, 1.00 equiv), toluene (4.5 mL) and DMPU (0.5 mL). 15-crown-5 ether (38 µL, 0.191 mmol, 2.10 equiv) and NaH (60% in paraffin oil, 12 mg, 0.28 mmol, 3.10 equiv) were added and the mixture was heated to 110 °C for 48 h. The mixture was allowed to cool to rt and sat. aq. NH_4Cl (2 mL) and EtOAc (2 mL) were added. The layers were separated, and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue was subjected to preparative thin-layer chromatography purification (silica, *i*-hexane/EtOAc 5:5) to afford the rotenoid derivative **80** as a yellow oil (10 mg, 0.026 mmol, 28% yield). Since there is no step, which involves a possible epimerization of the β-center bearing the OTBS group in **77h** we can assume, that the product **80** should not only be diastereomerically pure, but also enantiomerically pure. However, we did not perform the all synthesis with the enantiomer of **77h**.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.17 (s, 1H, H-14), 7.02 (d, *J* = 8.1 Hz, 1H, H-4), 6.81 (s, 1H, H-17), 6.44 (d, *J* = 2.4 Hz, 1H, H-7), 6.42 (dd, *J* = 8.1, 2.4 Hz, 1H, H-3), 5.21 (d, *J* = 6.9 Hz, 1H, H-20), 5.18 (d, *J* = 6.9 Hz, 1H, H-20'), 5.05 (s, 1H, H-8), 4.84 (d, *J* = 3.3 Hz, 1H, H-10), 4.22 (d, *J* = 10.6 Hz, 1H, H-13), 3.98 (dd, *J* = 10.6, 3.5 Hz, 1H, H-13'), 3.96 (s, 1H, H-9), 3.88 (s, 3H, H-18), 3.86 (s, 3H, H-19), 3.78 (s, 3H, H-1), 3.50 (s, 3H, H-21).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm): δ = 161.4 (C-2), 154.3 (C-6), 149.6 (C-12), 148.9 (C-16), 144.4 (C-15), 127.6 (C-4), 120.6 (C-5), 117.9 (C-11), 111.1 (C-14), 106.0 (C-3), 101.9 (C-7), 100.2 (C-17), 95.5 (C-20), 81.6 (C-10), 77.2 (C-8), 73.5 (C-13), 56.8 (C-19), 56.3 (C-21), 56.2 (C-18), 55.5 (C-1), 43.2 (C-9).

NOE-NMR shows a proximity of H-8 and H-9.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2958, 2935, 2840, 1623, 1587, 1508, 1465, 1444, 1314, 1272, 1210, 1189, 1148, 1122, 1106, 1092, 1068, 1050, 1008, 949, 921, 833, 790, 752, 666.

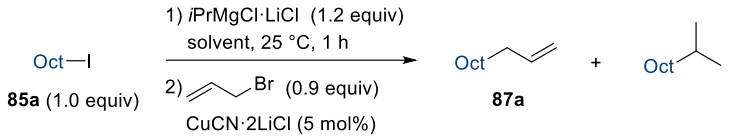
HR-MS (EI, 70 eV): [$C_{21}H_{25}O_7$] = [M+H], calcd.: 389.1600; found: 389.1601.

Optical Rotation: $[\alpha]_D^{20}$ = −18 (c = 1.0, $CHCl_3$).

3 Preparation of Primary and Secondary Dialkylmagnesiums *via* a Radical I/Mg-exchange Reaction using *s*Bu_2Mg in Toluene

3.1 Optimization of the Preparation of Primary Dialkylmagnesiums

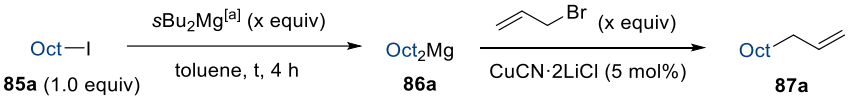
Table S2. Extended exchange reagent screening using octyl iodide (**85a**).



entry	solvent	GC-yield of **87a** [%][a]	GC-yield of 2-methyldecane [%]
1	THF	3	71[b]
2	toluene	21	14

[a] Reactions were performed on a 0.5 mmol scale. Yields were determined by GC-analysis using undecane ($C_{11}H_{24}$) as an internal standard. [b] Isolated yield.

Table S3. Extended optimization of reaction conditions.

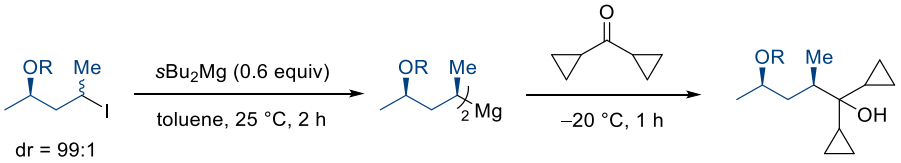


entry	t [°C]	equiv of *s*Bu_2Mg	equiv of allyl bromide	yield of **87a** [%][b]
1	25	0.6	1.0	55
2	25	0.6[c]	1.0	18
3	40	0.6	1.0	65
4	60	0.6	1.0	47
5	40	0.7	1.0	73
6	40	0.8	1.0	68
7	40	0.7	0.9	81
8	40	0.7	0.8	84
9	40	0.7	0.6	86

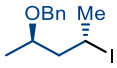
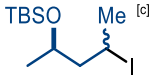
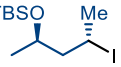
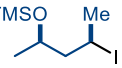
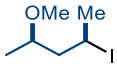
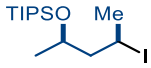
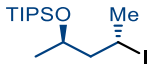
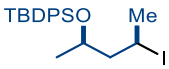
[a] Relevant formula is *s*$Bu_2Mg \cdot 0.5Et_2O$. [b] Reactions were performed on a 0.5 mmol scale. Yields were determined by GC-analysis using undecane ($C_{11}H_{24}$) as an internal standard. [c] Commercial *n*Bu_2Mg was used as an exchange reagent.

3.2 Protecting Group Effect on the Stereoconvergence of the Diorganomagnesium Formation

Table S4. Optimization of protecting group of 3-substituted secondary alkyl iodides.



dr = 99:1

entry	iodide	GC-yield[a] [%]	dr[b]
1		53	73:27
2		81	88:12
3		78[d]	88:12
4		43	82:18
5		41	60:40
6		72[d]	99:1
7		81[d]	99:1
8		traces	-

[a] Reactions were performed on a 0.25 mmol scale. Yields were determined by GC-analysis using undecane ($C_{11}H_{24}$) as an internal standard. [b] Diastereomeric ratio (dr) was determined by GC-analysis. [c] dr = 50:50. [d] Isolated yield.

3.3 Typical Procedure of Preparation 3-Substituted Secondary Alkyl Iodides

Protected alcohols were prepared according to the literature procedures[92a] from corresponding diastereomers of commercial 2,4-pentanediol or (2*R*, 4*R*)-(-)-2,4-pentanediol.

Iodine (1.2 eqiuv) was dissolved in CH_2Cl_2 (*ca.* 0.1 M) and cooled to −10 °C. Triphenylphosphine (1.2 eqiuv) was added and reaction mixture was stirred for 1 h at −10 °C. Then *N*-methylimidazole (1.2 equiv) was added dropwise and stirred for 10 min. Then solution of corresponding alcohol in CH_2Cl_2 (1 mL) was added. After further stirring

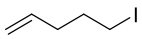
for 30 min reaction was quenched with sat. aq. ($NaHSO_3$+$Na_2S_2O_5$) solution and extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were dried over Na_2SO_4. The solvents were evaporated at 30 °C and the crude product was subjected to column chromatography furnishing the analytical pure iodide.[120] The analytical data were in full consistency with the data reported in the literature.[107]

3.4 Preparation of Starting Materials

Preparation of Primary Iodides TP2[121]

Triphenylphosphine (1.05 equiv) and imidazole (1.05 equiv) were dissolved in CH_2Cl_2 (0.3 M) and cooled to 0 °C. Iodine (1.05 equiv) was added over 15 min and the corresponding alcohol (1.00 equiv) was added dropwise. The reaction mixture was allowed to warm to room temperature and was stirred overnight. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution. The phases were separated and the aqueous layer was extracted 3× with CH_2Cl_2. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvents were evaporated and the crude product was subjected to column chromatography furnishing the analytical pure iodide.

1-Iodo-4-pentene (85b)

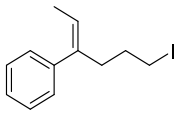


The title compound was prepared according to the literature procedure from 5-bromo-1-pentene (0.45 g, 3 mmol) and was obtained as a colorless oil (0.56 g, 2.9 mmol, 95% yield). The analytical data were in full consistency with the data reported in the literature.[122]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.75 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.15 – 4.95 (m, 2H), 3.19 (t, J = 6.9 Hz, 2H), 2.16 (dtt, J = 7.6, 6.3, 1.4 Hz, 2H), 1.99 – 1.85 (m, 2H).

[120] A. Kremsmair, H.R. Wilke, M.M. Simon, Q. Schmidt, K. Karaghiosoff, P. Knochel, *Chem. Sci.* **2021**, DOI: 10.1039/d1sc05315a.
[121] H. Helmboldt, D. Köhler, M. Hiersemann, *Org. Lett.* **2006**, *8*, 1573.
[122] K. Heckenbichler, A. Schweiger, L.A. Brandner, A. Binter, M. Toplak, P. Macheroux, K. Gruber, R. Breinbauer, *Angew. Chem. Int. Ed.* **2018**, *57*, 7240-7244.

(*Z*)-(6-Iodohex-2-en-3-yl)benzene (85c)



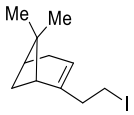
The title compound was prepared according **TP2** from (*Z*)-4-phenylhex-4-en-1-ol (1.76 g, 10 mmol) and was obtained as a pale pink oil (2.32 g, 8.1 mmol, 81% yield).[89]

Purification: *i*-hexane:ethyl acetate = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.35 – 7.29 (m, 4H), 7.25 – 7.20 (m, 1H), 5.81 (q, *J* = 6.9 Hz, 1H), 3.15 (t, *J* = 6.8 Hz, 2H), 2.69 – 2.59 (m, 2H), 1.87 (dd, *J* = 13.5, 7.2 Hz, 5H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 142.80, 139.08, 128.44, 126.81, 126.35, 124.48, 32.16, 30.04, 14.58, 6.90.

2-(2-Iodoethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (85d)

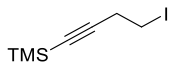


The title compound was prepared according to **TP2** from (*R*)-nopol (1.66 g, 10 mmol) and was obtained as a pale pink oil (2.57 g, 9.3 mmol, 93% yield). The analytical data were in full consistency with the data reported in the literature.[123]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.31 (s, 1H), 3.22 – 3.05 (m, 2H), 2.61 – 2.47 (m, 2H), 2.37 (dt, *J* = 8.6, 5.6 Hz, 1H), 2.31 – 2.12 (m, 2H), 2.12 – 2.05 (m, 1H), 2.00 (td, *J* = 5.6, 1.6 Hz, 1H), 1.27 (s, 3H), 1.18 (d, *J* = 8.6 Hz, 1H), 0.84 (s, 3H).

[123] C. Dai, J.M.R. Narayanam, C.R.J. Stephenson, *Nat. Chem.* **2011**, *3*, 140-145.

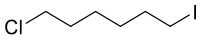
(4-Iodobut-1-yn-1-yl)trimethylsilane (85e)



The title compound was prepared according to **TP2** from 4-(trimethylsilyl)but-3-yn-1-ol (1.14 g, 8 mmol) and was obtained as a colorless oil (1.77 g, 7 mmol, 88% yield). The analytical data were in full consistency with the data reported in the literature.[124]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 3.22 (t, J = 7.5 Hz, 2H), 2.79 (t, J = 7.5 Hz, 2H), 0.16 (s, 9H).

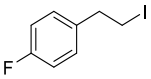
1-Chloro-6-iodohexane (85f)



The title compound was prepared according to **TP2** from 6-chloro-1-hexanol (0.41 g, 3 mmol) and was obtained as a colorless oil (0.52 g, 2.1 mmol, 70% yield). The analytical data were in full consistency with the data reported in the literature.[125]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 3.54 (t, J = 6.6 Hz, 2H), 3.19 (t, J = 6.9 Hz, 2H), 1.90 – 1.72 (m, 4H), 1.54 – 1.37 (m, 4H).

1-Fluoro-4-(2-iodoethyl)benzene (85g)

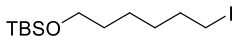


The title compound was prepared according to the literature procedure from 1-(2-bromoethyl)-4-fluorobenzene (2.03 g, 10 mmol) and was obtained as a colorless oil (2.22 g, 8.9 mmol, 89% yield). The analytical data were in full consistency with the data reported in the literature.[126]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.21 – 7.11 (m, 2H), 7.09 – 6.93 (m, 2H), 3.39 – 3.25 (m, 2H), 3.15 (t, J = 7.6 Hz, 2H).

[124] R. Frei, M.D. Wodrich, D. Prasad Hari, P.-A. Borin, C. Chauvier, J. Waser, *J. Am. Chem. Soc.* **2014**, *136*, 16563-16573.
[125] K. Mori, Y. Shikichi, S. Shankar, J. Y. Yew, *Tetrahedron* **2010**, *66*, 7161-7168.
[126] A.R. Mackenzie, S.M. Monaghan, US5677324A (**1997**).

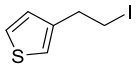
***Tert*-butyl((6-iodohexyl)oxy)dimethylsilane (85h)**



The title compound was prepared according to **TP2** from ((6-bromohexyl)oxy)(*tert*-butyl)dimethylsilane (1.16 g, 5 mmol) and was obtained as a colorless oil (1.42 g, 4.1 mmol, 83% yield). The analytical data were in full consistency with the data reported in the literature.[127]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 3.60 (t, J = 6.4 Hz, 2H), 3.19 (t, J = 7.0 Hz, 2H), 1.83 (p, J = 7.0 Hz, 2H), 1.63 – 1.45 (m, 2H), 1.45 – 1.21 (m, 3H), 0.89 (s, 10H), 0.04 (s, 6H).

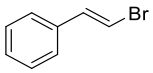
3-(2-Iodoethyl)thiophene (85i)



The title compound was prepared according to **TP2** from 2-(thiophen-3-yl)ethan-1-ol (0.64 g, 5 mmol) and was obtained as a colorless oil (1.04 g, 4.3 mmol, 87% yield). The analytical data were in full consistency with the data reported in the literature.[128]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.29 (dd, J = 5.0, 2.9 Hz, 1H), 7.06 (dd, J = 2.8, 1.3 Hz, 1H), 6.96 (dd, J = 5.0, 1.3 Hz, 1H), 3.41 – 3.31 (m, 2H), 3.22 (t, J = 7.6 Hz, 2H).

(*E*)-(2-Bromovinyl)benzene (S12)



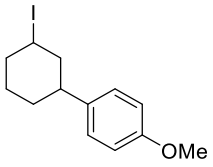
The title compound was prepared according to the literature procedure from *E*/*Z* mixture of *β*-bromostyrene. The analytical data were in full consistency with the data reported in the literature.[129]

[127] J.J.S. Lamba, J.M. Tour, *J. Am. Chem. Soc.* **1994**, *116*, 11723-11736.
[128] A.K.A. de Almeida, J.M.M. Dias, A.J.C. Silva, M. Navarro, S.A. Junior, J. Tonholo, A.S. Ribeiro, *Synth. Met.* **2013** *171*, 45-50; Y. Ikenoue, N. Outani, A.O. Patil, F. Wudl, A.J. Heeger, *Synth. Met.* **1989**, *30*, 305-319.

[129] D. Müller, A. Alexakis, *Org. Lett.* **2012**, *14*, 1842-1845.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.37 – 7.27 (m, 5H), 7.11 (d, J = 14.0 Hz, 1H), 6.78 (d, J = 14.0 Hz, 1H).

1-(3-Iodocyclohexyl)-4-methoxybenzene (88b)

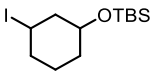


The title compound was prepared according to the literature procedure from 2-cyclohexenone. The analytical data were in full consistency with the data reported in the literature.[130]

dr = 99:1

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.22 – 7.02 (m, 2H), 6.92 – 6.69 (m, 2H), 3.79 (s, 3H), 3.10 (tt, *J* = 11.8, 3.4 Hz, 1H), 2.23 (dddd, *J* = 14.5, 5.3, 3.2, 2.0 Hz, 1H), 2.11 (dtt, *J* = 14.7, 3.4, 1.5 Hz, 1H), 2.02 – 1.83 (m, 2H), 1.80 – 1.61 (m, 2H), 1.61 – 1.38 (m, 2H), 0.92 – 0.79 (m, 1H).

***Tert*-butyl((3-iodocyclohexyl)oxy)dimethylsilane (88c)**

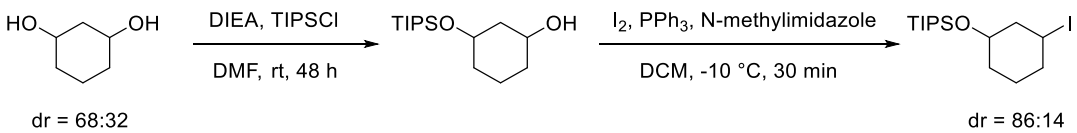


The title compound was prepared according to the literature procedure from 1,3-cyclohexanediol. The analytical data were in full consistency with the data reported in the literature.[131]

dr = 84:16

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.65 (tt, *J* = 8.5, 4.2 Hz, 1H), 4.00 – 3.95 (m, 1H), 2.22 – 1.85 (m, 3H), 1.85 – 1.70 (m, 1H), 1.57 (ddt, *J* = 18.4, 11.9, 5.4 Hz, 3H), 1.41 – 1.07 (m, 1H), 0.89 (s, 9H), 0.04 (d, *J* = 2.4 Hz, 6H).

((3-Iodocyclohexyl)oxy)triisopropylsilane (88d)



dr = 68:32

dr = 86:14

[130] L. Thomas, F.H. Lutter, M.S. Hofmayer, K. Karaghiosoff, P. Knochel, *Org. Lett.* **2018**, *20,* 2441-2444.
[131] T. Thaler, L.-N. Guo, P. Mayer, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50,* 2174-2177.

A dry and argon flushed Schlenk-tube, equipped with a magnetic stirrer and a septum, was charged with 1,3-cyclohexanediol (581 mg, 5 mmol), anhydrous *N*,*N*-dimethylformamide (DMF) (15 mL) and redistilled *N*,*N*-diisopropylethylamine (DIEA) (8.5 mL, 50 mmol) forming a biphasic mixture at room temperature. Triisopropylsilyl chloride (TIPSCl) (1.12 mL, 5.25 mmol) was added dropwise. The reaction mixture was stirred for 48 h. Upon completion, this mixture was quenched with cold water, extracted with diethyl ether (3×50 mL), and washed with 2N HCl, an aq. sat. $NaHCO_3$ and brine. The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue containing the crude protected alcohol (622 mg, 2.29 mmol, 46% yield) as a colorless oil was used in the next step without further purification.[132]

Iodine (697 mg, 2.75 mmol) was dissolved in CH_2Cl_2 (*ca.* 0.1 M) and cooled to -10 °C. Triphenylphosphine (721 mg, 2.75 mmol) was added and reaction mixture was stirred for 1 h at −10 °C. Then *N*-methylimidazole (0.22 mL, 2.75 mmol) was added dropwise and stirred for 10 min. Then the solution of alcohol in CH_2Cl_2 (1 mL) was added. After further stirring for 30 min reaction mixture was quenched with sat. aq. ($NaHSO_3$+$Na_2S_2O_5$) solution and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried over Na_2SO_4. The solvents were evaporated at 30 °C and the crude product was subjected to column chromatography furnishing the analytical pure iodide.[108]

Isolated yield: 444 mg, 1.16 mmol, 27%, colorless oil.

Purification: *i*-hexane:diethyl ether = 200:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.67 (dtd, *J* = 12.8, 6.4, 3.9 Hz, 1H), 4.08 (p, *J* = 4.5 Hz, 1H), 2.22 – 2.03 (m, 3H), 1.94 (dtd, *J* = 13.0, 9.0, 3.7 Hz, 1H), 1.81 (dtt, *J* = 17.5, 9.1, 3.9 Hz, 1H), 1.64 (h, *J* = 3.3 Hz, 2H), 1.61 – 1.48 (m, 1H), 1.05 (d, *J* = 2.2 Hz, 21H). (Signals for the main stereomer are given).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 69.1, 47.1, 38.8, 33.8, 29.3, 22.6, 18.2, 12.4.

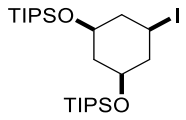
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2962, 2941, 2890, 2861, 2359, 2330, 1461, 1359, 1308, 1238, 1157, 1151, 1102, 1053, 1036, 883, 687, 685, 681, 679, 674, 668.

MS (EI, 70 eV): *m/z* (%) = 382 (1), 340 (11), 339 (68), 211 (10). 131 (11), 103 (14), 81 (100), 75 (25), 61 (16).

HR-MS (EI, 70eV): [$C_{15}H_{31}IOISi$], calcd.: 382.1189; found: 382.1185.

[132] C. Yu, B. Liu, L. Hu, *Tetrahedron Lett.* **2000**, *41,* 4281-4285.

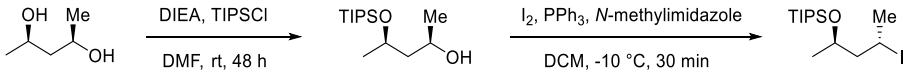
((5-Iodocyclohexane-1,3-diyl)bis(oxy))bis(triisopropylsilane) (88e)



The title compound was prepared by an analogous procedure of **88d** from commercial (1*α*,3*α*,5*α*)-1,3,5-cyclohexanetriol.

Isolated yield: 1385 mg, 2.50 mmol, 25%, colorless oil.
Purification: *i*-hexane:diethyl ether = 200:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.69 (p, *J* = 3.2 Hz, 1H), 4.21 (tt, *J* = 10.7, 4.0 Hz, 2H), 2.29 (dddt, *J* = 15.4, 9.4, 4.9, 2.2 Hz, 3H), 1.53 – 1.39 (m, 3H), 1.07 (d, *J* = 2.2 Hz, 42H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 68.0, 46.8, 44.5, 27.0, 18.2, 18.2, 12.4.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2943, 2892, 2866, 1463, 1382, 1233, 1116, 1087, 1075, 1064, 1013, 996, 906, 882, 866, 821, 781, 681, 657.
MS (EI, 70 eV): *m/z* (%) = 511 (15), 311 (13), 288 (24), 287 (100), 261 (20), 245 (26), 227 (18), 206 (20), 157 (18), 115 (20).
HR-MS (EI, 70eV): [$C_{21}H_{44}O_2ISi_2$], calcd.: 511.1925; found: 511.1919 [M-*i*Pr]$^+$.

(((2*R*,4*S*)-4-Iodopentan-2-yl)oxy)triisopropylsilane (91a)

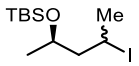


A dry and argon flushed Schlenk-tube, equipped with a magnetic stirrer and a septum, was charged with (2*R*, 4*R*)-(−)-2,4-pentanediol (520 mg, 5 mmol), anhydrous DMF (15 mL) and redistilled DIEA (8.5 mL, 50 mmol) forming a biphasic mixture at room temperature. TIPSCl (1.12 mL, 5.25 mmol) was added dropwise. The reaction mixture was stirred for 48 h. Upon completion, the reaction was quenched with cold water, extracted with diethyl ether (3×50 mL), and washed with 2N HCl, an aq. sat. $NaHCO_3$ and brine. The combined organic layers were dried over Na_2SO_4, the solvents were evaporated and the residue containing the crude chiral protected alcohol (1.05 g, 4.04 mmol, 81% yield) as a colorless oil was used in the next step without further purification.[121]
Iodine (1.23 g, 4.85 mmol) was dissolved in CH_2Cl_2 (*ca.* 0.1 M) and cooled to −10 °C. Triphenylphosphine (1.27 g, 4.85 mmol) was added and reaction mixture was stirred for

1 h at −10 °C. Then *N*-methylimidazole (0.39 mL, 4.85 mmol) was added dropwise and stirred for 10 min. Then solution of alcohol in CH_2Cl_2 (1 mL) was added. After further stirring for 30 min reaction mixture was quenched with sat. aq. ($NaHSO_3$+$Na_2S_2O_5$) solution and extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were dried over Na_2SO_4. The solvents were evaporated at 30 °C and the crude product was subjected to column chromatography furnishing the analytical pure iodide.[92b]

Isolated yield: 652 mg, 1.76 mmol, 44%, colorless oil.
Purification: *i*-hexane:diethyl ether = 200:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.15 – 4.00 (m, 2H), 2.21 (ddd, *J* = 14.6, 9.8, 5.1 Hz, 1H), 1.96 (d, *J* = 6.8 Hz, 3H), 1.60 (ddd, *J* = 14.3, 7.5, 5.2 Hz, 1H), 1.15 (d, *J* = 6.0 Hz, 3H), 1.07 (d, *J* = 1.4 Hz, 21H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 69.2, 52.6, 29.6, 25.8, 22.9, 18.3, 18.3, 12.6.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2964, 2943, 2921, 2890, 2865, 2361, 2339, 1462, 1373, 1252, 1149, 1127, 1058, 998, 962, 924, 881, 713.
MS (EI, 70 eV): *m/z* (%) = 355 (1), 327 (13), 286 (11), 285 (100), 241 (48), 213 (21), 199 (10), 185 (9), 75 (10), 69 (10).
HR-MS (EI, 70eV): [$C_{13}H_{28}IOSi$], calcd.: 355.0954; found: 355.0943 [M-Me]$^+$.
Optical rotation: $[\alpha]_D^{20}$ = 34 (c 1.00, $CHCl_3$).

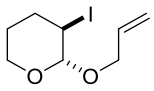
***Tert*-butyl(((2*R*)-4-iodopentan-2-yl)oxy)dimethylsilane (91b)**



The title compound was prepared according to the literature procedure from ethyl (*R*)-3-hydroxybutyrate. The analytical data were in full consistency with the data reported in the literature.[122]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.28 (dqd, *J* = 11.1, 6.9, 2.8 Hz, 1H), 4.16 (dp, *J* = 8.0, 6.8 Hz, 1H), 4.00 – 3.85 (m, 2H), 2.19 (ddd, *J* = 14.4, 8.1, 6.6 Hz, 1H), 1.96 (d, *J* = 6.9 Hz, 3H), 1.93 (d, *J* = 6.8 Hz, 3H), 1.86 (ddd, *J* = 14.8, 11.2, 2.3 Hz, 1H), 1.69 (ddd, *J* = 14.2, 6.8, 6.1 Hz, 1H), 1.57 – 1.47 (m, 1H), 1.17 (d, *J* = 6.1 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H), 0.89 (d, *J* = 0.7 Hz, 18H), 0.14 (s, 3H), 0.10 (s, 3H), 0.07 (s, 3H), 0.07 (s, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 68.9, 68.6, 52.8, 52.8, 29.9, 29.0, 28.9, 26.1, 26.0, 25.3, 24.1, 23.1, 18.2, 18.2, -3.8, -4.1, -4.2, -4.6.

2-(Allyloxy)-3-iodotetrahydro-2*H*-pyran (96)



The title compound was prepared according to the literature procedure from allylic alcohol (2.04 mL, 30 mmol), 3,4-dihydro-2*H*-pyran (3.30 mL, 36 mmol), *N*-iodosuccinimide (6.75 g, 30 mmol) and was obtained as a colorless oil (7.64 g, 28.5 mmol, 95% yield). The analytical data were in full consistency with the data reported in the literature.[133]

dr = 99:1

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.93 (dddd, *J* = 16.9, 10.4, 6.2, 5.2 Hz, 1H), 5.33 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.21 (dq, *J* = 10.4, 1.4 Hz, 1H), 4.68 (d, *J* = 5.3 Hz, 1H), 4.26 (ddt, *J* = 12.9, 5.2, 1.5 Hz, 1H), 4.11 (ddd, *J* = 8.1, 5.3, 4.3 Hz, 1H), 4.05 (ddt, *J* = 12.9, 6.2, 1.4 Hz, 1H), 4.02 – 3.95 (m, 1H), 3.58 (ddd, *J* = 11.2, 7.4, 3.5 Hz, 1H), 2.44 – 2.32 (m, 1H), 2.02 (dtd, *J* = 14.1, 8.3, 4.0 Hz, 1H), 1.77 (dtt, *J* = 14.3, 7.3, 3.8 Hz, 1H), 1.65 – 1.51 (m, 1H).

[133] C. Ollivier, P. Renaud, *J. Am. Chem. Soc.* **2001**, *123*, 4717-4727.

3.5 Preparation of Primary and Secondary Dialkylmagnesiums *via* a Radical I/Mg-exchange Reaction using *s*Bu_2Mg in Toluene

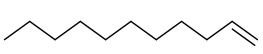
Preparation of primary dialkylmagnesiums *via* an I/Mg-exchange reaction using *s*Bu_2Mg in toluene (TP3)

A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum was charged with the respective primary alkyl iodide (0.50 mmol) and dry toluene (1.0 mL). Then a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol) was added *via* syringe at 40 °C and the reaction was stirred for 4 h. After that the corresponding electrophile (0.30 mmol) was added dropwise and the reaction mixture was stirred until completion. The reaction mixture was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3×50 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was subjected to column chromatography purification on silica yielding the corresponding product.

Preparation of secondary dialkylmagnesiums *via* an I/Mg-exchange reaction using *s*Bu_2Mg in toluene (TP4)

A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum was charged with the respective secondary alkyl iodide (0.50 mmol) and dry toluene (2.0 mL). Then a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol) was added *via* syringe at room temperature and the reaction was stirred for 2 h. After that the corresponding electrophile (0.40 mmol) was added dropwise at −20 °C and the reaction mixture was stirred until completion. The reaction mixture was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3×50 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was subjected to column chromatography purification on silica yielding the corresponding product.

1-Undecene (87a)

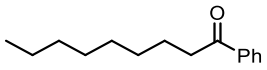


Following **TP3**, octyl iodide (**85a**, 120 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), allyl bromide (26 µL, 0.30 mmol) was added at −20 °C, following by 1.0 M CuCN·2LiCl solution in THF (15

µL, 0.015 mmol, 5 mol%) and was stirred for 30 min. The analytical data were in full consistency with the data reported in the literature.[134]

Isolated yield: 40 mg, 0.26 mmol, 86%, colorless oil.
Purification: pentane.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.82 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.05 – 4.83 (m, 2H), 2.10 – 1.98 (m, 2H), 1.42 – 1.23 (m, 14H), 0.88 (t, *J* = 6.8 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 139.4, 114.2, 34.0, 32.1, 29.7, 29.7, 29.5, 29.3, 29.1, 22.8, 14.3.

1-Phenylnonan-1-one (87b)

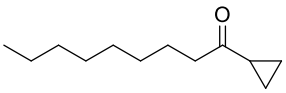


Following **TP3**, octyl iodide (**85a**, 120 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and was stirred for 30 min. Then, benzoyl chloride (35 µL, 0.30 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 56 mg, 0.26 mmol, 86%, yellow oil.
Purification: *i*-hexane:ethyl acetate = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 8.01 – 7.92 (m, 2H), 7.60 – 7.51 (m, 1H), 7.46 (dd, *J* = 8.3, 6.8 Hz, 2H), 3.04 – 2.91 (m, 2H), 1.73 (p, *J* = 7.4 Hz, 2H), 1.37 – 1.24 (m, 10H), 0.88 (h, J = 3.2, 2.8 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 200.8, 137.2, 133.0, 128.7, 128.2, 38.8, 32.0, 29.6, 29.5, 29.3, 24.5, 22.8, 14.3.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2953, 2923, 2869, 2853, 1683, 1597, 1448, 1359, 1273, 1215, 1179, 1001, 969, 749, 689.
MS (EI, 70 eV): *m/z* (%) = 218 (1), 147 (1), 133 (11), 120 (86), 105 (100), 78 (12).
HR-MS (EI, 70eV): [$C_{15}H_{22}O$], calcd.: 218.1671; found: 218.1665.

[134] C.M.R. Volla, D. Marcović, S.R. Dubbaka, P. Vogel, *Eur. J. Org. Chem.* **2009**, 6281-6288.

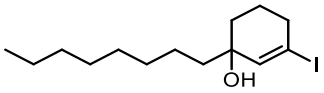
1-Cyclopropyl-1-nonanone (87c)



Following **TP3**, octyl iodide (**85a**, 120 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in tetrahydrofurane (THF) (0.55 mL, 0.55 mmol) was added at −40 °C and was stirred for 30 min. Then, cyclopropanecarbonyl chloride (27 µL, 0.30 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 38 mg, 0.21 mmol, 70%, colorless oil.
Purification: pentane:diethyl ether = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 2.52 (t, *J* = 7.5 Hz, 2H), 1.91 (tt, *J* = 7.9, 4.6 Hz, 1H), 1.59 (p, *J* = 7.1 Hz, 2H), 1.27 (qd, *J* = 7.6, 6.3, 3.8 Hz, 10H), 0.99 (dd, *J* = 4.4, 3.2 Hz, 2H), 0.91 – 0.80 (m, 5H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 211.5, 43.7, 32.0, 29.5, 29.4, 29.3, 24.2, 22.8, 20.4, 14.2, 10.7.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2954, 2923, 2853, 1698, 1463, 1456, 1384, 1194, 1130, 1078, 1060, 1018, 900, 818, 722.
MS (EI, 70 eV): *m/z* (%) = 183 (11), 182 (3), 153 (6), 139 (8), 111 (9), 97 (25), 84 (55), 83 (69), 69 (100).
HR-MS (EI, 70eV): [$C_{12}H_{23}O$], calcd.: 183.1749; found: 183.1740 $[M+H]^+$.

3-Iodo-1-octylcyclohex-2-en-1-ol (87d)

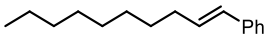


Following **TP3**, octyl iodide (**85a**, 120 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), 3-iodo-2-cyclohexen-1-one (67 mg, 0.30 mmol) was added at 0 °C and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 50 mg, 0.15 mmol, 50%, colorless oil.
Purification: *i*-hexane:ethyl acetate = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 6.31 (d, *J* = 2.0 Hz, 1H), 2.65 – 2.38 (m, 2H), 1.91 – 1.79 (m, 1H), 1.76 – 1.57 (m, 3H), 1.50 (dt, *J* = 8.1, 6.1 Hz, 2H), 1.38 – 1.19 (m, 13H), 0.88 (t, *J* = 6.7 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 142.8, 101.7, 73.2, 42.1, 39.8, 34.0, 32.0, 30.2, 29.7, 29.4, 23.4, 22.8, 21.8, 14.3.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2951, 2924, 2868, 2853, 1668, 1652, 1646, 1635, 1623, 1616, 1576, 1569, 1558, 1506, 1464, 1456.
MS (EI, 70 eV): *m/z* (%) = 318 (7), 233 (13), 223 (100), 220 (60), 93 (18).
HR-MS (EI, 70eV): [$C_{14}H_{23}I$], calcd.: 318.0844; found: 318.0838 [M-H_2O]$^+$.

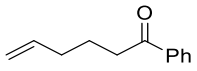
(1*E*)-Dec-1-en-1-ylbenzene (87e)



Following **TP3**, octyl iodide (**85a**, 120 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete, dialkylmagnesium solution (1.7 mL) was added to a mixture of $Fe(acac)_3$ (8.8 mg, 0.03 mmol, 5 mol%), tetramethylethylenediamine (TMEDA) (15 µl, 0.05 mmol, 10 mol%) and *β*-bromostyrene (55 mg, 0.30 mmol) at 0 °C. Then the reaction mixture was stirring for 30 min.

Isolated yield: 46 mg, 0.21 mmol, 71%, colorless oil.
Purification: *i*-hexane:ethyl acetate = 100:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.39 – 7.27 (m, 4H), 7.20 (t, *J* = 7.2 Hz, 1H), 6.39 (d, *J* = 15.8 Hz, 1H), 6.24 (dt, *J* = 15.8, 6.8 Hz, 1H), 2.21 (q, *J* = 7.2 Hz, 2H), 1.47 (p, *J* = 7.1 Hz, 2H), 1.31 (d, *J* = 12.1 Hz, 10H), 0.90 (t, *J* = 6.8 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 138.1, 131.4, 129.8, 128.6, 126.9, 126.0, 33.2, 32.0, 29.7, 29.5, 29.5, 29.4, 22.8, 14.3.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3024, 2954, 2922, 2867, 2852, 1598, 1494, 1465, 1455, 1449, 1377, 1071, 1028, 979, 962, 742, 722, 711, 691.
MS (EI, 70 eV): *m/z* (%) = 216 (18), 143 (2), 129 (13), 117 (99), 104 (100), 91 (26).
HR-MS (EI, 70eV): [$C_{16}H_{24}$], calcd.: 216.1878; found: 216.1872.

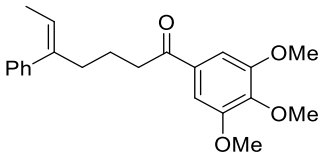
1-Phenylhex-5-en-1-one (87f)



Following **TP3**, iodide (**85i**, 98 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and was stirred for 30 min. Then, benzoyl chloride (35 µL, 0.30 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 39 mg, 0.22 mmol, 75%, colorless oil.
Purification: pentane:diethyl ether = 100:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 8.01 – 7.89 (m, 2H), 7.62 – 7.52 (m, 1H), 7.46 (dd, *J* = 8.3, 6.8 Hz, 2H), 5.83 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.14 – 4.92 (m, 2H), 2.98 (t, *J* = 7.4 Hz, 2H), 2.27 – 2.08 (m, 2H), 1.86 (p, *J* = 7.4 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 200.4, 138.2, 137.2, 133.1, 128.7, 128.2, 115.5, 37.9, 33.3, 23.4.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3065, 2973, 2932, 2894, 2866, 1682, 1640, 1597, 1580, 1448, 1366, 1231, 1203, 1179, 1001, 995, 972, 911, 753, 735, 689.
MS (EI, 70 eV): *m/z* (%) = 174 (4), 173 (6), 145 (5), 120 (54), 106 (8), 105 (100), 91 (3), 78 (10), 77 (35).
HR-MS (EI, 70eV): [$C_{12}H_{14}O$], calcd.: 174.1045; found: 174.1037.

(5*Z*)-5-Phenyl-1-(3,4,5-trimethoxyphenyl)hept-5-en-1-one (87g)



Following **TP3**, iodide (**85b**, 143 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and was stirred for 30 min. Then, 3,4,5-trimethoxybenzoyl chloride (69 mg, 0.30 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 84 mg, 0.24 mmol, 79%, *Z/E* = 99:1, colorless oil.

Purification: *i*-hexane:ethyl acetate = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.52 – 7.25 (m, 7H), 5.95 (q, *J* = 6.9 Hz, 1H), 4.03 (s, 3H), 3.99 (s, 6H), 3.02 (t, *J* = 7.3 Hz, 2H), 2.76 (t, *J* = 7.5 Hz, 2H), 1.95 (dd, *J* = 11.7, 7.1 Hz, 5H).

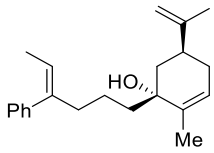
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 199.1, 153.1, 143.1, 142.4, 140.1, 132.4, 128.4, 126.7, 126.3, 123.9, 105.5, 61.0, 56.3, 37.9, 28.7, 23.3, 14.4.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2997, 2935, 2871, 2837, 1676, 1583, 1504, 1453, 1411, 1362, 1330, 1320, 1230, 1187, 1149, 1123, 1049, 1002, 850, 827, 759, 700.

MS (EI, 70 eV): *m/z* (%) = 334 (4), 211 (12), 210 (100), 207 (18), 195 (59).

HR-MS (EI, 70eV): [$C_{22}H_{26}O_4$], calcd.: 354.1831; found: 354.1827.

(1*R*,5*S*)-2-Methyl-1-((*Z*)-4-phenylhex-4-en-1-yl)-5-(prop-1-en-2-yl)cyclohex-2-en-1-ol (87h)



Following **TP3**, iodide (**85b**, 143 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), (*S*)-carvone[135] (47 µL, 0.30 mmol) was added at 0 °C, and the reaction mixture was allowed to warm to room temperature in 2 h.

Isolated yield: 50 mg, 0.16 mmol, 54%, *Z/E* = 99:1, dr = 95:5, colorless oil.

Purification: *i*-hexane:ethyl acetate = 8:2.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.38 – 7.25 (m, 4H), 7.24 – 7.17 (m, 1H), 5.76 (q, *J* = 6.8 Hz, 1H), 5.40 (tt, *J* = 3.1, 1.6 Hz, 1H), 4.72 – 4.63 (m, 2H), 2.60 – 2.44 (m, 2H), 2.17 (dddd, *J* = 12.0, 9.2, 5.4, 2.8 Hz, 1H), 2.10 – 2.00 (m, 1H), 1.93 (ddt, *J* = 16.0, 9.8, 2.7 Hz, 2H), 1.84 – 1.76 (m, 3H), 1.72 – 1.22 (m, 12H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 149.2, 143.3, 140.8, 138.8, 128.3, 126.6, 126.4, 123.4, 123.3, 109.3, 74.2, 40.0, 39.4, 38.0, 30.9, 29.6, 22.2, 20.9, 17.1, 14.4.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3415, 3026, 2941, 2918, 2857, 1644, 1598, 1494, 1441, 1373, 1315, 1288, 1263, 1166, 1085, 1075, 1030, 994, 950, 887, 831, 806, 752, 697.

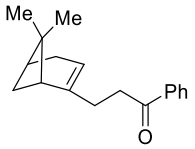
MS (EI, 70 eV): *m/z* (%) = 292 (6), 160 (12), 151 (62), 145 (24), 144 (36), 133 (19), 132 (13), 128 (28), 123 (31), 117 (20), 114 (16), 109 (100), 91 (47).

[135] T.P. Truong, S. J. Bailey, A.E. Golliher, E.Y. Monroy, U.K. Shrestha, W.A. Maio, *J. Chem. Educ.* **2018**, *95*, 438-444.

HR-MS (EI, 70eV): [$C_{22}H_{30}O$], calcd.: 310.2297; found: 310.2293.

Optical rotation: $[\alpha]_D^{20}$ = −13.3 (c = 0.15, $CHCl_3$).

3-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)-1-phenylpropan-1-one (87i)



Following **TP3**, iodide (**85d**, 138 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and was stirred for 30 min. Then, benzoyl chloride (35 µL, 0.30 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 57 mg, 0.22 mmol, 76%, yellow oil.

Purification: *i*-hexane:ethyl acetate = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 8.00 – 7.92 (m, 2H), 7.60 – 7.52 (m, 1H), 7.46 (tt, *J* = 6.6, 1.4 Hz, 2H), 5.26 (tp, *J* = 3.1, 1.5 Hz, 1H), 3.02 (dd, *J* = 8.3, 7.1 Hz, 2H), 2.38 (dtd, *J* = 12.5, 5.5, 2.6 Hz, 3H), 2.32 – 2.14 (m, 2H), 2.13 – 2.01 (m, 2H), 1.28 (s, 3H), 1.17 (d, *J* = 8.5 Hz, 1H), 0.84 (s, 3H).

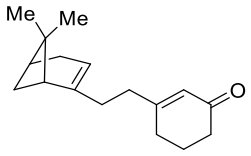
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 200.2, 147.2, 137.2, 133.1, 128.7, 128.2, 116.6, 46.1, 40.9, 38.1, 36.6, 31.8, 31.4, 26.4, 21.3.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2981, 2913, 2831, 1683, 1597, 1580, 1448, 1380, 1363, 1284, 1265, 1202, 1179, 1001, 973, 886, 759, 741, 688.

MS (EI, 70 eV): *m/z* (%) = 254 (2), 211 (13), 193 (13), 149 (13), 134 (26), 119 (100), 117 (14), 105 (63), 91 (90), 77 (35).

HR-MS (EI, 70eV): [$C_{18}H_{22}O$], calcd.: 254.1671; found: 254.1666.

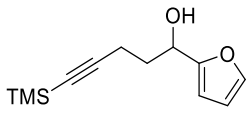
3-(2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl)cyclohex-2-en-1-one (87j)



Following **TP3**, iodide (**85d**, 138 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −25 °C and was stirred for 15 min. Then, 3-iodo-2-cyclohexen-1-one (36 µL, 0.30 mmol) was added, and the reaction mixture was stirred at this temperature for 4 h.

Isolated yield: 62 mg, 0.25 mmol, 84%, colorless oil.
Purification: pentane:diethyl ether = 8:2.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.87 (t, *J* = 1.4 Hz, 1H), 5.23 (dp, *J* = 3.0, 1.5 Hz, 1H), 2.40 – 2.33 (m, 3H), 2.32 – 2.11 (m, 8H), 2.11 – 2.04 (m, 1H), 2.03 – 1.94 (m, 3H), 1.27 (s, 3H), 1.12 (d, *J* = 8.5 Hz, 1H), 0.82 (s, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 200.1, 166.5, 147.0, 125.9, 117.0, 45.8, 40.9, 38.1, 37.5, 36.0, 34.2, 31.8, 31.4, 29.8, 26.4, 22.9, 21.3.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2917, 2874, 2831, 1719, 1666, 1623, 1454, 1428, 1415, 1380, 1371, 1364, 1346, 1324, 1253, 1240, 1191, 1129, 965.
MS (EI, 70 eV): *m/z* (%) = 225 (38), 209 (19), 207 (100), 191 (21), 119 (21), 117 (16), 110 (37), 105 (16), 91 (65).
HR-MS (EI, 70eV): [$C_{17}H_{24}O$], calcd.: 244.1827; found: 244.1824.

1-(Furan-2-yl)-5-(trimethylsilyl)pent-4-yn-1-ol (87k)



Following **TP3**, iodide (**85h**, 126 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), furfural (25 µl, 0.30 mmol) was added at 0 °C, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 53 mg, 0.24 mmol, 80%, colorless oil.

Purification: pentane:diethyl ether = 8:2.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.38 (dd, *J* = 1.8, 0.9 Hz, 1H), 6.33 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.26 (dt, *J* = 3.2, 0.8 Hz, 1H), 4.84 (td, *J* = 6.6, 4.0 Hz, 1H), 2.48 – 2.27 (m, 2H), 2.22 (d, *J* = 4.6 Hz, 1H), 2.05 (q, *J* = 6.9 Hz, 2H), 0.15 (s, 9H).

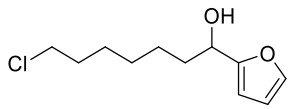
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 156.1, 142.2, 110.3, 106.3, 106.3, 85.7, 66.9, 34.2, 16.4, 0.2.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2956, 2923, 2853, 2178, 2175, 2172, 1737, 1696, 1459, 1377, 1249, 1090, 1051, 842, 760.

MS (EI, 70 eV): *m/z* (%) = 207 (13), 189 (31), 149 (21), 131 (42), 115 (83), 110 (100), 97 (40), 75 (50).

HR-MS (EI, 70eV): [$C_{12}H_{17}O_2Si$], calcd.: 221.0998; found: 221.0992 [M-H]$^+$.

7-Chloro-1-(furan-2-yl)heptan-1-ol (87l)



Following **TP3**, iodide (**85c**, 123 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), furfural (25 µL, 0.30 mmol) was added at 0 °C, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 56 mg, 0.26 mmol, 86%, colorless oil.

Purification: *i*-hexane:ethyl acetate = 8:2.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.37 (dd, *J* = 1.9, 0.8 Hz, 1H), 6.33 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.23 (d, *J* = 3.2 Hz, 1H), 4.67 (t, *J* = 6.8 Hz, 1H), 3.52 (t, *J* = 6.7 Hz, 2H), 1.94 – 1.70 (m, 5H), 1.55 – 1.19 (m, 6H).

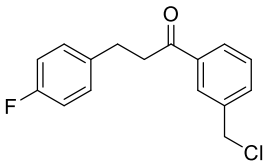
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 156.9, 142.1, 110.3, 106.0, 67.9, 45.2, 35.5, 32.6, 28.8, 26.9, 25.5.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3363, 2934, 2858, 1505, 1464, 1456, 1149, 1070, 1036, 1009, 884, 811, 735.

MS (EI, 70 eV): *m/z* (%) = 107 (24), 98 (5), 97 (100), 95 (3), 94 (22), 91 (5), 81 (4), 79 (22), 77 (11), 69 (10).

HR-MS (EI, 70eV): [$C_{11}H_{17}ClO_2$], calcd.: 216.0917; found: 216.0911.

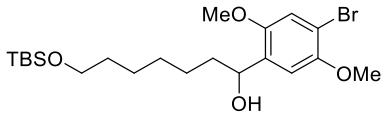
1-(3-(Chloromethyl)phenyl)-3-(4-fluorophenyl)propan-1-one (87m)



Following **TP3**, iodide (**85g**, 125 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and was stirred for 30 min. Then, 3-(chloromethyl)benzoyl chloride (43 µl, 0.30 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 60 mg, 0.22 mmol, 72%, colorless oil.
Purification: *i*-hexane:ethyl acetate = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.96 (d, *J* = 1.9 Hz, 1H), 7.90 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.60 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.24 – 7.16 (m, 2H), 7.03 – 6.93 (m, 2H), 4.62 (s, 2H), 3.29 (dd, *J* = 8.1, 6.9 Hz, 2H), 3.05 (t, *J* = 7.5 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 198.6, 161.5 (d, *J* = 243.9 Hz), 138.3, 137.4, 136.9 (d, *J* = 3.2 Hz), 133.3, 130.0 (d, *J* = 7.8 Hz), 129.3, 128.2, 128.1, 115.4 (d, *J* = 21.0 Hz), 45.7, 40.7, 29.3.
^{19}F-NMR (376 MHz, $CDCl_3$, ppm): δ = -117.20 (tt, *J* = 8.7, 5.3 Hz).
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3037, 2956, 2930, 2900, 1682, 1601, 1586, 1508, 1441, 1360, 1296, 1264, 1247, 1219, 1177, 1156, 1094, 1055, 1015, 987, 827, 795, 727, 704.
MS (EI, 70 eV): *m/z* (%) = 276 (6), 241 (10), 227 (58), 221 (7), 155 (33), 153 (100), 125 (26), 109 (15), 89 (19).
HR-MS (EI, 70eV): [$C_{16}H_{14}ClFO$], calcd.: 276.0717; found: 276.0711.

1-(4-Bromo-2,5-dimethoxyphenyl)-7-((*tert*-butyldimethylsilyl)oxy)heptan-1-ol (87n)



Following **TP3**, iodide (**85e**, 171 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), 4-bromo-2,5-dimethoxybenzaldehyde (74 mg, 0.30 mmol) was added at 0 °C, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 106 mg, 0.23 mmol, 77%, colorless oil.

Purification: *i*-hexane:ethyl acetate = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.04 (s, 1H), 6.95 (s, 1H), 4.91 – 4.80 (m, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 3.58 (t, *J* = 6.6 Hz, 2H), 2.35 (s, 1H), 1.79 – 1.64 (m, 2H), 1.55 – 1.41 (m, 2H), 1.40 – 1.23 (m, 6H), 0.88 (s, 9H), 0.04 (s, 6H).

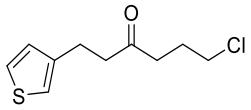
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 150.7, 150.3, 133.4, 116.1, 111.2, 109.8, 70.3, 63.4, 57.0, 56.2, 37.6, 33.0, 26.1, 26.1, 25.9, 18.5, -5.1.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2928, 2854, 1489, 1463, 1441, 1386, 1360, 1255, 1209, 1179, 1099, 1054, 1037, 1005, 835, 813, 775.

MS (EI, 70 eV): *m/z* (%) = 460 (3), 405 (15), 403 (15), 387 (10), 385 (9), 247 (189), 245 (22), 232 (26), 230 (10), 229 (100), 176 (25), 151 (11), 138 (11), 75 (33), 73 (13).

HR-MS (EI, 70eV): [$C_{21}H_{37}BrO_4Si$], calcd.: 460.1644; found: 460.1647.

6-Chloro-1-(thiophen-3-yl)hexan-3-one (87o)



Following **TP3**, iodide (**85f**, 119 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and was stirred for 30 min. Then, 4-chlorobutyryl chloride (34 µL, 0.30 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 55 mg, 0.25 mmol, 85%, colorless oil.

Purification: *i*-hexane:ethyl acetate = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.26 – 7.22 (m, 1H), 6.97 – 6.91 (m, 2H), 3.56 (t, *J* = 6.3 Hz, 2H), 2.97 – 2.89 (m, 2H), 2.76 (t, *J* = 7.5 Hz, 2H), 2.60 (t, *J* = 7.0 Hz, 2H), 2.09 – 1.98 (m, 2H).

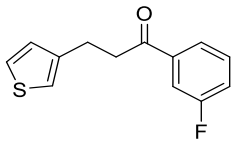
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 208.9, 141.2, 128.1, 125.8, 120.7, 44.6, 43.7, 39.6, 26.3, 24.3.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3102, 2957, 2924, 2895, 2854, 1710, 1537, 1437, 1408, 1372, 1310, 1296, 1206, 1155, 1090, 1002, 858, 831, 774, 738, 700.

MS (EI, 70 eV): *m/z* (%) = 216 (6), 180 (4), 139 (3), 112 (7), 111 (100), 97 (33).

HR-MS (EI, 70eV): [$C_{10}H_{13}ClOS$], calcd.: 216.0376; found: 216.0370.

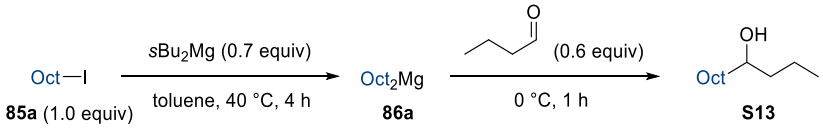
1-(3-Fluorophenyl)-3-(thiophen-3-yl)propan-1-one (87p)



Following **TP3**, iodide (**85f**, 119 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and was stirred for 30 min. Then, 3-fluorobenzoyl chloride (37 µL, 0.30 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 57 mg, 0.24 mmol, 81%, colorless oil.
Purification: *i*-hexane:ethyl acetate = 95:5.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.39 – 7.27 (m, 4H), 7.20 (t, *J* = 7.2 Hz, 1H), 6.39 (d, *J* = 15.8 Hz, 1H), 6.24 (dt, *J* = 15.8, 6.8 Hz, 1H), 2.21 (q, *J* = 7.2 Hz, 2H), 1.47 (p, *J* = 7.1 Hz, 2H), 1.31 (d, *J* = 12.1 Hz, 10H), 0.90 (t, *J* = 6.8 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 198.0 (d, *J* = 2.1 Hz), 163.0 (d, *J* = 248.0 Hz), 141.3, 139.0 (d, *J* = 6.0 Hz), 130.4 (d, *J* = 7.6 Hz), 128.3, 125.9, 123.9 (d, *J* = 3.0 Hz), 120.8, 120.3 (d, *J* = 21.4 Hz), 114.9 (d, *J* = 22.2 Hz), 39.8, 24.5.
^{19}F-NMR (376 MHz, $CDCl_3$, ppm): δ = -111.82 (ddd, *J* = 9.5, 8.2, 5.7 Hz).
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2928, 1688, 1588, 1484, 1442, 1409, 1359, 1295, 1271, 1258, 1240, 1167, 1149, 880, 860, 777, 681.
MS (EI, 70 eV): *m/z* (%) = 234 (9), 124 (2), 123 (31), 111 (100), 95 (15), 77 (6), 75 (6).
HR-MS (EI, 70eV): [$C_{13}H_{11}FOS$], calcd.: 234.0515; found: 234.0510.

Dodecan-4-ol (S13)



Following **TP3**, octyl iodide (**85a**, 120 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), freshly distilled butyraldehyde (22 mg, 0.30 mmol) was added at 0 °C, and the reaction mixture was allowed to warm to room temperature in 1 h.

Isolated yield: 29 mg, 0.15 mmol, 51%, colorless oil.

Purification: pentane:diethyl ether = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.30 (s, 1H), 1.44 – 1.35 (m, 4H), 1.26 (d, *J* = 5.0 Hz, 15H), 0.90 (dt, *J* = 13.4, 7.0 Hz, 6H).

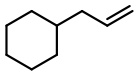
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 74.6, 41.9, 39.4, 32.0, 30.4, 29.8, 29.5, 23.6, 22.8, 16.9, 14.9, 14.3.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3418, 2956, 2924, 2871, 2853, 1464, 1457, 1378, 1260, 1140, 1110, 1078, 1031, 979, 934, 904, 861, 800, 722, 700.

MS (EI, 70 eV): *m/z* (%) = 186 (11), 185 (100), 9 (12), 55(13), 43 (11).

HR-MS (EI, 70eV): [$C_{12}H_{26}O$], calcd.: 186.1984; found: 186.1927.

Allylcyclohexane (90a)



Following **TP4**, iodide (**88a**, 105 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), allyl bromide (26 µL, 0.30 mmol) was added at −20 °C, following by 1.0 M CuCN·2LiCl solution in THF (15 µL, 0.015 mmol, 5 mol%) and the reaction mixture was stirred for 30 min. The analytical data were in full consistency with the data reported in the literature. [136]

Isolated yield: 30 mg, 0.24 mmol, 48%, colorless oil.

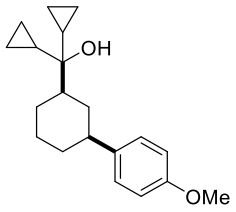
Purification: pentane.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.81 – 5.57 (m, 1H), 5.56 – 4.89 (m, 2H), 2.02 – 1.90 (m, 2H), 1.70 – 1.63 (m, 4H), 1.41 – 1.33 (m, 1H), 1.21 – 0.98 (m, 4H), 0.88 – 0.70 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 137.8, 115.8, 42.0, 37.7, 33.3, 27.0, 25.3

[136] D. Zhu, L. Lv, C.-C. Li, S. Ung, J. Gao, C.-J. Li, *Angew. Chem. Int. Ed.* **2018**, *57*, 16520-16524; *Angew. Chem.* **2018**, *130*, 16758-1672.

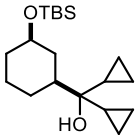
Dicyclopropyl(3-(4-methoxyphenyl)cyclohexyl)methanol (90b)



Following **TP4**, iodide (**88b**, 158 mg, 0.50 mmol, dr = 99:1) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), dicyclopropyl ketone (45 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h.

Isolated yield: 66 mg, 0.22 mmol, 55%, dr = 99:1, colorless oil.
Purification: *i*-hexane:diethyl ether = 8:2.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.20 – 7.12 (m, 2H), 6.91 – 6.81 (m, 2H), 3.79 (s, 3H), 2.51 (tt, *J* = 11.9, 3.4 Hz, 1H), 2.19 – 2.09 (m, 1H), 2.08 – 2.00 (m, 1H), 1.95 (dq, *J* = 11.9, 3.0 Hz, 1H), 1.88 (ddd, *J* = 10.5, 4.9, 2.5 Hz, 1H), 1.69 (tt, *J* = 12.0, 3.0 Hz, 1H), 1.46 – 1.34 (m, 3H), 1.30 (td, *J* = 12.5, 3.4 Hz, 1H), 0.89 – 0.79 (m, 3H), 0.45 – 0.34 (m, 6H), 0.32 – 0.21 (m, 2H).
Relative stereochemistry was assigned based on observation of NOE for 1,3-diaxial protons.
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 157.8, 140.3, 127.8, 113.8, 72.3, 55.4, 50.7, 44.0, 36.0, 34.7, 27.3, 27.0, 16.6, 16.5, 1.4, 1.2, -0.8, -0.9.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3011, 3001, 2926, 2854, 2362, 2334, 2320, 1611, 1512, 1465, 1448, 1247, 1176, 1035, 1025, 989, 912, 824.
MS (EI, 70 eV): *m/z* (%) = 300 (1), 190 (46), 147 (14), 121 (33), 111 (100), 91 (14), 69 (58).
HR-MS (EI, 70eV): [$C_{20}H_{28}O_2$], calcd.: 300.2089; found: 300.2084.

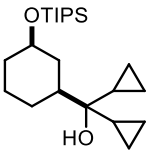
(3-((*Tert*-butyldimethylsilyl)oxy)cyclohexyl)dicyclopropylmethanol (90c)



Following **TP4**, iodide (**88c**, 170 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), dicyclopropyl ketone (45 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h.

Isolated yield: 72 mg, 0.22 mmol, 56%, dr = 99:1, colorless oil.
Purification: *i*-hexane:ethyl acetate = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 3.56 (tt, *J* = 10.4, 4.4 Hz, 1H), 2.12 (ddq, *J* = 11.6, 4.6, 2.2 Hz, 1H), 1.92 – 1.74 (m, 3H), 1.58 – 1.46 (m, 1H), 1.33 – 1.07 (m, 4H), 0.89 (s, 9H), 0.84 – 0.73 (m, 2H), 0.38 (qdt, *J* = 6.5, 5.0, 2.1 Hz, 6H), 0.25 (tdd, *J* = 8.7, 6.0, 2.1 Hz, 2H), 0.06 (s, 6H).
Relative stereochemistry was assigned based on observation of NOE for 1,3-diaxial protons.
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 72.5, 72.0, 49.0, 37.7, 36.5, 26.7, 26.1, 24.5, 18.4, 16.6, 16.4, 1.4, 1.2, -0.9, -1.0, -4.4, -4.4.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3085, 3007, 2950, 2927, 2857, 2357, 2342, 1472, 1463, 1373, 1360, 1255, 1249, 1106, 1086, 1083, 1021, 1005, 989, 969, 881, 867, 836, 773.
MS (EI, 70 eV): *m/z* (%) = 324 (1), 265 (2), 133 (11), 111 (100), 95 (11), 93 (12), 91 (11), 82 (31), 81 (22), 75 (56).
HR-MS (EI, 70eV): [$C_{19}H_{36}O_2Si$], calcd.: 324.2485; found: 324.2466.

Dicyclopropyl(3-((triisopropylsilyl)oxy)cyclohexyl)methanol (90d)



Following **TP4**, iodide (**88d**, 191 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), dicyclopropyl ketone (45 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h.

Isolated yield: 44 mg, 0.21 mmol, 52%, dr = 99:1, colorless oil.

Purification: *i*-hexane:diethyl ether = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 3.64 (tt, *J* = 10.3, 4.2 Hz, 1H), 2.23 (ddt, *J* = 12.0, 4.7, 2.3 Hz, 1H), 1.95 (dtd, *J* = 8.9, 4.4, 2.1 Hz, 1H), 1.88 – 1.77 (m, 2H), 1.57 – 1.45 (m, 1H), 1.32 – 1.11 (m, 4H), 1.06 (d, *J* = 2.2 Hz, 21H), 0.80 (dddd, *J* = 17.4, 11.5, 4.8, 2.9 Hz, 3H), 0.44 – 0.31 (m, 6H), 0.31 – 0.19 (m, 2H).

Relative stereochemistry was assigned based on observation of NOE for 1,3-diaxial protons.

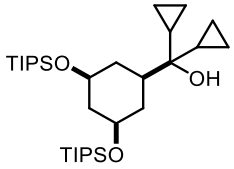
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 72.3, 72.0, 49.2, 38.0, 36.7, 26.7, 24.6, 18.3, 18.3, 17.0, 16.2, 12.5, 1.4, 1.0, -0.8, -0.9.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3615, 3509, 3085, 3008, 2954, 2938, 2892, 2863, 2362, 1680, 1463, 1425, 1387, 1381, 1370, 1355, 1312, 1255, 1247, 1180, 1094, 1066, 1020, 991, 968, 928, 914, 906, 881, 858, 830, 808, 784, 735, 677.

MS (EI, 70 eV): *m/z* (%) = 348 (2), 305 (21), 263 (8), 173 (17), 171 (29), 159 (23), 145 (26), 133 (14), 131 (54), 129 (20), 117 (30), 105 (15), 103 (100).

HR-MS (EI, 70eV): [$C_{22}H_{40}OSi$], calcd.: 348.2848; found: 348.2841 [M-H_2O]$^+$.

(3,5-Bis((triisopropylsilyl)oxy)cyclohexyl)dicyclopropylmethanol (90e)



Following **TP4**, iodide (**88e**, 139 mg, 0.25 mmol) was treated with a solution of *s*Bu_2Mg (0.30 mL, 0.15 mmol). After the exchange was complete (2 h), dicyclopropyl ketone (23 µL, 0.20 mmol) was added at −20 °C and the reaction mixture was stirred for 2 h.

Isolated yield: 58 mg, 0.11 mmol, 54%, dr = 99:1, colorless oil.

Purification: *i*-hexane:diethyl ether = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 3.65 (tt, *J* = 10.9, 4.2 Hz, 2H), 2.26 (ddq, *J* = 11.5, 3.9, 2.0 Hz, 1H), 2.16 (dq, *J* = 12.8, 2.6 Hz, 2H), 1.46 (tt, *J* = 12.7, 2.9 Hz, 1H), 1.38 (q, *J* = 11.4 Hz, 1H), 1.25 (td, *J* = 12.4, 10.6 Hz, 2H), 1.15 – 0.97 (m, 42H), 0.84 – 0.78 (m, 2H), 0.77 (s, 1H), 0.44 – 0.34 (m, 6H), 0.32 – 0.22 (m, 2H).

Relative stereochemistry was assigned based on observation of NOE for 1,3,5-triaxial protons.

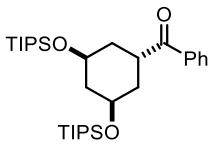
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 71.8, 69.9, 46.7, 44.9, 37.0, 18.2, 18.2, 16.7, 12.5, 1.3, -0.9.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2942, 2891, 2865, 1464, 1382, 1373, 1158, 1083, 1061, 1021, 1014, 994, 935, 916, 881, 832, 815, 786, 679, 655.

MS (EI, 70 eV): *m/z* (%) = 519 (1), 495 (12), 477 (32), 321 (45), 287 (55), 211 (75), 191 (57), 173 (93), 131 (64), 111 (56), 69 (100).

HR-MS (EI, 70eV): [$C_{31}H_{59}O_2Si_2$], calcd.: 519.4054; found: 519.4049 [M-H_3O]$^+$.

(3,5-Bis((triisopropylsilyl)oxy)cyclohexyl)(phenyl)methanone (90f)



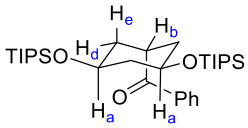
Following **TP4**, iodide (**88e**, 139 mg, 0.25 mmol) was treated with a solution of *s*Bu_2Mg (0.30 mL, 0.15 mmol). After the exchange was complete (2 h), benzaldehyde (20 µL, 0.20 mmol) was added at −30 °C and the reaction mixture was stirred for 1 h. The reaction mixture was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3×30 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*.

Pyridinium chlorochromate (43 mg, 0.2 mmol) was dissolved in CH_2Cl_2 (*ca.* 1 M) and alcohol was added at rt. The reaction mixture was stirred for 3 h, then was diluted with ether and filtered through the silica. The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*.[137]

Isolated yield: 54 mg, 0.10 mmol, 51%, dr = 99:1, yellowish oil.

Purification: *i*-hexane:diethyl ether = 95:5.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.88 – 7.84 (m, 2H), 7.56 – 7.51 (m, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 3.97 (tt, *J* = 10.3, 4.1 Hz, 2H), 3.83 (tt, *J* = 5.8, 2.9 Hz, 1H), 2.23 – 2.21 (m, 1H), 2.21 – 2.15 (m, 2H), 1.58 (ddd, *J* = 13.1, 10.3, 5.7 Hz, 2H), 1.40 (q, *J* = 10.8 Hz, 1H), 1.06 – 0.94 (m, 42H).



Relative stereochemistry was assigned based on the coupling constants of H^b (H^1). The value of $^3J_H{}^a$-$_H{}^e$ is 10.3 Hz, which is consistent for $^3J_{ax\text{-}ax}$. Small couplings $^3J_H{}^b$-$_H{}^d$ and $^3J_H{}^b$-$_H{}^e$ of 2.9 Hz and 5.8 Hz correspondingly are characteristic for $^3J_{eq\text{-}eq}$ and $^3J_{eq\text{-}ax}$.[138]

[137] G. Piancatelli, A. Scettri, M. D'Auria, *Synthesis* **1982**, *4*, 245-258.
[138] K. L. Williamson, *J. Am. Chem. Soc.* **1963**, *85*, 516-519; D. Höfner, S.A. Lesko, G. Binsch, *Org. Magn. Reson.* **1978**, *11*, 179-196.

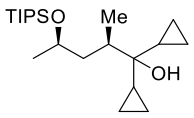
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 203.9, 136.4, 132.9, 128.7, 128.4, 66.4, 46.0, 40.3, 36.4, 18.1, 18.1, 12.3.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2942, 2892, 2866, 1682, 1463, 1448, 1382, 1215, 1119, 1082, 1060, 1012, 1004, 997, 954, 908, 881, 822, 794, 782, 733, 702, 679.

MS (EI, 70 eV): *m/z* (%) = 532 (1), 490(20), 489 (59), 315 (18), 287 (22), 245 (15), 185 (100), 105 (71).

HR-MS (EI, 70eV): [$C_{31}H_{56}O_3Si_2$], calcd.: 532.3768; found: 532.3760.

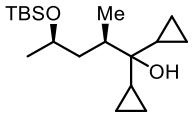
(2*R*,4*R*)-1,1-Dicyclopropyl-2-methyl-4-((triisopropylsilyl)oxy)pentan-1-ol (93a)



Following **TP4**, iodide (**91a**, 185 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), dicyclopropyl ketone (45 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h.

Isolated yield: 115 mg, 0.32 mmol, 81%, dr = 99:1, 98% *ee*, colorless oil.
Purification: *i*-hexane:diethyl ether = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.02 (dtt, *J* = 12.1, 6.0, 3.0 Hz, 1H), 1.89 (ddd, *J* = 13.2, 9.0, 2.9 Hz, 1H), 1.67 (ddt, *J* = 10.7, 6.9, 3.5 Hz, 1H), 1.56 (s, 1H), 1.55 – 1.47 (m, 1H), 1.20 – 1.16 (m, 4H), 1.07 (d, *J* = 1.7 Hz, 20H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.82 (dqd, *J* = 8.4, 5.7, 3.4 Hz, 2H), 0.47 – 0.33 (m, 6H), 0.25 (tddd, *J* = 7.3, 5.4, 3.5, 1.5 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 72.3, 67.8, 41.9, 41.8, 22.9, 18.3, 18.3, 16.5, 15.9, 15.7, 12.6, 1.4, 1.3, -0.9, -1.1.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2966, 2939, 2924, 2864, 2360, 2357, 2334, 1462, 1457, 1377, 1125, 1094, 1028, 1021, 996, 881.
MS (EI, 70 eV): *m/z* (%) = 311 (1), 175 (32), 174 (12), 163 (14), 157 (13), 139 (12), 133 (20), 131 (86), 129 (11), 121 (26), 111 (100).
HR-MS (EI, 70eV): [$C_{18}H_{35}O_2Si$], calcd.: 311.2406; found: 311.2394 [M-*i*Pr]$^+$.
Optical rotation: $[\alpha]_D^{20}$ = −12.5 (c = 0.17, $CHCl_3$).

(2*R*,4*R*)-4-((*Tert*-butyldimethylsilyl)oxy)-1,1-dicyclopropyl-2-methylpentan-1-ol (93b)



Following **TP4**, iodide (**91b**, 164 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), dicyclopropyl ketone (45 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h.

Isolated yield: 98 mg, 0.31 mmol, 78%, dr = 88:12, 98% *ee*, colorless oil.

Purification: *i*-hexane:diethyl ether = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 3.93 (dqd, *J* = 7.9, 6.1, 4.4 Hz, 1H), 1.92 (ddd, *J* = 13.5, 7.8, 3.5 Hz, 1H), 1.70 (tdd, *J* = 10.3, 7.9, 5.2 Hz, 1H), 1.39 (ddd, *J* = 13.5, 8.9, 4.5 Hz, 1H), 1.34 (s, 1H), 1.15 (d, *J* = 6.1 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.81 (dtd, *J* = 13.8, 7.8, 7.0, 4.1 Hz, 2H), 0.47 – 0.31 (m, 6H), 0.29 – 0.18 (m, 2H), 0.07 (s, 6H) (signals of one stereomer are given).

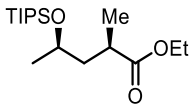
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 72.2, 68.3, 41.8, 41.7, 26.1, 23.0, 18.4, 16.5, 16.3, 16.0, 1.4, 1.2, -0.8, -1.2, -4.3, -4.5 (signals of one stereomer are given).

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3086, 3008, 2957, 2927, 2883, 2855, 1472, 1462, 1376, 1364, 1255, 1128, 1095, 1067, 1051, 1022, 999, 986, 977, 937, 932, 914, 905, 834, 807, 773.

MS (EI, 70 eV): *m/z* (%) = 293 (1), 159 (4), 139 (18), 121 (11), 119 (25), 111 (46), 107 (16), 103 (13), 93 (24), 91 (11), 79 (14), 75 (100).

HR-MS (EI, 70eV): [$C_{18}H_{33}OSi$], calcd.: 293.2301; found: 293.2292 [M-H_3O]$^+$.

Ethyl (2*R*,4*R*)-2-methyl-4-((triisopropylsilyl)oxy)pentanoate (94a)



Following **TP4**, iodide (**91a**, 185 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), ethyl cyanoformate (40 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h.

Isolated yield: 100 mg, 0.32 mmol, 79%, dr = 99:1, 98% *ee*, colorless oil.

Purification: *i*-hexane:diethyl ether = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.11 (qd, *J* = 7.1, 2.4 Hz, 2H), 4.02 – 3.91 (m, 1H), 2.64 (dqd, *J* = 8.7, 7.1, 5.3 Hz, 1H), 1.84 (ddd, *J* = 13.7, 8.7, 5.1 Hz, 1H), 1.55 – 1.43 (m, 1H), 1.28 – 1.22 (m, 3H), 1.20 – 1.13 (m, 6H), 1.05 (d, *J* = 1.7 Hz, 21H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 177.1, 67.2, 60.3, 44.0, 36.4, 24.2, 18.4, 18.3, 18.3, 14.3, 12.7.

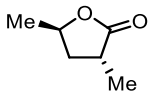
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2966, 2941, 2892, 2865, 2360, 1733, 1462, 1373, 1344, 1275, 1243, 1178, 1151, 1131, 1104, 1096, 1054, 1030, 1014, 997, 972, 949, 919, 882.

MS (EI, 70 eV): *m/z* (%) = 315 (1), 273 (54), 228 (11), 227 (100), 159 (41), 131 (55), 127 (10), 117 (13), 103 (67).

HR-MS (EI, 70eV): [$C_{17}H_{35}O_3Si$], calcd.: 315.2355; found: 315.2346 [M-H]$^+$.

Optical rotation: $[\alpha]_D^{20}$ = −10 (c = 0.70, $CHCl_3$).

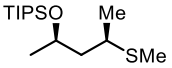
(3*R*,5*R*)-3,5-Dimethyldihydrofuran-2(3*H*)-one (S14)



According to the literature procedure[92b], to a solution of **94a** (158 mg, 0.50 mmol, dr = 99:1) in CH_2Cl_2 (2 mL) was added TfOH (1 drop) at room temperature and the mixture was stirred for 2 h. Then the reaction mixture was quenched with sat. aq. $NaHCO_3$ and the mixture was passed through a plug of $MgSO_4$. The filtrate was concentrated and subjected to the column chromatography. The analytical data is in full consistency with the data reported in the literature.[92a,139]

Isolated yield: 29 mg, 0.25 mmol, 85%, dr = 99:1, colorless oil.
Purification: pentane:diethyl ether = 7:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = δ 4.75 – 4.62 (m, 1H), 2.79 – 2.66 (m, 1H), 2.09 – 2.02 (m, 2H), 1.37 (d, *J* = 6.4 Hz, 3H), 1.28 (d, *J* = 7.3 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 180.1, 74.8, 37.2, 34.1, 21.2, 15.8.
Optical rotation: $[\alpha]_D^{20}$ = 26 (c = 0.80, $CHCl_3$), lit.[140] $[\alpha]_D^{20}$ = 36.5 (c = 1.10, $CHCl_3$).

Triisopropyl(((2*R*,4*R*)-4-(methylthio)pentan-2-yl)oxy)silane (94b)



Following **TP4**, iodide (**91a**, 185 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), *S*-methyl benzenethiosulfonate (58 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h.

Isolated yield: 94 mg, 0.32 mmol, 81%, dr = 93:7, 98% *ee*, colorless oil.
Purification: *i*-hexane:diethyl ether = 95:5.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.20 – 4.07 (m, 1H), 2.86 – 2.72 (m, 1H), 2.04 (s, 3H), 1.69 – 1.53 (m, 2H), 1.28 (d, *J* = 6.7 Hz, 3H), 1.17 (d, *J* = 6.0 Hz, 3H), 1.07 (s, 21H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 66.6, 47.1, 38.0, 24.3, 21.6, 18.4, 18.3, 12.8, 12.8.

[139] L. Coulombel, E. Duñach, *Synth. Commun.* **2005**, *35*, 153.
[140] M. Korpak, J. Pietruszka, *Adv. Synth. Catal.* **2011**, *353*, 1420-1424.

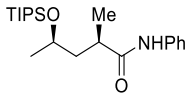
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2960, 2941, 2922, 2894, 2864, 1462, 1454, 1446, 1376, 1372, 1246, 1148, 1125, 1105, 1080, 1065, 1052, 1030, 1013, 996, 985, 970, 932, 918, 881, 761, 720, 674.

MS (EI, 70 eV): *m/z* (%) = 247 (36), 205 (13), 163 (24), 161 (100), 133 (17), 131 (22), 119 (63), 105 (15), 103 (12).

HR-MS (EI, 70eV): [$C_{12}H_{27}OSSi$], calcd.: 247.1552; found: 247.1546 [M-*i*Pr]$^+$.

Optical rotation: $[\alpha]_D^{20}$ = −7.1 (c = 0.51, $CHCl_3$).

(2*R*,4*R*)-2-Methyl-*N*-phenyl-4-((triisopropylsilyl)oxy)pentanamide (94c)



Following **TP4**, iodide (**91a**, 185 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), phenyl isocyanate (43 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 2 h.

Isolated yield: 103 mg, 0.28 mmol, 71%, dr = 99:1, 98% *ee*, colorless crystals.

m.p.: 67.2 – 69.1 °C

Purification: *i*-hexane:diethyl ether = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): *δ* = 7.54 – 7.47 (m, 2H), 7.35 – 7.27 (m, 2H), 7.24 (s, 1H), 7.13 – 7.05 (m, 1H), 4.03 (dtd, *J* = 7.8, 6.1, 4.5 Hz, 1H), 2.61 (dqd, *J* = 8.7, 7.0, 4.9 Hz, 1H), 1.95 (ddd, *J* = 13.5, 8.8, 4.5 Hz, 1H), 1.56 (ddd, *J* = 13.8, 7.8, 5.0 Hz, 1H), 1.23 (dd, *J* = 14.7, 6.5 Hz, 6H), 1.05 (d, *J* = 1.5 Hz, 21H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): *δ* = 174.9, 138.1, 129.1, 124.2, 119.8, 67.3, 44.5, 39.0, 24.2, 18.4, 18.3, 12.9.

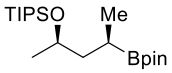
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3305, 2964, 2941, 2890, 2865, 1661, 1602, 1542, 1500, 1462, 1441, 1378, 1308, 1249, 1152, 1128, 1106, 1055, 1013, 997, 948, 882, 753.

MS (EI, 70 eV): *m/z* (%) = 348 (1), 321 (20), 320 (100), 206 (18), 190 (17), 178 (17), 172 (28), 150 (15), 136 (21).

HR-MS (EI, 70eV): [$C_{20}H_{34}O_2NSi$], calcd.: 348.2359; found: 348.2355 [M-CH_3]$^+$.

Optical rotation: $[\alpha]_D^{20}$ = −33 (c = 1.00, $CHCl_3$).

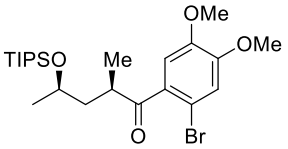
Triisopropyl(((2*R*,4*R*)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-yl)oxy)silane (94d)



Following **TP4**, iodide (**91a**, 185 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), MeOBpin (66 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h.

Isolated yield: 93 mg, 0.25 mmol, 63%, dr = 99:1, 98% *ee*, colorless oil.
Purification: *i*-hexane:diethyl ether = 100:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 3.96 (dp, *J* = 7.4, 5.9 Hz, 1H), 1.57 (dt, *J* = 13.4, 7.2 Hz, 1H), 1.47 (ddd, *J* = 13.4, 7.7, 5.6 Hz, 1H), 1.22 (s, 12H), 1.15 (d, *J* = 6.0 Hz, 3H), 1.05 (s, 22H), 0.96 (d, *J* = 7.2 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 83.0, 68.3, 43.3, 24.9, 24.8, 23.7, 18.4, 18.3, 15.9, 12.7.
^{11}B-NMR (128 MHz, $CDCl_3$, ppm): δ = 35.0.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2962, 2943, 2928, 2892, 2866, 1463, 1386, 1379, 1370, 1317, 1144, 1063, 1013, 882, 675.
MS (EI, 70 eV): *m/z* (%) = 355 (1), 227 (39), 226 (17), 185 (100), 184 (25), 157 (21), 143 (17), 75 (16).
HR-MS (EI, 70eV): [$C_{20}H_{43}BO_3Si$], calcd.: 355.2840; found: 355.2831 [M-CH_3]$^+$.
Optical rotation: $[\alpha]_D^{20}$ = +3.1 (c = 1.00, $CHCl_3$).

(2*R*,4*R*)-1-(2-Bromo-4,5-dimethoxyphenyl)-2-methyl-4-((triisopropylsilyl)oxy)pentan-1-one (95a)



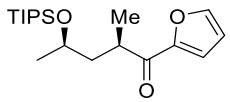
Following **TP4**, iodide (**91a**, 185 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), 2-bromo-4,5-dimethoxybenzaldehyde (98 mg, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h. This mixture was quenched with an aq. sat. NH_4Cl solution

and extracted with ethyl acetate (3×50 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*.

The intermediate alcohol was dissolved in CH_2Cl_2 (*ca.* 0.2 M) and Dess-Martin periodinane[93] (339 mg, 0.8 mmol) was added at rt. The reaction mixture was stirred for 10 min and then was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3×50 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*.

Isolated yield: 136 mg, 0.28 mmol, 56%, dr = 99:1, 98% *ee*, colorless oil.
Purification: *i*-hexane:diethyl ether = 7:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.04 (s, 1H), 6.94 (s, 1H), 4.00 (h, *J* = 6.3 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.50 (td, *J* = 7.2, 6.2 Hz, 1H), 1.93 (dt, *J* = 13.6, 6.3 Hz, 1H), 1.63 – 1.49 (m, 1H), 1.20 (d, *J* = 0.9 Hz, 3H), 1.18 (d, *J* = 1.7 Hz, 3H), 1.05 (d, *J* = 2.4 Hz, 1H), 1.04 – 1.03 (m, 2H), 1.01 (d, *J* = 2.4 Hz, 18H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 116.5, 112.1, 77.5, 77.2, 76.8, 67.2, 56.4, 56.3, 43.3, 41.5, 23.9, 18.3, 18.3, 17.2, 12.7.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2961, 2941, 2929, 2891, 2864, 1693, 1593, 1508, 1504, 1462, 1455, 1439, 1376, 1372, 1257, 1214, 1168, 1151, 1129, 1102, 1045, 1029, 1019, 996, 988, 882, 678.
MS (EI, 70 eV): *m/z* (%) = 443 (1), 243 (9), 218 (38), 217 (38), 203 (32), 190 (14), 173 (100), 103 (12), 75 (35).
HR-MS (EI, 70eV): [$C_{20}H_{32}BrO_4Si$], calcd.: 443.1253; found: 443.1245 [M-*i*Pr]$^+$.
Optical rotation: $[\alpha]_D^{20}$ = +0.9 (c = 1.00, $CHCl_3$).

(2*R*,4*R*)-1-(Furan-2-yl)-2-methyl-4-((triisopropylsilyl)oxy)pentan-1-one (95b)



Following **TP4**, iodide (**91a**, 185 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.60 mL, 0.30 mmol). After the exchange was complete (2 h), furaldehyde (33 µL, 0.40 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h. This mixture was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3×50 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*.

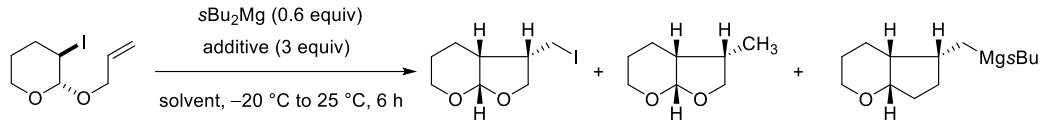
The intermediate alcohol was dissolved in CH_2Cl_2 (*ca.* 0.2 M) and Dess-Martin periodinane[131] (339 mg, 0.8 mmol) was added at rt. The reaction mixture was stirred for 10 min and then was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3×50 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*.

Isolated yield: 96 mg, 0.29 mmol, 57%, dr = 99:1, 98% *ee*, colorless oil.
Purification: *i*-hexane:diethyl ether = 8:2.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.57 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.18 (dd, *J* = 3.6, 0.8 Hz, 1H), 6.52 (dd, *J* = 3.5, 1.7 Hz, 1H), 4.01 – 3.92 (m, 1H), 3.51 – 3.40 (m, 1H), 2.04 (ddd, *J* = 13.6, 8.0, 5.5 Hz, 1H), 1.54 (ddd, *J* = 13.7, 6.8, 5.7 Hz, 1H), 1.20 (dd, *J* = 6.6, 5.8 Hz, 6H), 1.07 (s, 1H), 1.06 (s, 2H), 0.99 (d, *J* = 1.0 Hz, 18H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 193.3, 152.6, 146.3, 117.2, 112.2, 67.2, 43.1, 38.3, 24.1, 18.4, 18.3, 18.2, 12.7.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2962, 2941, 2931, 2892, 2865, 2361, 1723, 1708, 1677, 1641, 1567, 1466, 1463, 1382, 1251, 1151, 1131, 1097, 1050, 1014, 921, 883, 757, 679.
MS (EI, 70 eV): *m/z* (%) = 295 (100), 277 (37), 227 (10), 199 (10), 185 (10), 147 (74), 131 (16), 119 (17), 103 (30).
HR-MS (EI, 70eV): [$C_{16}H_{27}O_3Si$], calcd.: 295.1729; found: 295.1722 [M-*i*Pr]$^+$.
Optical rotation: $[\alpha]_D^{20}$ = −1.3 (c = 1.00, $CHCl_3$).

3.6 Mechanistic Studies

3.6.1 Optimization of the reaction of cyclic iodo-acetal 96

Table S5. Optimization of reaction conditions of cyclization of iodo-acetal **96**.

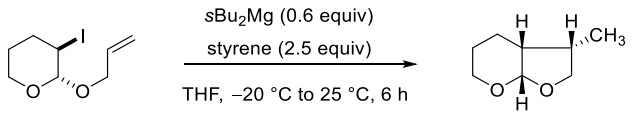


96, dr = 99:1 **97** **98a** **99**

entry	solvent	additive	yield of **97** [%][a]	yield of **98a** [%]	yield of **99** [%]	dr[b]
1	THF	no	33	13	18	92:8
2	THF	*s*BuI[c]	47	17	6	95:5
3	THF	*s*BuI	64	3	5	95:5
4	THF	*i*PrI	58	3	3	93:7
5	Et_2O	*s*BuI	31	22	6	94:6
6	Bu_2O	*s*BuI	27	23	6	94:6
7	dioxane	*s*BuI	52	6	3	92:8
8	toluene	*s*BuI	30	19	4	95:5
9	*n*-hexane	*s*BuI	12	6	4	92:8
10	THF	*s*BuI[d]	67[e]	2	3	95:5

[a] The reactions were performed on a 0.5 mmol scale. Yields were determined by GC-analysis using undecane ($C_{11}H_{24}$) as an internal standard. [b] Diastereomerical ratio (dr) was determined by GC-analysis. [c] The reaction was performed in the presence of 1 equiv of additive. [d] The reaction was performed in the presence of 3 equiv of additive. [e] Isolated yield.

3.6.2 Reaction with the cyclic iodo-acetal 96 in the presence of styrene

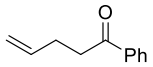


96 **98a**, 4%[a]

Scheme S3. Addition of styrene to the rection of cyclic iodo-acetal **96**. [a] The reaction was performed on a 0.5 mmol scale. Yield was determined by GC-analysis using undecane ($C_{11}H_{24}$) as an internal standard.

3.6.3 Radical clocks

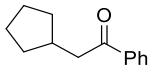
1-Phenylpent-4-en-1-one (87q)



Following **TP3**, iodide (**85j**, 91 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and the reaction mixture was stirred for 30 min. Then, benzoyl chloride (35 µL, 0.30 mmol) was added, and the reaction was allowed to warm to room temperature in 1 h. The analytical data were in full consistency with the data reported in the literature.[141]

Isolated yield: 26 mg, 0.14 mmol, 54%, colorless oil.
Purification: pentane:diethyl ether = 100:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 8.01 – 7.93 (m, 2H), 7.59 – 7.53 (m, 1H), 7.46 (dd, *J* = 8.3, 6.9 Hz, 2H), 5.91 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H), 5.09 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.01 (dq, *J* = 10.2, 1.5 Hz, 1H), 3.12 – 3.05 (m, 2H), 2.55 – 2.46 (m, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 199.6, 137.4, 137.0, 133.2, 128.7, 128.2, 115.4, 37.9, 28.3.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3080, 3062, 2918, 1684, 1641, 1597, 1580, 1448, 1411, 1361, 1278, 1252, 1206, 1180, 1001, 970, 912, 743, 689.
MS (EI, 70 eV): *m/z* (%) = 160 (1), 158 (2), 129 (2), 115 (4), 106 (8), 105 (100), 91 (2), 78 (3), 77 (44), 53 (2), 50 (3), 43 (2).
HR-MS (EI, 70eV): [$C_{11}H_{14}O$], calcd.: 160.0888; found: 160.0880.

2-Cyclopentyl-1-phenylethan-1-one (87s)



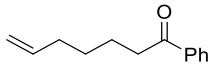
Following **TP3**, iodide (**85k**, 105 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and the reaction mixture was stirred for 30 min. Then, benzoyl chloride (35 µL, 0.30 mmol) was added, and the reaction

[141] W.E. Brenzovich. D. Benitez, A.D. Lackner, H.P. Shunatona, E. Tkatchouk, W.A. Goddard III, F. Dean Toste, *Angew. Chem. Int. Ed.* **2010**, *49*, 5519-5522.

mixture was allowed to warm to room temperature in 1 h. The analytical data were in full consistency with the data reported in the literature.[142]

Isolated yield: 14 mg, 0.08 mmol, 25%, colorless oil.
Purification: pentane:diethyl ether = 100:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.99 – 7.93 (m, 2H), 7.59 – 7.51 (m, 1H), 7.49 – 7.43 (m, 2H), 2.99 (d, *J* = 7.1 Hz, 2H), 2.39 (ddd, *J* = 8.7, 7.2, 1.5 Hz, 1H), 1.94 – 1.82 (m, 2H), 1.73 – 1.50 (m, 3H), 1.25 – 1.10 (m, 1H), 0.94 – 0.80 (m, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 200.6, 137.4, 133.0, 128.7, 128.3, 45.0, 36.2, 32.9, 25.1.

1-Phenylhept-6-en-1-one (87t)

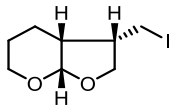


Following **TP3**, iodide (**85k**, 105 mg, 0.50 mmol) was treated with a solution of *s*Bu_2Mg (0.70 mL, 0.35 mmol). After the exchange was complete (4 h), a 1.0 M CuCN·2LiCl solution in THF (0.55 mL, 0.55 mmol) was added at −40 °C and the reaction mixture was stirred for 30 min. Then, benzoyl chloride (35 µL, 0.30 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 1 h. The analytical data were in full consistency with the data reported in the literature.[143]

Isolated yield: 19 mg, 0.10 mmol, 33%, colorless oil.
Purification: pentane:diethyl ether = 100:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.99 – 7.93 (m, 2H), 7.60 – 7.52 (m, 1H), 7.51 – 7.43 (m, 2H), 5.82 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.02 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.96 (ddt, *J* = 10.2, 2.2, 1.3 Hz, 1H), 2.98 (t, *J* = 7.4 Hz, 2H), 2.17 – 2.07 (m, 2H), 1.76 (p, *J* = 7.4 Hz, 2H), 1.49 (tt, *J* = 10.0, 6.6 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 200.5, 138.7, 137.1, 133.1, 128.7, 128.2, 114.8, 38.5, 33.7, 28.7, 23.9.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2915, 2854, 2848, 2364, 2359, 2355, 2332, 2165, 1711, 1684, 1653, 1571, 1558, 1548, 1539, 1469, 1445, 1326, 1215, 979.
MS (EI, 70 eV): *m/z* (%) = 188 (1), 164 (9), 133 (15), 120 (57), 105 (100), 77 (44).
HR-MS (EI, 70eV): [$C_{13}H_{16}O$], calcd.: 188.1201; found: 188.1193.

[142] C.F. Malosh, J.M. Ready, *J. Am. Chem. Soc.* **2004**, *126*, 10240-10241.
[143] J.-J. Cao, F. Zhou, J. Zhou, *Angew. Chem. Int. Ed.* **2010**, *49*, 4976-4980.

(3*S*,3a*R*,7a*S*)-3-(Iodomethyl)hexahydro-4*H*-furo[2,3-b]pyran (97)

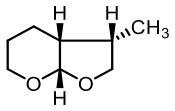


A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum was charged with the iodide (**96**, 134 mg, 0.50 mmol, dr = 99:1), *s*BuI (276 mg, 1.50 mmol) and dry toluene (1.0 mL). Then a solution of sBu_2Mg in toluene (0.60 mL, 0.30 mmol) was added *via* syringe at −20 °C and the reaction mixture was stirred for 6 h. This mixture was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3 x 50 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was subjected to column chromatography purification on silica yielding the corresponding product. The analytical data were in full consistency with the data reported in the literature.[144]

Isolated yield: 90 mg, 0.34 mmol, 67%, dr = 95:5, yellow oil.
Purification: *i*-hexane:ethyl acetate = 8:2.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.27 (d, *J* = 3.6 Hz, 1H), 4.01 (t, *J* = 8.2 Hz, 1H), 3.80 – 3.71 (m, 1H), 3.67 (dd, *J* = 9.4, 8.4 Hz, 1H), 3.61 (dtd, *J* = 11.2, 3.8, 1.6 Hz, 1H), 3.14 (d, *J* = 8.1 Hz, 2H), 2.81 (dqd, *J* = 9.2, 8.0, 6.1 Hz, 1H), 2.08 (dtd, *J* = 10.1, 6.3, 3.6 Hz, 1H), 1.76 (dddd, *J* = 12.6, 6.2, 4.2, 1.5 Hz, 1H), 1.64 – 1.53 (m, 2H), 1.47 – 1.35 (m, 1H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 101.8, 70.2, 61.3, 44.4, 38.4, 22.8, 18.8, 2.3.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3120, 3032, 2926, 2869, 2858, 1610, 1560, 1488, 1454, 1419, 1402, 1310, 1276, 1257, 1244, 1227, 1191, 1150, 1082, 1060, 1046, 1026, 912, 871, 814, 753, 697.
MS (EI, 70 eV): *m/z* (%) = 268 (9), 267 (100), 141 (14), 111 (65), 97 (15), 95 (28), 93 (12), 83 (16), 79 (10), 71 (41), 69 (20), 67 (21), 41 (9).
HR-MS (EI, 70eV): [$C_8H_{13}IO_2$], calcd.: 267.9960; found: 267.9911.

[144] H. Yorimitsu, T. Nakamura, H. Shinokubo, K. Oshima, K. Omoto, H. Fujimoto, *J. Am. Chem. Soc.* **2000**, *122*, 11041-11047; S.H. Kyne, C. Lévêque, S. Zheng, L. Fensterbank, A. Jutand, C. Ollivier, *Tetrahedron* **2016**, *72*, 7727-7737.

(3*S*,3a*R*,7*aS*)-3-Methylhexahydro-4*H*-furo[2,3-b]pyran (98a)



A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum was charged with the iodide (**96**, 134 mg, 0.50 mmol, dr = 99:1), *s*BuI (276 mg, 1.50 mmol) and dry toluene (1.0 mL). Then a solution of sBu_2Mg in toluene (0.60 mL, 0.30 mmol) was added *via* syringe at −20 °C and the reaction mixture was stirred for 6 h. This mixture was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3 x 50 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was subjected to column chromatography purification on silica yielding the corresponding product. The analytical data were in full consistency with the data reported in the literature.[145]

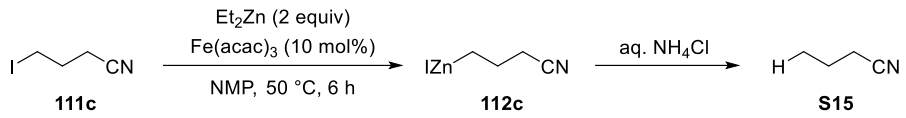
Isolated yield: 5 mg, 0.05 mmol, 5%, dr = 95:5, colorless oil.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.27 (d, *J* = 3.8 Hz, 1H), 3.93 (t, *J* = 8.0 Hz, 1H), 3.73 (ddd, *J* = 10.8, 9.4, 3.7 Hz, 1H), 3.66 – 3.56 (m, 2H), 2.51 – 2.34 (m, 1H), 1.89 (dtd, *J* = 10.4, 6.3, 3.8 Hz, 1H), 1.73 – 1.45 (m, 4H), 0.95 (d, *J* = 6.9 Hz, 3H).

[145] A. Ekomié, G. Lefèvre, L. Fensterbank, E. Lacôte, M. Malacria, C. Ollivier, A. Jutand, *Angew. Chem. Int. Ed.* **2012**, *51*, 6942-6946.

4 Iron-Catalyzed Zincations of Alkyl Iodides

4.1 Optimization of the Reaction Conditions

Table S6. Optimization of the zincation of 4-iodobutyronitrile (**111c**).



111c **112c** **S15**

Entry	Deviation from standard conditions	GC-Yield of **112c** (%)[a]
1	None	83
2	THF as a solvent	44
3	Bu_2O as a solvent	56
4	2-Me-THF as a solvent	58
5	Performing the reaction at 25 °C	3

[a] All reactions were performed on a 0.5 mmol scale. Yields are calibrated by GC-yields, determined after aqueous work-up of a reaction aliquot using $C_{11}H_{24}$ as internal standard.

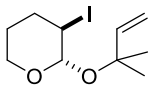
4.2 Preparation of Starting Materials

Preparation of Iodooxanyl Acetals TP5[146]

3,4-Dihydropyrane (1.01 equiv) was dropwise added to a mixture of *N*-iodosuccinimide (1.02 equiv) and allyl alcohol (1.00 equiv) in CH_2Cl_2 (1.8 M) at −10 °C. The reaction mixture was allowed to warm to room temperature and was stirred overnight. The reaction mixture was quenched with sat. aqueous $Na_2S_2O_3$ solution. The phases were separated and the aqueous layer was extracted 3× with CH_2Cl_2. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvents were evaporated and the crude product was subjected to column chromatography furnishing the analytical pure iodooxanyl acetal.

[146] F. T. Pulikottil, R. Pilli, V. Murugesan, C. G. Krishnan, R. Rasappan, *ChemCatChem* **2019**, *11*, 2438-2442.

3-Iodo-2-((2-methylbut-3-en-2-yl)oxy)tetrahydro-2*H*-pyran (103)

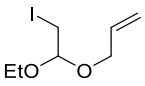


The title compound was prepared according to **TP5** from 2-methylbut-3-en-2-ol (0.86 g, 1.05 mL, 10.0 mmol), 3,4-dihydro-2*H*-pyran (0.85 g, 0.92 mL, 10.1 mmol), *N*-iodosuccinimide (2.30 g, 10.2 mmol) and was obtained as a colorless oil (2.14 g, 7.2 mmol, 72% yield). The analytical data were in full consistency with the data reported in the literature.[147]

dr = 99:1

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 6.00 (ddd, *J* = 17.6, 10.8, 1.7 Hz, 1H), 5.20 – 5.09 (m, 2H), 4.65 (d, *J* = 6.3 Hz, 1H), 4.07 – 3.94 (m, 2H), 3.50 (ddd, *J* = 11.7, 8.2, 3.8 Hz, 1H), 2.48 – 2.36 (m, 1H), 2.03 (dtd, *J* = 13.8, 9.2, 4.7 Hz, 1H), 1.60 (dddd, *J* = 13.6, 9.4, 8.0, 4.1 Hz, 2H), 1.33 (d, *J* = 6.9 Hz, 6H).

3-(1-Ethoxy-2-iodoethoxy)prop-1-ene (108b)



The title compound was prepared according to **TP5** from allylic alcohol (0.23 g, 7 mL, 4.0 mmol), ethyl vinyl ether (0.35 g, 0.47 mL, 4.8 mmol), *N*-iodosuccinimide (0.99 g, 4.4 mmol) and was obtained as a colorless oil (0.78 g, 7.2 mmol, 76% yield). The analytical data were in full consistency with the data reported in the literature.[148]

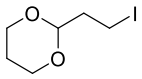
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.92 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H), 5.31 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.20 (dq, *J* = 10.4, 1.4 Hz, 1H), 4.66 (t, *J* = 5.5 Hz, 1H), 4.19 – 4.01 (m, 2H), 3.62 (ddq, *J* = 43.0, 9.4, 7.1 Hz, 2H), 3.23 (d, *J* = 5.5 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 134.2, 117.5, 101.3, 67.5, 62.3, 15.3, 5.4.

HR-MS (EI, 70eV): [$C_7H_{12}IO_2$], calcd.: 254.9882; found: 254.9877 $[M-H]^+$.

[147] J. Y. Hwang, J. H. Baek, T. I. Shin, J. H. Shin, J. W. Oh, K. P. Kim, Y. You, E. J. Kang, *Org. Lett*. **2016**, *18*, 4900-4903.
[148] A. Vaupel, P. Knochel, *J. Org. Chem*. **1996**, *61*, 5743-5753.

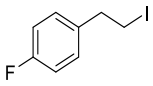
2-(2-Iodoethyl)-1,3-dioxane (111a)



The title compound was prepared according to the literature procedure from 2-(2-bromoethyl)-1,3-dioxane. The analytical data were in full consistency with the data reported in the literature.[149]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.62 (t, J = 5.0 Hz, 1H), 4.10 (ddt, J = 10.5, 5.0, 1.4 Hz, 2H), 3.85 – 3.71 (m, 2H), 3.20 (t, J = 7.1 Hz, 2H), 2.17 – 1.99 (m, 3H), 1.35 (dtt, J = 13.5, 2.6, 1.4 Hz, 1H).

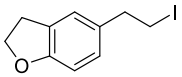
1-Fluoro-4-(2-iodoethyl)benzene (111b)



The title compound was prepared according to the literature procedure from 1-(2-bromoethyl)-4-fluorobenzene. The analytical data were in full consistency with the data reported in the literature.[150]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.21 – 7.11 (m, 2H), 7.09 – 6.93 (m, 2H), 3.39 – 3.25 (m, 2H), 3.15 (t, J = 7.6 Hz, 2H).

5-(2-Iodoethyl)-2,3-dihydrobenzofuran (111d)

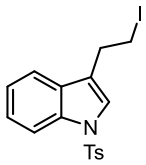


The title compound was prepared according to the literature procedure from 5-(2-bromoethyl)-2,3-dihydro-benzofuran. The analytical data were in full consistency with the data reported in the literature.[151]

[149] T.K. Olszewski, C. Grison, *Heteroatom Chem.* **2010**, *21*, 139-147.
[150] A.R. Mackenzie, S.M. Monaghan, US5677324A (**1997**).
[151] P.-F. Yang, l. Zhu, J.-X. Liang, H.-T. Zhao, J.-X- Zhang, X.-W. Zeng, Q. Ouyang, W. Shu, *ACS Catal.* **2022**, *12*, 5795-5805.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.02 (d, *J* = 1.8 Hz, 1H), 6.92 (dd, *J* = 8.1, 1.9 Hz, 1H), 6.72 (d, *J* = 8.1 Hz, 1H), 4.56 (t, *J* = 8.7 Hz, 2H), 3.30 (td, *J* = 7.6, 0.6 Hz, 2H), 3.20 (t, *J* = 8.7 Hz, 2H), 3.10 (t, *J* = 7.9 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 159.1, 132.9, 128.0, 127.5, 125.0, 109.3, 71.4, 40.0, 29.8, 6.8.

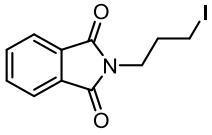
3-(2-Iodoethyl)-1-tosyl-1*H*-indole (111e)



The title compound was prepared according to literature procedure from 2-(1*H*-indol-3-yl)ethan-1-ol. The analytical data is in full consistency with the data reported in the literature. [152]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.99 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.80 – 7.73 (m, 2H), 7.45 (dt, *J* = 6.5, 1.0 Hz, 2H), 7.32 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.25 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.23 – 7.17 (m, 2H), 3.41 (t, *J* = 7.5 Hz, 2H), 3.24 (t, *J* = 7.5 Hz, 2H), 2.32 (s, 3H).

2-(3-Iodopropyl)isoindoline-1,3-dione (111f)



The title compound was prepared according to literature procedure from 2-(3-bromopropyl)-1*H*-isoindole-1,3(2*H*)-dione. The analytical data is in full consistency with the data reported in the literature. [153]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.4, 3.1 Hz, 2H), 3.78 (t, *J* = 6.8 Hz, 2H), 3.17 (t, *J* = 7.2 Hz, 2H), 2.25 (p, *J* = 7.0 Hz, 2H).

[152] S. Rezazadeh, V. Devannah, D. A. Watson *J.Am.Chem.Soc.* **2017**, *139*, 8110-8113.
[153] J. Zhou, G.C. Fu, *J.Am.Chem.Soc.* **2003**, *125*, 12527-12530.

4.3 Iron-Catalyzed Radical Zincations of Alkyl Iodides

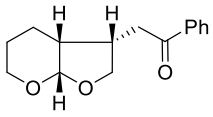
Iron-Catalyzed Radical Zincation of Alkenyl and Secondary Alkyl Iodides (TP6)

A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum was charged with the respective alkyl iodide (0.5 mmol), $Fe(acac)_3$ (18 mg, 0.05 mmol), dry *N*-methylpyrrolidone (NMP) (0.48 mL) and tetrahydrofurane (THF) (1.0 mL). Then a 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.0 mmol) was added *via* syringe at indicated temperature and the reaction was stirred until completion. After that the corresponding electrophile (1.5 mmol) was added dropwise and the reaction mixture was stirred until completion as indicated by GC-analysis of worked-up reaction aliquots. The reaction mixture was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3×20 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was subjected to column chromatography purification on silica yielding the corresponding product.

Iron-Catalyzed Radical Zincation of Primary Alkyl Iodides (TP7)

A dry and argon flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a septum was charged with the respective iodide (0.5 mmol), $Fe(acac)_3$ (18 mg, 0.05 mmol) and dry *N*-methylpyrrolidone (NMP) (1.0 mL). Then a 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.0 mmol) was added *via* syringe at 50 °C and the reaction was stirred for 6 h. After that the corresponding electrophile (1.5 mmol) was added dropwise and the reaction mixture was stirred until completion. The mixture was quenched with an aq. sat. NH_4Cl solution and extracted with ethyl acetate (3×20 mL). The organic phase was then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was subjected to column chromatography purification on silica yielding the corresponding product.

2-(Hexahydro-4*H*-furo[2,3-b]pyran-3-yl)-1-phenylethan-1-one (98c)

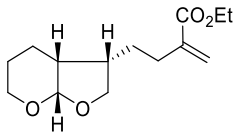


Following **TP6**, iodooxanyl acetal (**96**, 134 mg, 0.50 mmol, dr = 99:1) was treated with 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.00 mmol) at −20 °C and the mixture was let to warm up to 25 °C. After the insertion was complete after 16 h, a 1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −40 °C and was stirred for 30 min.

Then, benzoyl chloride (211 mg, 174 µL, 1.50 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 2 h and worked-up as usual.

Isolated yield: 94 mg, 0.38 mmol, 76%, dr = 95:5, colorless oil.
Purification: *i*-hexane:ethyl acetate = 7:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.97 – 7.90 (m, 2H), 7.62 – 7.52 (m, 1H), 7.45 (dd, *J* = 8.4, 7.0 Hz, 2H), 5.30 (d, *J* = 3.7 Hz, 1H), 4.13 (t, *J* = 8.0 Hz, 1H), 3.81 – 3.66 (m, 2H), 3.62 (dtd, *J* = 11.2, 3.8, 1.6 Hz, 1H), 3.22 – 3.10 (m, 1H), 3.05 – 2.90 (m, 2H), 2.18 (dtd, *J* = 10.2, 6.2, 3.8 Hz, 1H), 1.72 – 1.37 (m, 4H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 198.7, 136.6, 133.4, 128.8, 128.0, 101.9, 70.1, 61.3, 36.8, 36.4, 36.2, 23.1, 19.9.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2940, 2873, 1718, 1682, 1597, 1580, 1449, 1404, 1383, 1356, 1312, 1276, 1253, 1229, 1215, 1180, 1145, 1119, 1098, 1050, 1020, 1002, 996, 948, 901, 884, 870, 754, 714, 690.
MS (EI, 70 eV): *m/z* (%) = 246 (1), 229 (1), 145 (19), 144 (7), 126 (8), 120 (8), 117 (11), 105 (100), 77 (40).
HR-MS (EI, 70eV): [$C_{15}H_{18}O_3$], calcd.: 246.1256; found: 246.1249 [M]$^+$.

Ethyl 4-(hexahydro-4*H*-furo[2,3-b]pyran-3-yl)-2-methylenebutanoate (98d)



Following **TP6**, iodooxanyl acetal (**96**, 134 mg, 0.50 mmol, dr = 99:1) was treated with 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.00 mmol) at −20 °C and the mixture was let to warm up to 25 °C. After the insertion was complete after 16 h, a 1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −20 °C and was stirred for 30 min. Then, ethyl bromomethacrylate (203 mg, 146 µl, 1.05 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 2 h and worked-up as usual.

Isolated yield: 101 mg, 0.40 mmol, 80%, dr = 95:5, colorless oil.
Purification: *i*-hexane:ethyl acetate = 7:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 6.19 – 6.10 (m, 1H), 5.53 (q, *J* = 1.7 Hz, 1H), 5.27 (d, *J* = 3.8 Hz, 1H), 4.26 – 4.13 (m, 2H), 3.96 (tt, *J* = 8.0, 2.6 Hz, 1H), 3.74 (ddt, *J* = 10.6, 8.1, 2.8 Hz, 1H), 3.69 – 3.59 (m, 2H), 2.42 – 2.12 (m, 2H), 2.02 – 1.91 (m, 1H), 1.75 – 1.34 (m, 6H), 1.29 (td, *J* = 7.2, 2.4 Hz, 3H), 1.26 – 1.18 (m, 1H).

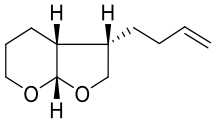
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 167.1, 140.5, 125.0, 102.1, 70.0, 61.1, 60.8, 40.7, 36.4, 30.8, 26.3, 23.3, 19.3, 14.3.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2939, 2873, 1723, 1449, 1371, 1268, 1252, 1225, 1204, 1189, 1143, 1111, 1096, 1071, 1019, 945, 895, 870, 732, 701.

MS (EI, 70 eV): *m/z* (%) = 253 (1), 179 (60), 163 (82), 125 (61), 123 (59), 93 (58), 79 (100).

HR-MS (EI, 70eV): [$C_{14}H_{21}O_4$], calcd.: 253.1440; found: 253.1434 [M-H]$^+$.

3-(But-3-en-1-yl)hexahydro-4*H*-furo[2,3-b]pyran (98e)



Following **TP6**, iodooxanyl acetal (**96**, 134 mg, 0.50 mmol, dr = 99:1) was treated with 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.00 mmol) at −20 °C and the mixture was let to warm up to 25 °C. After the insertion was complete after 16 h, allyl bromide (181 mg, 130 µl, 1.50 mmol) was added at −20 °C, following by 1.0 M CuCN·2LiCl solution in THF (15 µL, 0.015 mmol, 5 mol%), and was stirred for 2 h and then worked-up as usual.

Isolated yield: 66 mg, 0.36 mmol, 72%, dr = 95:5, colorless oil.

Purification: *i*-hexane:ethyl acetate = 8:2.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.76 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 5.25 (d, *J* = 3.7 Hz, 1H), 4.99 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.94 (dq, *J* = 10.1, 1.5 Hz, 1H), 3.93 (t, *J* = 8.0 Hz, 1H), 3.77 – 3.68 (m, 1H), 3.66 – 3.58 (m, 2H), 2.32 (dqd, *J* = 10.3, 7.7, 6.0 Hz, 1H), 2.05 – 1.87 (m, 3H), 1.69 – 1.29 (m, 6H) (signals of major diastereomer are given).

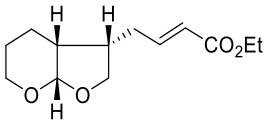
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 138.2, 115.0, 102.0, 70.0, 61.0, 40.4, 36.5, 32.4, 26.4, 23.3, 19.3 (signals of major diastereomer are given).

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2926, 2873, 1685, 1675, 1504, 1454, 1439, 1433, 1403, 1300, 1263, 1144, 1112, 1022, 990, 893.

MS (EI, 70 eV): *m/z* (%) = 181 (1), 153 (100), 125 (92), 97 (79), 93 (39), 81 (49), 79 (93), 67 (39).

HR-MS (EI, 70eV): [$C_{11}H_{17}O_2$], calcd.: 181.1229; found: 181.1222 [M-H]$^+$.

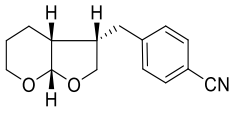
Ethyl (*E*)-4-(hexahydro-4*H*-furo[2,3-b]pyran-3-yl)but-2-enoate (98f)



Following **TP6**, iodooxanyl acetal (**96**, 134 mg, 0.50 mmol, dr = 99:1) was treated with 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.00 mmol) at −20 °C and the mixture was let to warm up to 25 °C. After the insertion was complete after 16 h, a 1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −40 °C and was stirred for 30 min. Then, ethyl propiolate (147 mg, 152 µl, 1.50 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 3 h and worked-up as usual.

Isolated yield: 76 mg, 0.32 mmol, 63%, dr = 94:6, *E/Z* = 99:1, yellow oil.
Purification: *i*-hexane:ethyl acetate = 8:2.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 6.84 (dt, *J* = 15.6, 7.1 Hz, 1H), 5.84 (dt, *J* = 15.6, 1.6 Hz, 1H), 5.26 (d, *J* = 3.7 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.95 (t, *J* = 8.1 Hz, 1H), 3.79 – 3.57 (m, 3H), 2.46 (dtd, *J* = 10.0, 7.8, 6.0 Hz, 1H), 2.31 (dtd, *J* = 14.9, 7.4, 1.5 Hz, 1H), 2.20 (dtd, *J* = 14.7, 7.3, 1.6 Hz, 1H), 1.99 (dtd, *J* = 10.2, 6.2, 3.7 Hz, 1H), 1.71 – 1.32 (m, 4H), 1.27 (t, *J* = 7.1 Hz, 3H) (signals of major diastereomer are given).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 166.4, 146.4, 122.7, 101.9, 69.7, 61.1, 60.5, 39.8, 36.4, 30.2, 23.1, 19.4, 14.3 (signals of major diastereomer are given).
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2932, 2891, 2873, 1718, 1655, 1461, 1446, 1368, 1314, 1267, 1235, 1199, 1171, 1147, 1114, 1102, 1042, 1024, 988, 947, 902, 871.
MS (EI, 70 eV): *m/z* (%) = 239 (14), 165 (16), 155 (19), 149 (15), 125 (100), 123 (25), 97 (28).
HR-MS (EI, 70eV): [$C_{13}H_{19}O_4$], calcd.: 239.1283; found: 239.1277 [M-H]$^+$.

4-((Hexahydro-4*H*-furo[2,3-b]pyran-3-yl)methyl)benzonitrile (98g)

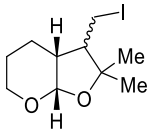


Following **TP6**, iodooxanyl acetal (**96**, 134 mg, 0.50 mmol, dr = 99:1) was treated with 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.00 mmol) at −20 °C and the mixture was let to warm up to 25 °C. After the insertion was complete after 16 h, $Pd(OAc)_2$ (5.6 mg, 0.025

mmol, 5 mol %), CPhos[154] (21.8 mg, 0.05 mmol, 10 mol %) and 4-iodobenzonitrile (229 mg, 1.00 mmol) were added and the mixture was stirred until completion.

Isolated yield: 85 mg, 0.35 mmol, 75%, dr = 95:5, colorless oil.
Purification: *i*-hexane:ethyl acetate = 1:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.56 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 5.25 (d, *J* = 3.7 Hz, 1H), 3.84 (t, *J* = 7.7 Hz, 1H), 3.74 (td, *J* = 9.6, 8.4, 4.5 Hz, 2H), 3.62 (ddt, *J* = 11.1, 3.4, 2.0 Hz, 1H), 2.84 – 2.75 (m, 1H), 2.73 – 2.58 (m, 2H), 1.94 (td, *J* = 10.7, 5.9 Hz, 1H), 1.77 – 1.66 (m, 1H), 1.56 (dddd, *J* = 20.3, 16.9, 9.4, 4.3 Hz, 3H) (signals of major diastereomer are given).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 145.9, 132.5, 129.3, 118.9, 110.3, 101.9, 69.6, 61.0, 42.1, 36.5, 33.8, 23.1, 19.7 (signals of major diastereomer are given).
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2940, 2897, 2871, 2227, 1607, 1505, 1252, 1145, 1110, 1051, 1021, 991, 947, 901, 882, 868, 820.
MS (EI, 70 eV): *m/z* (%) = 242 (86), 154 (58), 142 (100), 117 (37), 116 (68), 97 (33).
HR-MS (EI, 70eV): [$C_{15}H_{16}NO_2$], calcd.: 242.1181; found: 242.1176 [M-H]$^+$.

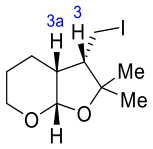
3-(Iodomethyl)-2,2-dimethylhexahydro-4*H*-furo[2,3-b]pyran



Following **TP6**, iodooxanyl acetal (**103**, 148 mg, 0.50 mmol, dr = 99:1) was treated with a 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.00 mmol) at room temperature and then the reaction mixture was heated up to 50 °C. After the cyclization was complete after 8 h, then I_2 (381 mg, 1.50 mmol) was added at 0 °C and the mixture was stirred for 3 h and worked-up as usual. The crude product obtained as a mixture of diastereomers **105a** and **105b**, which have been separated by column chromatography.

[154] C. Han, S. L. Buchwald, *J. Am. Chem. Soc.* **2009**, *131*, 7532-7533.

3-(Iodomethyl)-2,2-dimethylhexahydro-4*H*-furo[2,3-b]pyran (105a)



Isolated yield: 38 mg, 0.13 mmol, 26%, dr = 99:1, colorless oil.

Purification: *i*-hexane:ethyl acetate = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.23 (d, J = 3.8 Hz, 1H), 3.84 – 3.77 (m, 1H), 3.70 – 3.62 (m, 1H), 3.17 (s, 1H), 3.16 (d, J = 1.6 Hz, 1H), 2.53 (dt, J = 9.1, 7.0 Hz, 1H), 2.19 (dtd, J = 10.4, 6.5, 3.7 Hz, 1H), 1.85 – 1.77 (m, 1H), 1.66 – 1.48 (m, 3H), 1.30 (s, 3H), 1.27 (s, 3H).

Relative stereochemistry was assigned based on observation of NOE for 3,3a-protons.

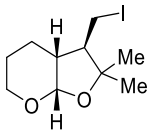
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 97.8, 79.1, 61.1, 53.3, 39.9, 31.1, 24.9, 23.3, 19.1, 1.2.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2955, 2928, 2883, 2866, 1706, 1479, 1465, 1366, 1228, 1120, 1089, 1059, 1036, 1016, 999, 973, 900, 886, 877, 869.

MS (EI, 70 eV): *m/z* (%) = 295 (1), 123 (11), 111 (100), 95 (14), 93 (13), 81 (46), 79 (20).

HR-MS (EI, 70eV): [$C_{10}H_{16}IO_2$], calcd.: 295.0195; found: 295.0182 [M-H]$^+$.

3-(Iodomethyl)-2,2-dimethylhexahydro-4*H*-furo[2,3-b]pyran (105b)



Isolated yield: 77 mg, 0.26 mmol, 52%, dr = 1:99, colorless crystals.

Purification: *i*-hexane:ethyl acetate = 9:1.

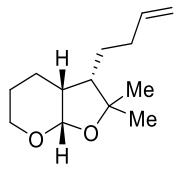
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.79 (d, J = 3.6 Hz, 1H), 3.88 (ddt, J = 11.8, 4.3, 2.1 Hz, 1H), 3.36 (td, J = 11.8, 2.3 Hz, 1H), 3.28 (dd, J = 10.3, 4.3 Hz, 1H), 2.98 (t, J = 10.3 Hz, 1H), 2.54 (ddd, J = 11.9, 10.2, 4.3 Hz, 1H), 1.91 (ddq, J = 14.2, 4.4, 2.2 Hz, 1H), 1.89 – 1.84 (m, 1H), 1.81 (ddt, J = 14.0, 12.9, 5.0 Hz, 1H), 1.75 – 1.65 (m, 1H), 1.50 (s, 3H), 1.34 (ddq, J = 13.7, 4.7, 2.3 Hz, 1H), 1.17 (s, 3H).

Relative stereochemistry was assigned based on X-ray structure, see page SI24 of SI.

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 100.0, 85.0, 64.7, 48.0, 45.8, 31.3, 23.5, 22.4, 20.3, 2.6.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2971, 2938, 2875, 2866, 2838, 1383, 1367, 1312, 1273, 1254, 1226, 1186, 1164, 1135, 1112, 1095, 1055, 1035, 1011, 902, 880, 874.
MS (EI, 70 eV): *m/z* (%) = 295 (1), 123 (25), 111 (100), 95 (15), 93 (14), 81 (55), 79 (20).
HR-MS (EI, 70eV): [$C_{10}H_{16}IO_2$], calcd.: 295.0195; found: 295.0183 [M-H]$^+$.
m.p.: 58.4 – 59.6 °C

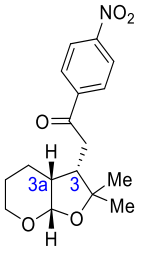
3-(But-3-en-1-yl)-2,2-dimethylhexahydro-4*H*-furo[2,3-b]pyran (106a)



Following **TP6**, iodide (**105a**, 148 mg, 0.40 mmol, dr = 99:1) was treated with 1.0 M solution of Et_2Zn in toluene (0.8 mL, 0.80 mmol) at room temperature and then the reaction mixture was heated up to 50 °C. After the insertion was complete after 16 h, allyl bromide (145 mg, 104 µL, 1.20 mmol) was added at −30 °C, followed by 1.0 M CuCN·2LiCl solution in THF (0.4 mL, 0.4 mmol) and the mixture was stirred for 3 h and worked-up as usual.

Isolated yield: 72 mg, 0.34 mmol, 86%, dr = 99:1, colorless oil.
Purification: pentane:ethyl acetate = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.80 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 5.21 (d, *J* = 3.3 Hz, 1H), 5.06 – 4.93 (m, 2H), 3.80 (ddt, *J* = 11.0, 6.6, 3.7 Hz, 1H), 3.70 – 3.58 (m, 1H), 2.16 – 1.90 (m, 4H), 1.68 – 1.44 (m, 5H), 1.35 (dddd, *J* = 14.0, 9.7, 6.6, 4.3 Hz, 1H), 1.24 (d, *J* = 7.7 Hz, 6H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 138.4, 115.0, 98.8, 79.3, 60.9, 49.2, 38.2, 33.1, 31.2, 25.5, 25.1, 23.7, 20.1.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2967, 2931, 2869, 1706, 1479, 1465, 1366, 1228, 1120, 1090, 1059, 1036, 1000, 973, 901, 878, 869, 807, 799, 746, 728.
MS (EI, 70 eV): *m/z* (%) = 195 (17), 123 (41), 121 (52), 109 (43), 107 (23), 97 (47), 95 (40), 93 (55), 91 (26), 81 (100).
HR-MS (EI, 70eV): [$C_{12}H_{19}O_2$], calcd.: 195.1385; found: 195.1376 [M-CH_3]$^+$.

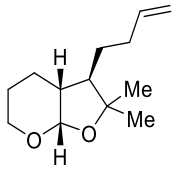
2-(2,2-dimethylhexahydro-4*H*-furo[2,3-b]pyran-3-yl)-1-(4-nitrophenyl)ethan-1-one (106b)



Following **TP6**, iodide (**105a**, 148 mg, 0.40 mmol, dr = 99:1) was treated with 1.0 M solution of Et_2Zn in toluene (0.8 mL, 0.80 mmol) at room temperature and then the reaction mixture was heated up to 50 °C. After the insertion was complete after 16 h, a 1.0 M CuCN·2LiCl solution in THF (0.4 mL, 0.4 mmol) was added at −30 °C and was stirred for 30 min. Then, 4-nitrobenzoyl chloride (223 mg, 1.20 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 3 h and worked-up as usual.

Isolated yield: 75 mg, 0.24 mmol, 59%, dr = 99:1, colorless crystals.
Purification: pentane:ethyl acetate = 1:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 8.36 – 8.29 (m, 2H), 8.16 – 8.10 (m, 2H), 5.22 (d, *J* = 3.9 Hz, 1H), 3.83 (ddd, *J* = 11.3, 9.0, 3.2 Hz, 1H), 3.66 – 3.56 (m, 1H), 3.18 – 3.09 (m, 2H), 2.76 (q, *J* = 7.3 Hz, 1H), 2.34 (qd, *J* = 9.6, 8.1, 5.0 Hz, 1H), 1.55 (tq, *J* = 9.5, 4.5 Hz, 4H), 1.33 (s, 3H), 1.30 (s, 3H).
Relative stereochemistry was assigned based on observation of NOE for 3,3a-protons.
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 197.6, 150.6, 141.2, 129.1, 124.1, 99.5, 80.1, 61.5, 44.3, 38.5, 36.3, 30.9, 26.1, 23.3, 21.0.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2966, 2947, 2921, 2896, 2875, 2851, 1685, 1605, 1525, 1407, 1385, 1371, 1349, 1333, 1322, 1304, 1280, 1264, 1242, 1210, 1167, 1156, 1143, 1125, 1104, 1093, 1030, 1004, 987, 952, 910, 877, 852, 833, 788, 753, 746, 688.
MS (EI, 70 eV): *m/z* (%) = 319 (1), 150 (89), 120 (24), 109 (100), 104 (58), 97 (46).
HR-MS (EI, 70eV): [$C_{17}H_{21}O_5N$], calcd.: 319.1420; found: 319.1409 [M]$^+$.
m.p.: 121.6 – 124.6 °C

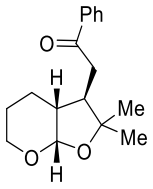
3-(But-3-en-1-yl)-2,2-dimethylhexahydro-4*H*-furo[2,3-b]pyran (107a)



Following **TP6**, iodide (**105b**, 148 mg, 0.50 mmol, dr = 1:99) was treated with 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.00 mmol) at room temperature and then the reaction mixture was heated up to 50 °C. After the insertion was complete after 16 h, allyl bromide (181 mg, 130 µL, 1.50 mmol) was added at −20 °C, following by 1.0 M CuCN·2LiCl solution in THF (15 *µ*L, 0.015 mmol, 5 mol%) and was stirred for 3 h and worked-up as usual.

Isolated yield: 65 mg, 0.31 mmol, 61%, dr = 1:99, colorless oil.
Purification: *i*-hexane:ethyl acetate = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.80 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H), 5.07 – 5.00 (m, 1H), 4.98 (dq, *J* = 10.2, 1.5 Hz, 1H), 4.85 (d, *J* = 3.4 Hz, 1H), 3.86 (ddt, *J* = 11.7, 4.4, 2.0 Hz, 1H), 3.36 (td, *J* = 11.7, 2.4 Hz, 1H), 2.23 – 1.99 (m, 3H), 1.91 – 1.60 (m, 4H), 1.58 – 1.45 (m, 1H), 1.40 (s, 3H), 1.38 – 1.22 (m, 2H), 1.10 (s, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 138.5, 115.0, 100.7, 85.0, 64.6, 44.6, 44.5, 32.6, 31.4, 28.3, 24.2, 22.4, 20.6.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2967, 2958, 2931, 2909, 2869, 1706, 1479, 1465, 1382, 1366, 1228, 1120, 1090, 1059, 1036, 1015, 1000, 973, 901, 885, 878, 869.
MS (EI, 70 eV): *m/z* (%) = 209 (1), 109 (59), 97 (57), 93 (66), 91 (65), 81 (99), 79 (100), 67 (96).
HR-MS (EI, 70eV): [$C_{13}H_{21}O_2$], calcd.: 209.1542; found: 209.1532 [M-H]$^+$.

2-(2,2-dimethylhexahydro-4*H*-furo[2,3-b]pyran-3-yl)-1-phenylethan-1-one (107b)

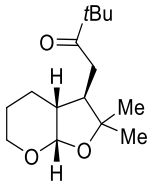


Following **TP6**, iodide (**105b**, 148 mg, 0.50 mmol, dr = 1:99) was treated with 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.00 mmol) at room temperature and then the reaction mixture was heated up to 50 °C. After the insertion was complete after 16 h, a

1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −40 °C and was stirred for 30 min. Then, benzoyl chloride (211 mg, 174 *µ*L, 1.50 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 3 h and worked-up as usual.

Isolated yield: 130 mg, 0.47 mmol, 95%, dr = 1:99, colorless crystals.
Purification: *i*-hexane:ethyl acetate = 1:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.99 – 7.92 (m, 2H), 7.62 – 7.55 (m, 1H), 7.49 (dd, *J* = 8.4, 7.0 Hz, 2H), 4.90 (d, *J* = 3.5 Hz, 1H), 3.95 – 3.84 (m, 1H), 3.44 – 3.33 (m, 1H), 3.00 (d, *J* = 7.3 Hz, 2H), 2.96 – 2.86 (m, 1H), 2.03 – 1.95 (m, 1H), 1.83 – 1.68 (m, 3H), 1.45 (s, 3H), 1.34 – 1.23 (m, 1H), 1.12 (s, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 199.4, 137.0, 133.4, 128.9, 128.2, 100.7, 84.9, 64.8, 44.7, 41.2, 38.8, 30.6, 24.9, 22.5, 20.5.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2970, 2937, 2864, 1684, 1597, 1580, 1464, 1448, 1383, 1366, 1338, 1315, 1298, 1276, 1251, 1228, 1216, 1207, 1176, 1171, 1133, 1118, 1097, 1087, 1056, 1036, 1021, 1001, 994, 975, 901, 879, 869, 756, 750, 724, 691.
MS (EI, 70 eV): *m/z* (%) = 273 (1), 173 (9), 155 (9), 109 (43), 105 (100), 97 (15), 96 (10), 93 (13), 81 (10), 79 (10), 77 (46).
HR-MS (EI, 70eV): [$C_{17}H_{21}O_3$], calcd.: 273.1491; found: 273.1483 [M-H]$^+$.
m.p.: 68.4 – 69.3 °C

1-(2,2-dimethylhexahydro-4*H*-furo[2,3-b]pyran-3-yl)-3,3-dimethylbutan-2-one (107c)



Following **TP6**, iodide (**105b**, 148 mg, 0.50 mmol, dr = 1:99) was treated with 1.0 M solution of Et_2Zn in toluene (1.0 mL, 1.00 mmol) at room temperature and then the reaction mixture was heated up to 50 °C. After the insertion was complete after 16 h, a 1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −40 °C and was stirred for 30 min. Then, *tert*-butylacetyl chloride (202 mg, 1.50 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 3 h and worked-up as usual.

Isolated yield: 82 mg, 0.32 mmol, 64%, dr = 1:99, colorless oil.

Purification: *i*-hexane:ethyl acetate = 9:1→7:3.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 4.84 (d, *J* = 3.5 Hz, 1H), 3.87 (dp, *J* = 11.8, 2.0 Hz, 1H), 3.33 (td, *J* = 11.6, 2.3 Hz, 1H), 2.74 (dt, *J* = 12.5, 6.5 Hz, 1H), 2.57 – 2.41 (m, 2H), 1.88 – 1.65 (m, 3H), 1.55 (ddd, *J* = 13.7, 4.0, 2.0 Hz, 1H), 1.39 (s, 3H), 1.31 – 1.22 (m, 1H), 1.14 (s, 9H), 1.02 (s, 3H).

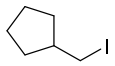
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 214.5, 100.5, 84.7, 64.7, 44.6, 44.4, 39.9, 36.8, 30.5, 26.7, 24.8, 22.5, 20.4.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2924, 2901, 2848, 1704, 1473, 1463, 1456, 1446, 1424, 1380, 1365, 1315, 1228, 1120, 1089, 1056, 1034, 1008, 998, 972, 900, 884, 880, 869.

MS (EI, 70 eV): *m/z* (%) = 253 (1), 139 (46), 111 (18), 109 (100), 97 (32), 93 (27), 91 (13), 81 (34), 79 (26).

HR-MS (EI, 70eV): [$C_{15}H_{25}O_3$], calcd.: 253.1804; found: 253.1804 [M-H]$^+$.

(Iodomethyl)cyclopentane (110a)



Following **TP6**, 6-iodo-1-hexene (**108a**, 105 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 16 h, then I_2 (381 mg, 1.50 mmol) was added at 0 °C. The mixture was stirred for 3 h and worked-up as usual. The analytical data were in full consistency with the data reported in the literature.[155]

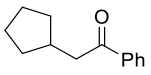
Isolated yield: 56 mg, 0.27 mmol, 53%, colorless oil.

Purification: pentane:diethyl ether = 100:3.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 3.14 (d, *J* = 7.0 Hz, 2H), 2.10 (dq, *J* = 15.1, 7.6 Hz, 1H), 1.78 (ddtd, *J* = 12.7, 7.0, 4.5, 4.0, 2.0 Hz, 3H), 1.68 – 1.49 (m, 3H), 1.24 – 1.11 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 42.9, 33.6, 25.7, 14.5.

2-Cyclopentyl-1-phenylethan-1-one (110b)

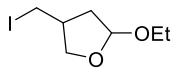


[155] T. Cohen, H. Gibney, R. Ivanov, E.A.-H. Yeh, I. Marek, D.P. Curran, *J. Am. Chem. Soc.* **2007**, *129*, 15405-15409.

Following **TP6**, 6-iodo-1-hexene (**108a**, 105 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 16 h, a 1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −40 °C and the mixture was stirred for 30 min. Then, benzoyl chloride (211 mg, 174 µL, 1.50 mmol) was added, and the reaction mixture was allowed to warm to room temperature in 3 h and worked-up as usual. The analytical data were in full consistency with the data reported in the literature.[156]

Isolated yield: 69 mg, 0.37 mmol, 73%, colorless oil.
Purification: pentane:diethyl ether = 100:3.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.99 – 7.93 (m, 2H), 7.59 – 7.51 (m, 1H), 7.49 – 7.43 (m, 2H), 2.99 (d, *J* = 7.1 Hz, 2H), 2.39 (ddd, *J* = 8.7, 7.2, 1.5 Hz, 1H), 1.94 – 1.82 (m, 2H), 1.73 – 1.50 (m, 3H), 1.25 – 1.10 (m, 1H), 0.94 – 0.80 (m, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 200.6, 137.4, 133.0, 128.7, 128.3, 45.0, 36.2, 32.9, 25.1.

2-Ethoxy-4-(iodomethyl)tetrahydrofuran (110c)



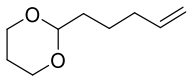
Following **TP6**, 6-iodo-1-hexene (**108b**, 105 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 16 h, then I_2 (381 mg, 1.50 mmol) was added at 0 °C. The mixture was stirred for 3 h and worked-up as usual.

Isolated yield: 82 mg, 0.32 mmol, 64%, dr = 83:17, yellowish oil.
Purification: *i*-hexane:ethyl acetate = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.20 (dd, *J* = 5.4, 1.9 Hz, 1H), 4.03 (dd, *J* = 8.8, 7.4 Hz, 1H), 3.71 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.59 (dd, *J* = 8.7, 7.2 Hz, 1H), 3.47 – 3.35 (m, 1H), 3.30 – 3.24 (m, 2H), 2.68 (ddtd, *J* = 16.2, 9.1, 7.2, 5.1 Hz, 1H), 2.23 (ddd, *J* = 13.6, 9.6, 5.4 Hz, 1H), 1.65 (ddd, *J* = 13.5, 5.2, 1.9 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H) (signals of a major diastereomer are given).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 104.1, 72.5, 63.0, 41.4, 40.3, 15.4, 8.8 (signals of a major diastereomer are given).

[156] C.F. Malosh, J.M. Ready, *J. Am. Chem. Soc.* **2004**, *126*, 10240-10241.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2946, 2902, 2876, 1781, 1706, 1475, 1440, 1426, 1372, 1337, 1321, 1274, 1234, 1183, 1150, 1139, 1087, 1028, 975, 922, 874, 844, 808.
MS (EI, 70 eV): *m/z* (%) = 254 (46), 211 (100), 210 (37), 83 (68), 55 (82).
HR-MS (EI, 70eV): [$C_7H_{12}IO_2$], calcd.: 254.9882; found: 254.9878 [M-H]$^+$.

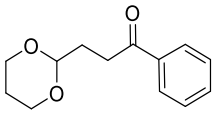
2-(Pent-4-en-1-yl)-1,3-dioxane (113a)



Following **TP7**, alkyl iodide **111a** (121 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 6 h, allyl bromide (181 mg, 130 µl, 1.50 mmol) was added at −20 °C, following by 1.0 M CuCN·2LiCl solution in THF (15 µL, 0.015 mmol, 5 mol%) and the mixture was stirred for 2 h and worked-up as usual.

Isolated yield: 43 mg, 0.28 mmol, 55%, colorless oil.
Purification: pentane:diethyl ether = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 5.78 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 4.99 (dq, *J* = 17.2, 1.7 Hz, 1H), 4.93 (dq, *J* = 10.1, 1.5 Hz, 1H), 4.51 (t, *J* = 5.1 Hz, 1H), 4.09 (ddd, *J* = 12.1, 5.0, 1.6 Hz, 2H), 3.75 (ddt, *J* = 12.2, 10.3, 2.3 Hz, 2H), 2.10 – 2.00 (m, 3H), 1.60 (ddd, *J* = 9.3, 6.8, 4.6 Hz, 2H), 1.53 – 1.43 (m, 2H), 1.33 (dtt, *J* = 13.4, 2.7, 1.4 Hz, 1H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 138.7, 114.8, 102.4, 67.0, 34.8, 33.6, 26.0, 23.4.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2955, 2926, 2849, 1641, 1470, 1460, 1431, 1405, 1378, 1286, 1243, 1143, 1116, 1084, 1051, 1038, 994, 944, 909, 859, 842, 810.
MS (EI, 70 eV): *m/z* (%) = 155 (7), 113 (14), 87 (100), 80(15), 79 (6), 59 (15).
HR-MS (EI, 70eV): [$C_9H_{15}O_2$], calcd.: 155.1072; found: 155.1066 [M-H]$^+$.

3-(1,3-Dioxan-2-yl)-1-phenylpropan-1-one (113b)

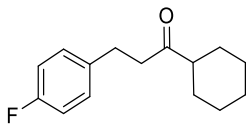


Following **TP7**, alkyl iodide **111a** (121 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 6 h, a 1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −40 °C and the mixture was stirred for 30 min. Then, benzoyl chloride (211 mg, 174 µL, 1.50 mmol) was added

and the reaction mixture was allowed to warm to room temperature in 3 h and worked-up as usual.

Isolated yield: 59 mg, 0.27 mmol, 54%, colorless oil.
Purification: *i*-hexane: ethyl acetate = 4:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 8.01 – 7.92 (m, 2H), 7.58 – 7.50 (m, 1H), 7.44 (dd, *J* = 8.3, 7.0 Hz, 2H), 4.66 (t, *J* = 4.9 Hz, 1H), 4.09 (ddd, *J* = 12.0, 5.0, 1.5 Hz, 2H), 3.84 – 3.69 (m, 2H), 3.11 (t, *J* = 7.3 Hz, 2H), 2.05 (pd, *J* = 8.8, 8.2, 5.1 Hz, 3H), 1.33 (dtt, *J* = 13.5, 2.6, 1.4 Hz, 1H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 199.7, 137.0, 133.1, 128.6, 128.2, 101.1, 67.0, 32.7, 29.4, 25.9.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2957, 2924, 2853, 1686, 1598, 1581, 1468, 1449, 1432, 1407, 1376, 1364, 1321, 1288, 1277, 1242, 1217, 1208, 1181, 1147, 1134, 1085, 1046, 1008, 972, 924, 888, 853, 742, 691.
MS (EI, 70 eV): *m/z* (%) = 219 (3), 144 (64), 133 (35), 120 (1), 116 (13), 115 (83), 105 (100), 100 (56), 87 (41).
HR-MS (EI, 70eV): [$C_{13}H_{15}O_3$], calcd.: 219.1016; found: 219.1012 [M-H]$^+$.

1-Cyclohexyl-3-(4-fluorophenyl)propan-1-one (113c)

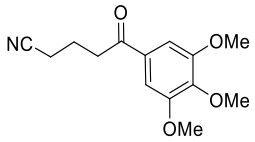


Following **TP7**, alkyl iodide **111b** (125 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 6 h, a 1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −40 °C and the mixture was stirred for 30 min. Then, cyclohexanoyl chloride (88 mg, 80 µL, 0.60 mmol) was added and the reaction mixture was allowed to warm to room temperature in 3 h and worked-up as usual.

Isolated yield: 71 mg, 0.31 mmol, 61%, colorless oil.
Purification: *i*-hexane: diethyl ether = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.16 – 7.09 (m, 2H), 6.98 – 6.91 (m, 2H), 2.84 (t, *J* = 7.4 Hz, 2H), 2.77 – 2.69 (m, 2H), 2.29 (tt, *J* = 11.3, 3.3 Hz, 1H), 1.86 – 1.70 (m, 4H), 1.70 – 1.60 (m, 1H), 1.37 – 1.14 (m, 5H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 213.1, 161.4 (d, *J* = 243.6 Hz), 137.2 (d, *J* = 3.2 Hz), 129.9 (d, *J* = 7.8 Hz), 115.3 (d, *J* = 21.2 Hz), 51.1, 42.4, 29.0, 28.5, 25.9, 25.7.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2929, 2855, 1708, 1510, 1450, 1222, 1158, 829.
MS (EI, 70 eV): *m/z* (%) = 234 (1), 151 (82), 123 (51), 122 (26), 111 (13), 109 (100), 103 (17), 83 (77).
HR-MS (EI, 70eV): [$C_{15}H_{19}FO$], calcd.: 234.1420; found: 234.1410 [M]$^+$.

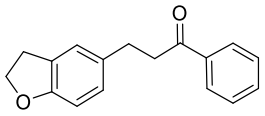
5-Oxo-5-(3,4,5-trimethoxyphenyl)pentanenitrile (113d)



Following **TP7**, alkyl iodide **111c** (98 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 6 h (83%), a 1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −40 °C and the mixture was stirred for 30 min. Then, 3,4,5-trimethoxybenzoyl chloride (231 mg, 1.00 mmol) was added and the reaction mixture was allowed to warm to room temperature in 3 h and worked-up as usual.

Isolated yield: 56 mg, 0.21 mmol, 51%, colorless crystals.
Purification: *i*-hexane:ethyl acetate = 7:3→6:4.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.20 (s, 2H), 3.91 (d, *J* = 1.4 Hz, 9H), 3.14 (t, *J* = 6.8 Hz, 2H), 2.52 (t, *J* = 6.9 Hz, 2H), 2.10 (p, *J* = 6.8 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 197.1, 153.2, 142.9, 131.8, 119.6, 105.5, 61.1, 56.4, 36.1, 20.0, 16.7.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3001, 2942, 2840, 1713, 1676, 1585, 1504, 1456, 1413, 1370, 1333, 1325, 1231, 1188, 1155, 1123, 1001, 868, 847, 830, 771, 713.
MS (EI, 70 eV): *m/z* (%) = 263 (25), 210 (7), 196 (10), 195 (100), 167 (9), 152 (9), 137 (5).
HR-MS (EI, 70eV): [$C_{14}H_{17}NO_4$], calcd.: 263.1158; found: 263.1149 [M]$^+$.
m.p.: 92.2 – 93.9 °C

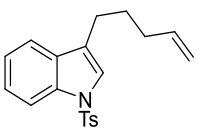
3-(2,3-Dihydrobenzofuran-5-yl)-1-phenylpropan-1-one (113e)



Following **TP7**, alkyl iodide **111d** (137 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 6 h, a 1.0 M CuCN·2LiCl solution in THF (0.5 mL, 0.5 mmol) was added at −40 °C and the mixture was stirred for 30 min. Then, benzoyl chloride (141 mg, 116 µL, 1.00 mmol) was added and the reaction mixture was allowed to warm to room temperature in 3 h and worked-up as usual.

Isolated yield: 78 mg, 0.31 mmol, 62%, colorless oil.
Purification: *i*-hexane:ethyl acetate = 9:1.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 8.00 – 7.94 (m, 2H), 7.61 – 7.53 (m, 1H), 7.46 (dd, *J* = 8.3, 6.9 Hz, 2H), 7.10 (d, *J* = 1.9 Hz, 1H), 6.99 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.72 (d, *J* = 8.1 Hz, 1H), 4.55 (t, *J* = 8.7 Hz, 2H), 3.27 (dd, *J* = 8.4, 6.9 Hz, 2H), 3.18 (t, *J* = 8.7 Hz, 2H), 3.00 (dd, *J* = 8.4, 7.0 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 199.5, 158.6, 137.0, 133.3, 133.1, 128.7, 128.1, 127.9, 127.3, 125.1, 109.2, 71.3, 41.1, 29.9, 29.7.
FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2956, 2924, 2855, 1683, 1598, 1492, 1448, 1361, 1288, 1272, 1243, 1203, 1102, 982, 944, 814, 743, 690.
MS (EI, 70 eV): *m/z* (%) = 252 (15), 134 (10), 133 (100), 131 (7), 115 (10), 105 (7), 105 (13), 91 (9), 77(20).
HR-MS (EI, 70eV): [$C_{17}H_{16}O_2$], calcd.: 252.1150; found: 252.1142 [M]$^+$.

3-(Pent-4-en-1-yl)-1-tosyl-1*H*-indole (113f)



Following **TP7**, alkyl iodide **111e** (213 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 6 h, allyl bromide (181 mg, 130 µl, 1.50 mmol) was added at −20 °C, following by 1.0 M CuCN·2LiCl solution in THF (15 µL, 0.015 mmol, 5 mol%) and the mixture was stirred for 2 h and worked-up as usual.

Isolated yield: 110 mg, 0.32 mmol, 65%, colorless oil.

Purification: *i*-hexane:ethyl acetate = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 8.00 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.79 – 7.71 (m, 2H), 7.48 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.35 – 7.27 (m, 2H), 7.26 – 7.16 (m, 3H), 5.84 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.10 – 4.93 (m, 2H), 2.71 – 2.63 (m, 2H), 2.32 (s, 3H), 2.16 – 2.05 (m, 2H), 1.78 (p, *J* = 7.5 Hz, 2H).

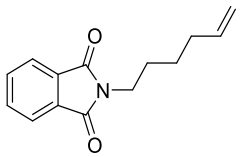
^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 144.8, 138.4, 135.4, 131.2, 129.9, 126.8, 124.7, 123.4, 123.1, 122.8, 119.6, 115.1, 113.9, 33.4, 28.1, 24.3, 21.7.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3066, 2976, 2929, 2859, 1640, 1598, 1494, 1447, 1400, 1366, 1306, 1293, 1278, 1205, 1187, 1172, 1120, 1094, 1020, 975, 912, 812, 746, 703, 669.

MS (EI, 70 eV): *m/z* (%) = 339 (1), 297 (4), 285 (6), 284 (8), 281 (2).

HR-MS (EI, 70eV): [$C_{20}H_{21}O_2NS$], calcd.: 339.1293; found: 339.1282 [M]$^+$.

2-(Hex-5-en-1-yl)isoindoline-1,3-dione (113g)



Following **TP7**, alkyl iodide **111f** (158 mg, 0.50 mmol) was treated with a solution of Et_2Zn (1.0 mL, 1.00 mmol) at 50 °C. After the insertion was complete after 6 h, allyl bromide (181 mg, 130 *µ*l, 1.50 mmol) was added at −20 °C, following by 1.0 M CuCN·2LiCl solution in THF (15 *µ*L, 0.015 mmol, 5 mol%) and the mixture was stirred for 2 h and worked-up as usual.

Isolated yield: 70 mg, 0.3 mmol, 61%, colorless oil.

Purification: *i*-hexane:ethyl acetate = 9:1.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ = 7.87 – 7.77 (m, 2H), 7.74 – 7.65 (m, 2H), 5.76 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 4.99 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.93 (ddt, *J* = 10.2, 2.2, 1.2 Hz, 1H), 3.67 (t, *J* = 7.3 Hz, 2H), 2.13 – 2.03 (m, 2H), 1.74 – 1.62 (m, 2H), 1.43 (p, *J* = 7.6 Hz, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ = 168.5, 138.4, 134.0, 132.2, 123.3, 115.0, 37.9, 33.4, 28.1, 26.2.

FT-IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2926, 2856, 1773, 1711, 1467, 1438, 1396, 1371, 1042, 913, 720.

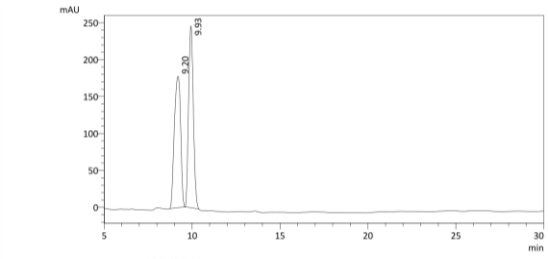
MS (EI, 70 eV): *m/z* (%) = 229 (1), 186 (10), 161 (20), 160 (100), 148 (45), 133 (19), 130 (31), 117 (13), 105 (10), 104 (10), 77 (10).

HR-MS (EI, 70eV): [$C_{14}H_{15}O_2N$], calcd.: 229.1103; found: 229.1094 [M]$^+$.

VI Appendix

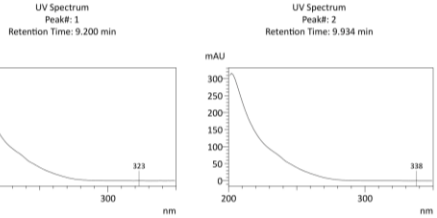
Chiral HPLC spectra

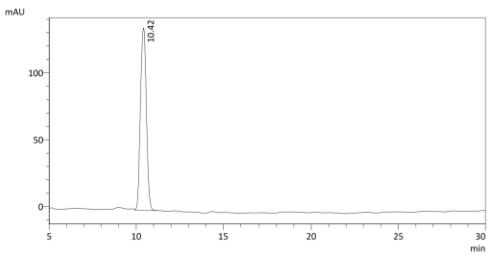
(3*S*,4*R*)-3-Bromo-4-((*tert*-butyldimethylsilyl)oxy)dihydrofuran-2(3*H*)-one (75a)



PDA Ch2 209nm

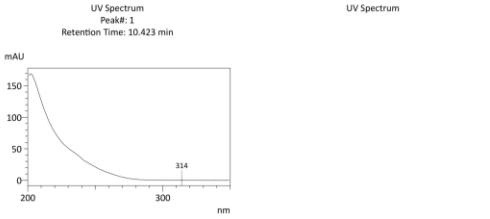
Peak#	Ret. Time	Area	Height	Area%
1	9.20	4437846	177899	49.0
2	9.93	4626221	246193	51.0
Total				100.0



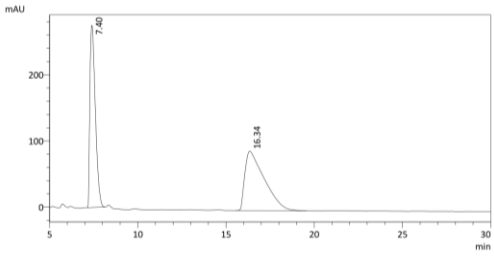


PDA Ch2 209nm

Peak#	Ret. Time	Area	Height	Area%
1	10.42	3227314	136222	100.0
Total				100.0

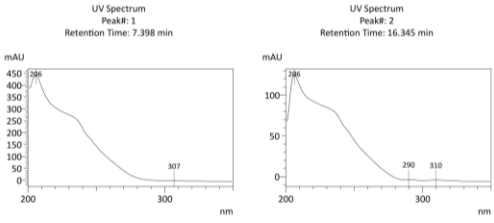


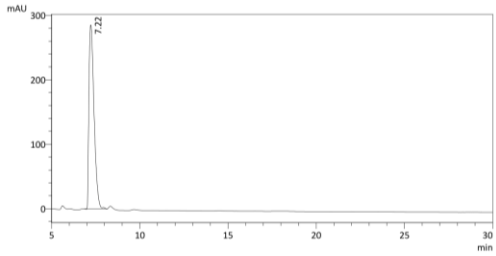
(2*R*,5*R*,6*R*)-5-Bromo-2-(*tert*-butyl)-6-methyl-1,3-dioxan-4-one (78a)



PDA Ch2 230nm

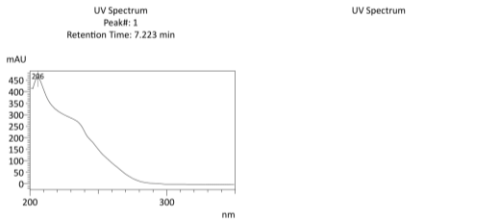
Peak#	Ret. Time	Area	Height	Area%
1	7.40	5933223	275159	46.4
2	16.34	6856051	89713	53.6
Total				100.0



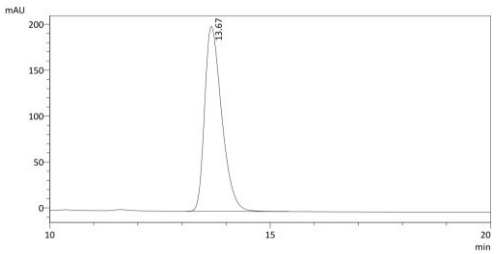


PDA Ch2 230nm

Peak#	Ret. Time	Area	Height	Area%
1	7.22	5741116	285611	100.0
Total				100.0

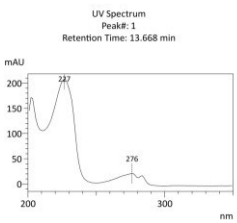


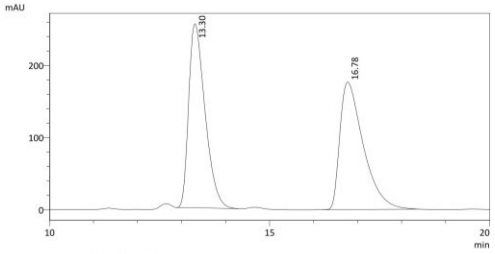
(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (77a)



PDA Ch2 227nm

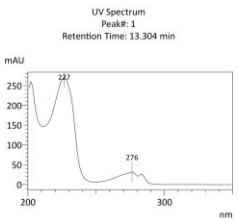
Peak#	Ret. Time	Area	Height	Area%
1	13.67	5419681	201373	100.0
Total				100.0

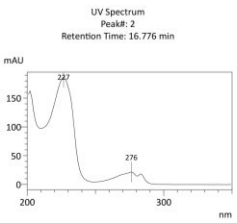




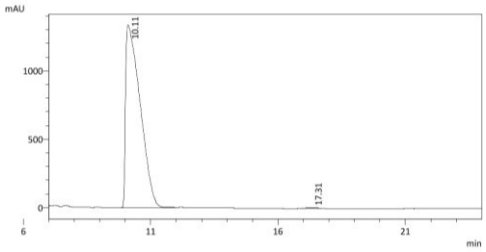
PDA Ch2 227nm

Peak#	Ret. Time	Area	Height	Area%
1	13.30	6593172	255131	50.2
2	16.78	6548808	176712	49.8
Total				100.0



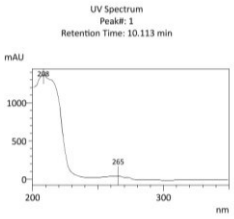


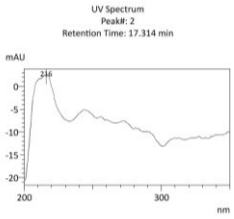
(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(4-(trifluoromethoxy)phenyl)dihydrofuran-2(3*H*)-one (77b)

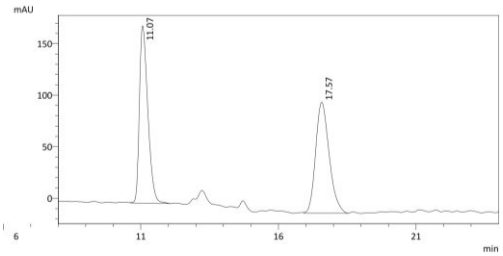


PDA Ch2 210nm

Peak#	Ret. Time	Area	Height	Area%
1	10.11	52806526	1334501	99.7
2	17.31	160492	5970	0.3
Total				100.0

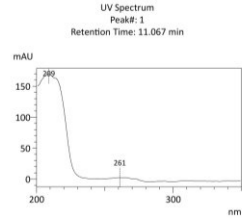


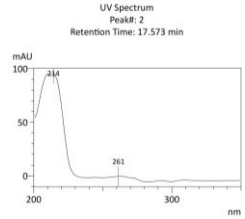




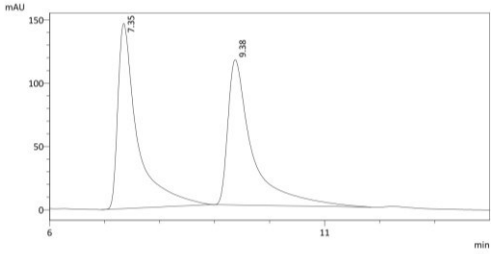
PDA Ch2 210nm

Peak#	Ret. Time	Area	Height	Area%
1	11.07	3659053	172151	49.9
2	17.57	3675601	107635	50.1
Total				100.0



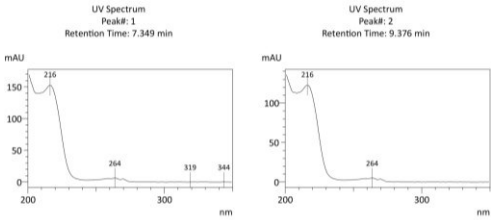


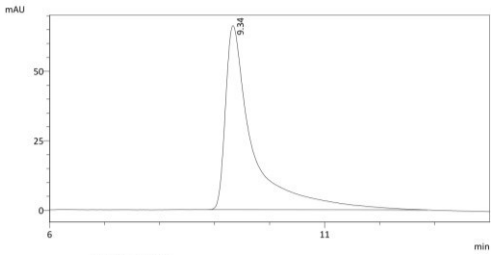
(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(4-(trifluoromethyl)phenyl)dihydrofuran-2(3*H*)-one (77c)



PDA Ch2 216nm

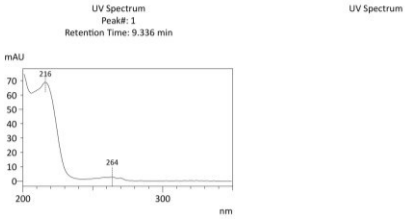
Peak#	Ret. Time	Area	Height	Area%
1	7.35	3619350	146326	50.5
2	9.38	3550754	114801	49.5
Total				100.0



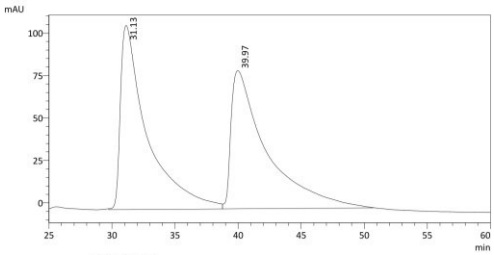


PDA Ch2 216nm

Peak#	Ret. Time	Area	Height	Area%
1	9.34	2302357	66226	100.0
Total				100.0

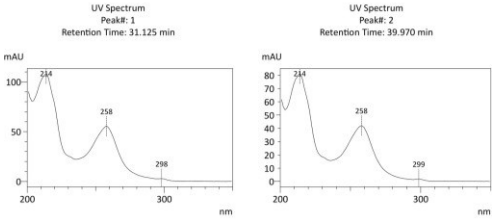


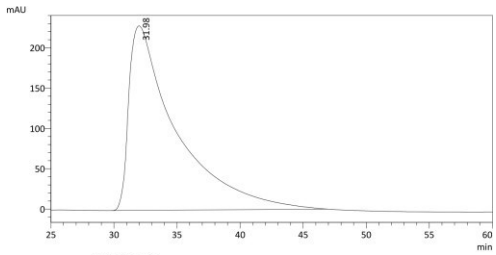
(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(3-(methylthio)phenyl)dihydrofuran-2(3*H*)-one (77d)



PDA Ch2 213nm

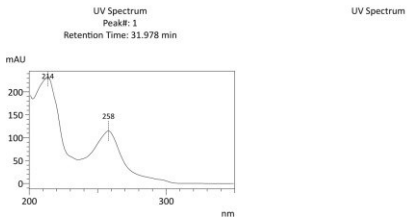
Peak#	Ret. Time	Area	Height	Area%
1	31.13	15954875	108406	50.1
2	39.97	15921832	81380	49.9
Total				100.0



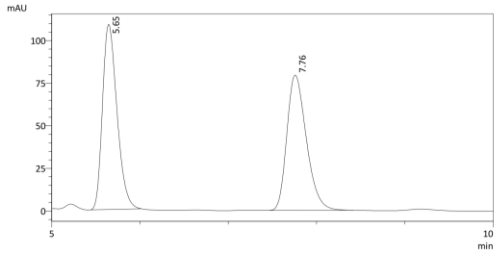


PDA Ch2 213nm

Peak#	Ret. Time	Area	Height	Area%
1	31.98	60054289	228959	100.0
Total				100.0



(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(3-((*tert*-butyldimethylsilyl)oxy)phenyl)-dihydrofuran- 2(3*H*)-one (77e)



PDA Ch2 270nm

Peak#	Ret. Time	Area	Height	Area%
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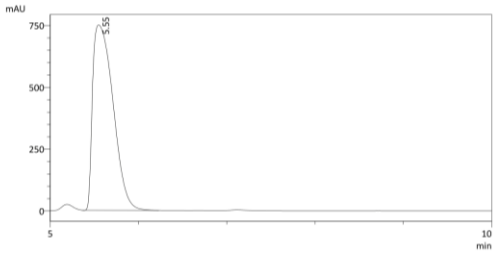
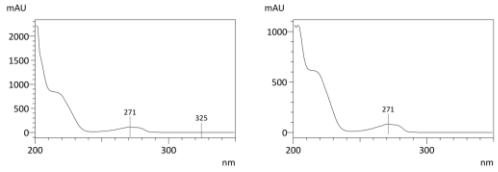
2	7.76	1220033	79452	49.6
Total				100.0



PDA Ch2 270nm

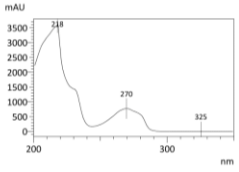
Peak#	Ret. Time	Area	Height	Area%
1	5.55	12049572	749349	100.0
Total				100.0

UV Spectrum
Peak#: 1
Retention Time: 5.646 min



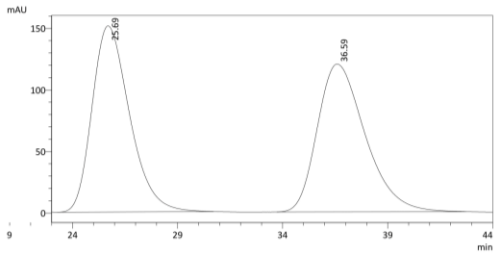
UV Spectrum
Peak#: 2
Retention Time: 7.758 min

UV Spectrum
Peak#: 1
Retention Time: 5.549 min



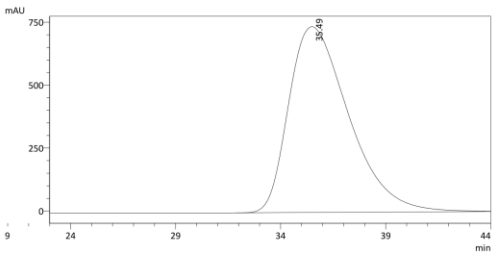
UV Spectrum

(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(6-methoxynaphthalen-2-yl)dihydrofuran-2(3*H*)-one (77f)



PDA Ch2 233nm

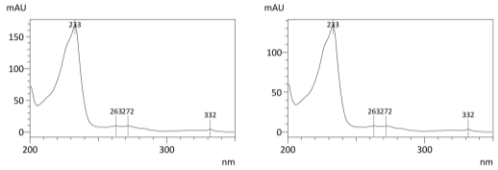
Peak#	Ret. Time	Area	Height	Area%
1	25.69	18794588	151193	49.7
2	36.59	19030070	120140	50.3
Total				100.0



PDA Ch2 233nm

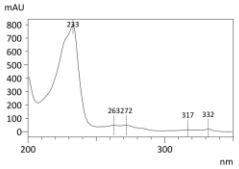
Peak#	Ret. Time	Area	Height	Area%
1	35.49	146832400	738248	100.0
Total				100.0

UV Spectrum
Peak#: 1
Retention Time: 25.686 min



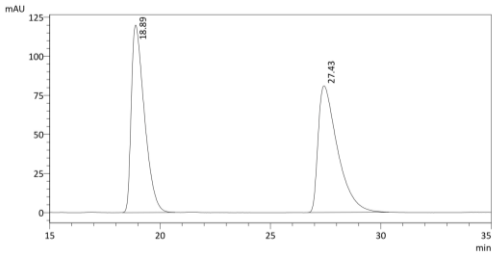
UV Spectrum
Peak#: 2
Retention Time: 36.585 min

UV Spectrum
Peak#: 1
Retention Time: 35.490 min



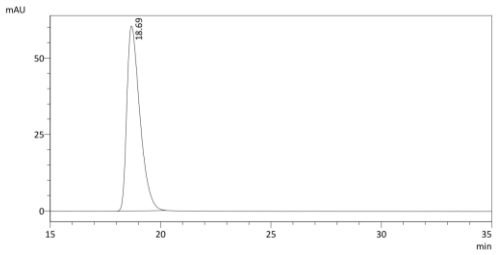
UV Spectrum

(3*S*,4*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(benzo[*d*][1,3]dioxol-5-yl)dihydrofuran-2(3*H*)-one (77g)



PDA Ch2 289nm

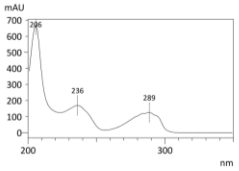
Peak#	Ret. Time	Area	Height	Area%
1	18.89	4947976	119967	49.9
2	27.43	4958881	81005	50.1
Total				100.0



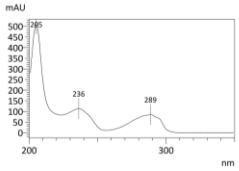
PDA Ch2 289nm

Peak#	Ret. Time	Area	Height	Area%
1	18.69	2480261	60575	100.0
Total				100.0

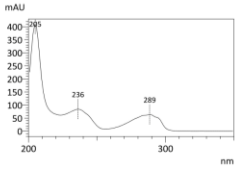
UV Spectrum
Peak#: 1
Retention Time: 18.894 min



UV Spectrum
Peak#: 2
Retention Time: 27.430 min

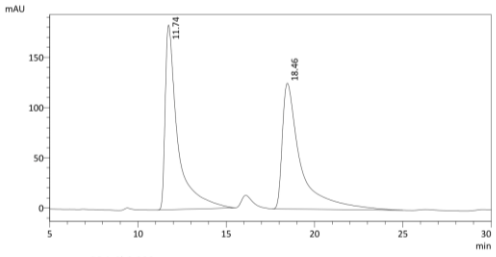


UV Spectrum
Peak#: 1
Retention Time: 18.687 min



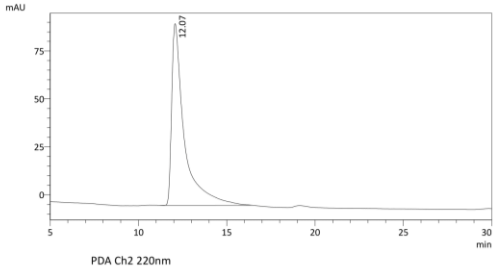
UV Spectrum

(3*S*,4*S*)-3-(2-(Benzyloxy)-4,5-dimethoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)-dihydrofuran-2(3*H*)- one (77h)



PDA Ch2 220nm

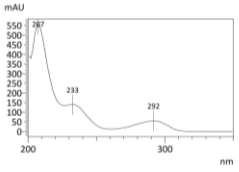
Peak#	Ret. Time	Area	Height	Area%
1	11.74	9055746	183932	50.0
2	18.46	9039755	125313	50.0
Total				100.0



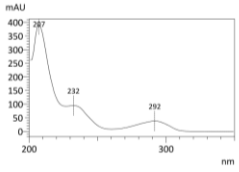
PDA Ch2 220nm

Peak#	Ret. Time	Area	Height	Area%
1	12.07	4707572	94811	100.0
Total				100.0

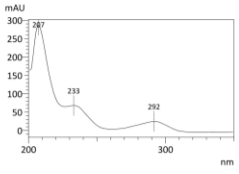
UV Spectrum
Peak#: 1
Retention Time: 11.736 min



UV Spectrum
Peak#: 2
Retention Time: 18.462 min

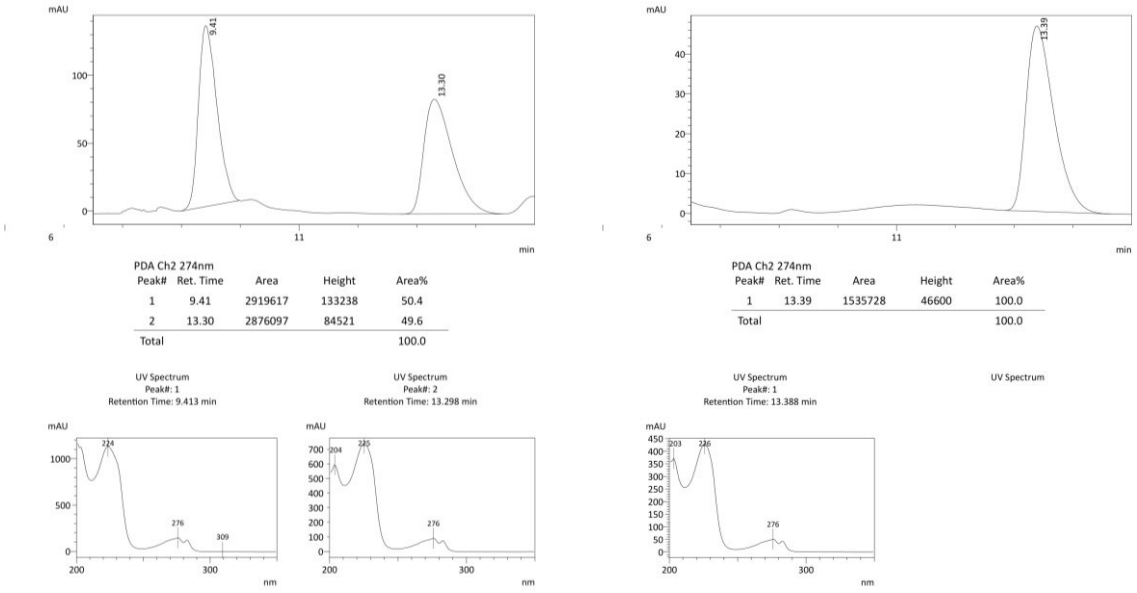


UV Spectrum
Peak#: 1
Retention Time: 12.074 min

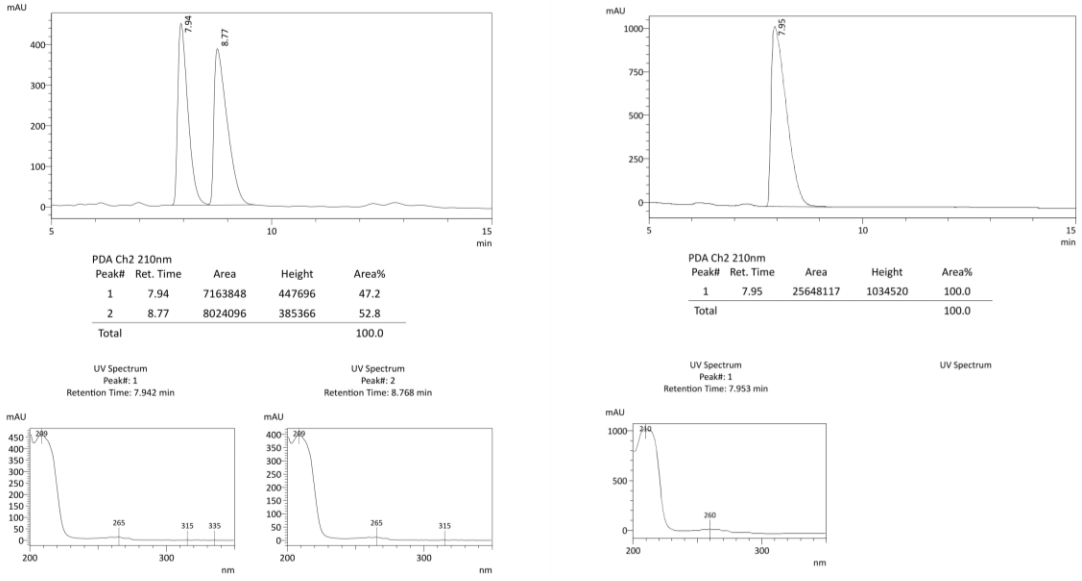


UV Spectrum

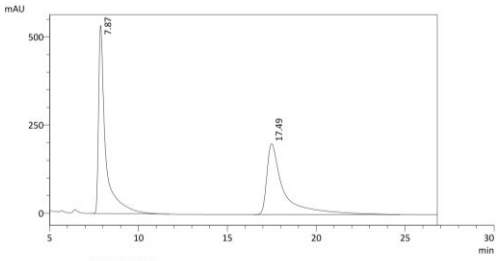
(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-5-(4-methoxyphenyl)-6-methyl-1,3-dioxan-4-one (79a)



(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-6-methyl-5-(4-(trifluoromethoxy)phenyl)-1,3-dioxan-4-one (79b)

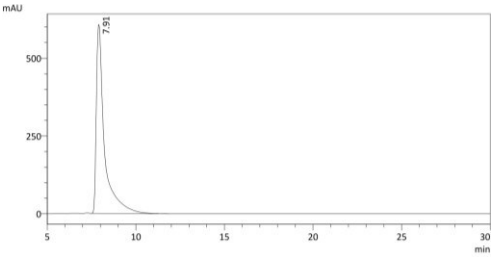


(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-6-methyl-5-(4-(trifluoromethyl)phenyl)-1,3-dioxan-4-one (79c)



PDA Ch2 215nm

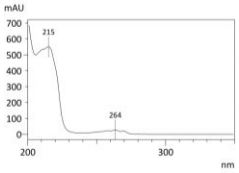
Peak#	Ret. Time	Area	Height	Area%
1	7.87	14704038	533512	52.5
2	17.49	13304145	200563	47.5
Total				100.0



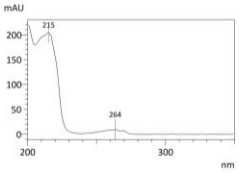
PDA Ch2 321nm

Peak#	Ret. Time	Area	Height	Area%
1	7.91	19233363	607030	100.0
Total				100.0

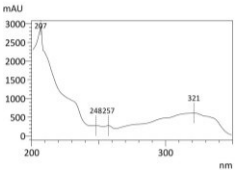
UV Spectrum
Peak#: 1
Retention Time: 7.872 min



UV Spectrum
Peak#: 2
Retention Time: 17.490 min

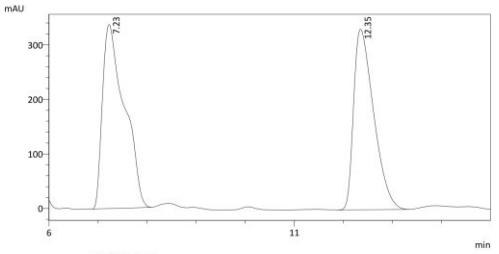


UV Spectrum
Peak#: 1
Retention Time: 7.908 min



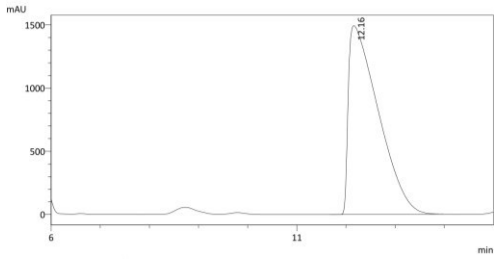
UV Spectrum

(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-5-(3-((*tert*-butyldimethylsilyl)oxy)phenyl)-6-methyl-1,3-dioxan-4-one (79d)



PDA Ch2 218nm

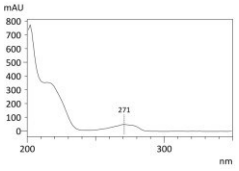
Peak#	Ret. Time	Area	Height	Area%
1	7.23	10480131	337200	52.7
2	12.35	9396053	331161	47.3
Total				100.0



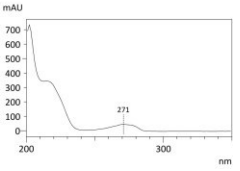
PDA Ch2 218nm

Peak#	Ret. Time	Area	Height	Area%
1	12.16	63191232	1494972	100.0
Total				100.0

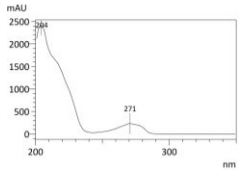
UV Spectrum
Peak#: 1
Retention Time: 7.227 min



UV Spectrum
Peak#: 2
Retention Time: 12.352 min

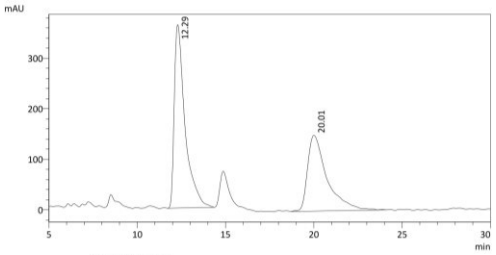


UV Spectrum
Peak#: 1
Retention Time: 12.162 min



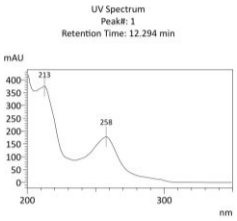
UV Spectrum

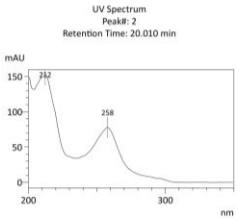
(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-6-methyl-5-(3-(methylthio)phenyl)-1,3-dioxan-4-one (79e)

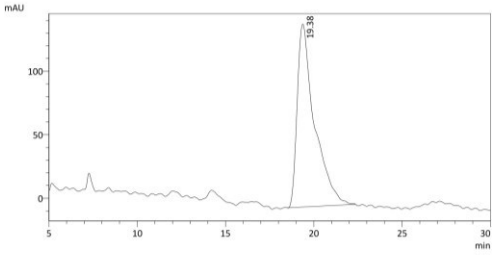


PDA Ch2 211nm

Peak#	Ret. Time	Area	Height	Area%
1	12.29	15392013	362969	57.4
2	20.01	11427046	150066	42.6
Total				100.0

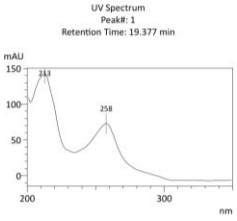




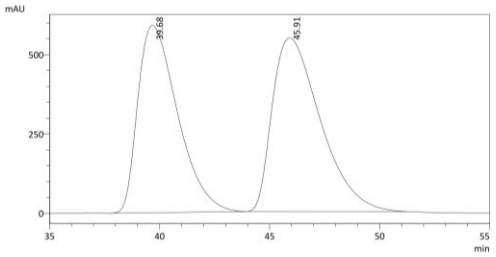


PDA Ch2 211nm

Peak#	Ret. Time	Area	Height	Area%
1	19.38	9829367	144048	100.0
Total				100.0

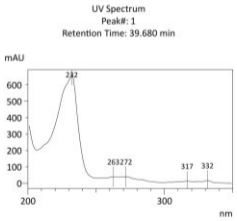


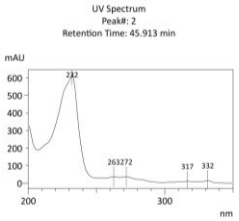
(2*R*,5*R*,6*R*)-2-(*tert*-Butyl)-5-(6-methoxynaphthalen-2-yl)-6-methyl-1,3-dioxan-4-one (79f)

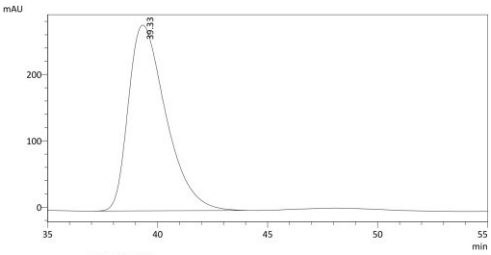


PDA Ch2 232nm

Peak#	Ret. Time	Area	Height	Area%
1	39.68	74226513	590802	47.2
2	45.91	83076242	546642	52.8
Total				100.0

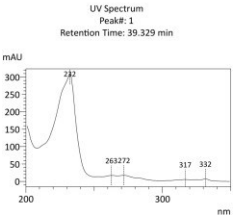




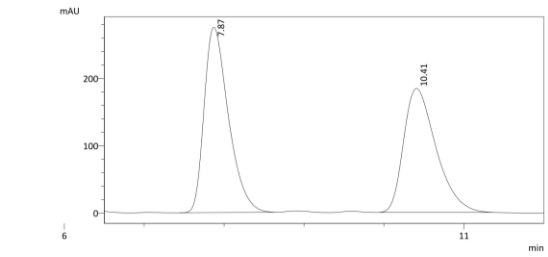


PDA Ch2 232nm

Peak#	Ret. Time	Area	Height	Area%
1	39.33	33269803	280188	100.0
Total				100.0

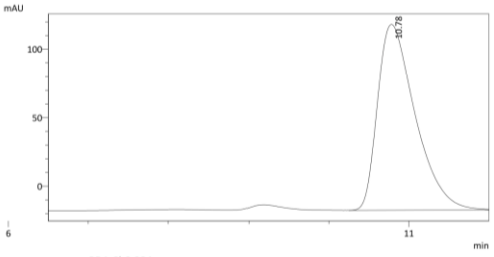


(2*R*,5*R*,6*R*)-5-(Benzo[*d*][1,3]dioxol-5-yl)-2-(*tert*-butyl)-6-methyl-1,3-dioxan-4-one (79g)



PDA Ch2 234nm

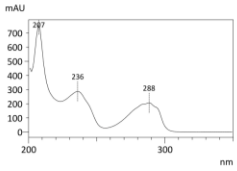
Peak#	Ret. Time	Area	Height	Area%
1	7.87	5821669	275413	52.9
2	10.41	5192871	183992	47.1
Total				100.0



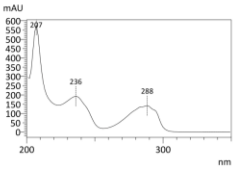
PDA Ch2 234nm

Peak#	Ret. Time	Area	Height	Area%
1	10.78	4441420	135745	100.0
Total				100.0

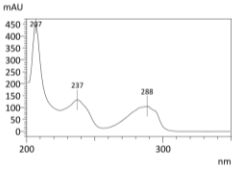
UV Spectrum
Peak#: 1
Retention Time: 7.872 min



UV Spectrum
Peak#: 2
Retention Time: 10.406 min



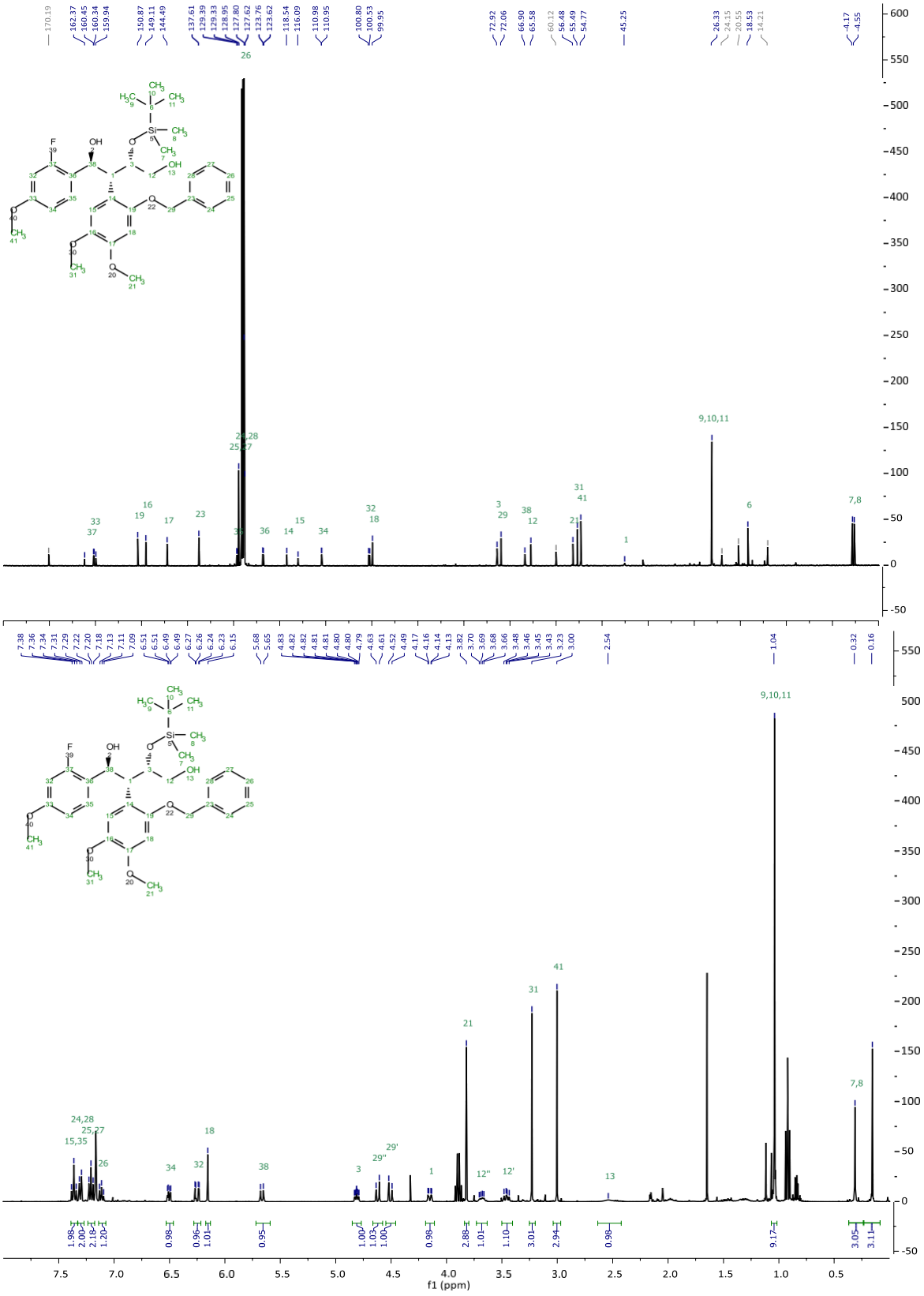
UV Spectrum
Peak#: 1
Retention Time: 10.782 min



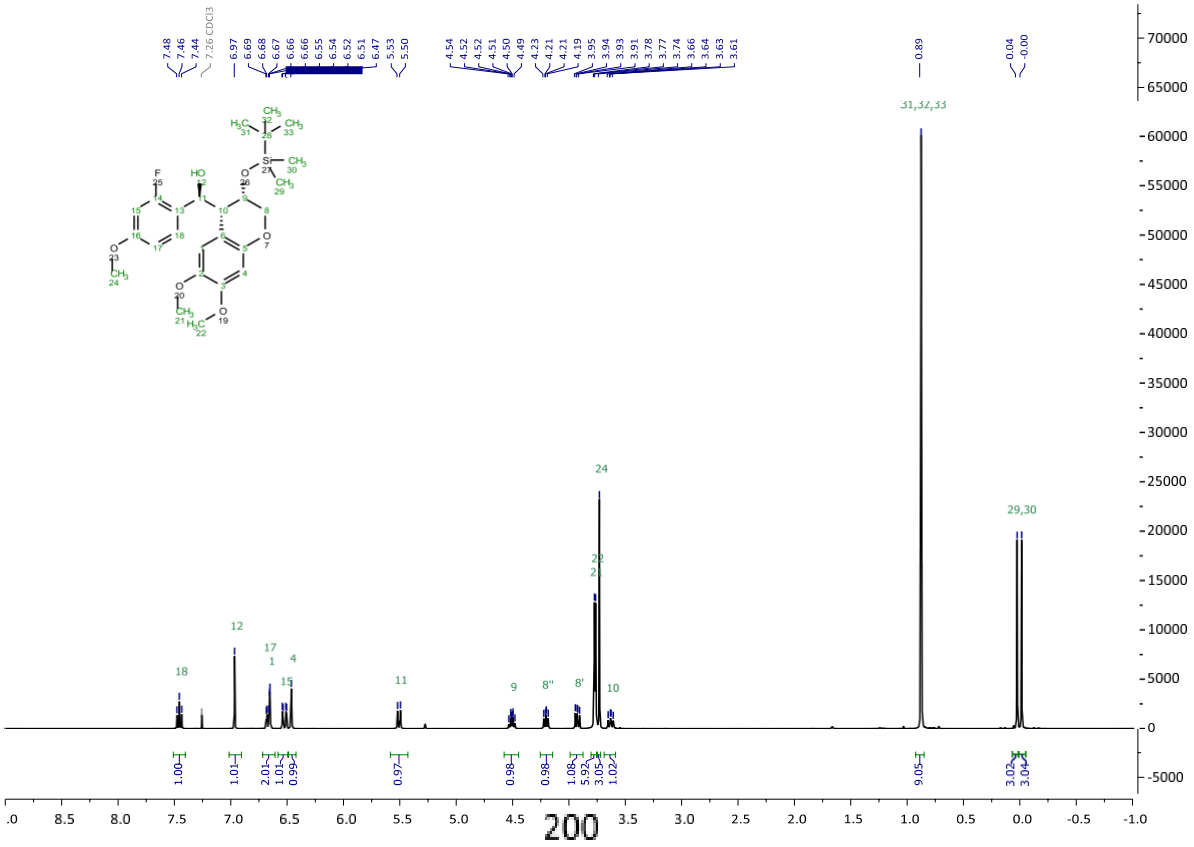
UV Spectrum

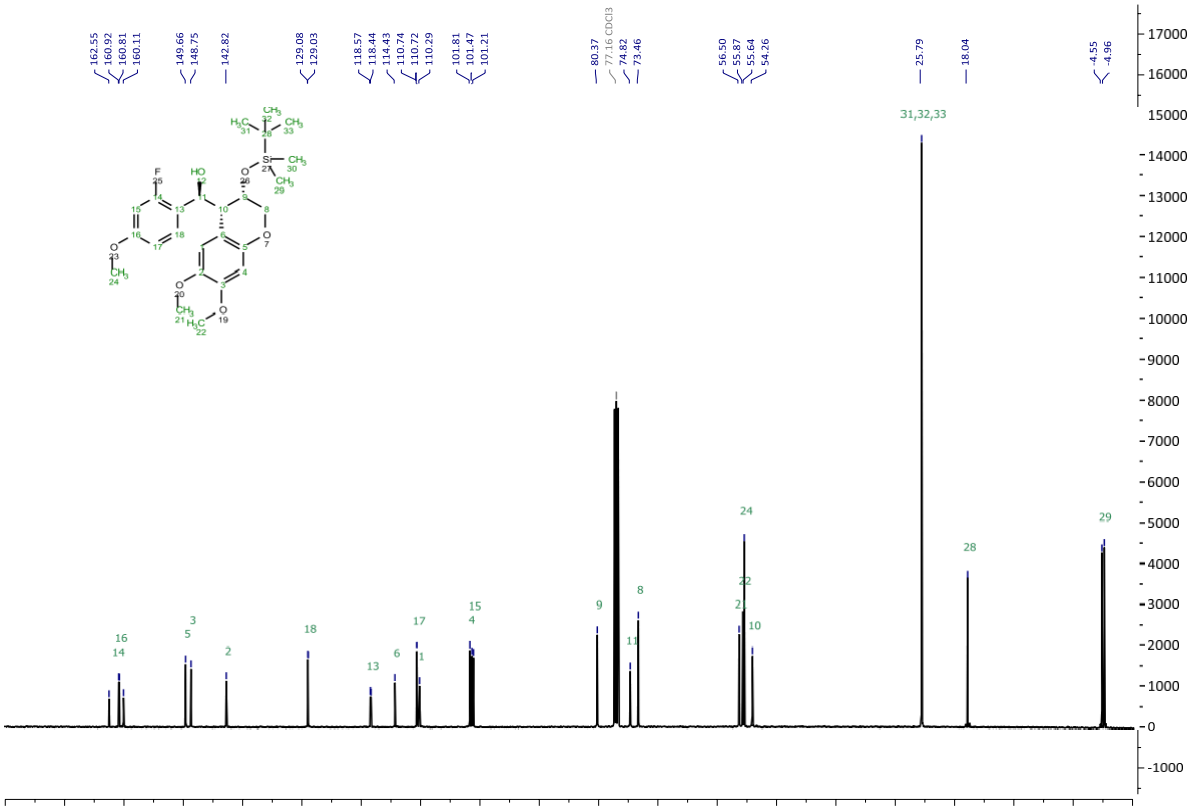
Selected NMR studies

(1*S*,2*R*,3*S*)-2-(2-(Benzyloxy)-4,5-dimethoxyphenyl)-3-((*tert*-butyldimethylsilyl)oxy)-1-(2-fluoro-4-methoxy-phenyl)butane-1,4-diol (82)

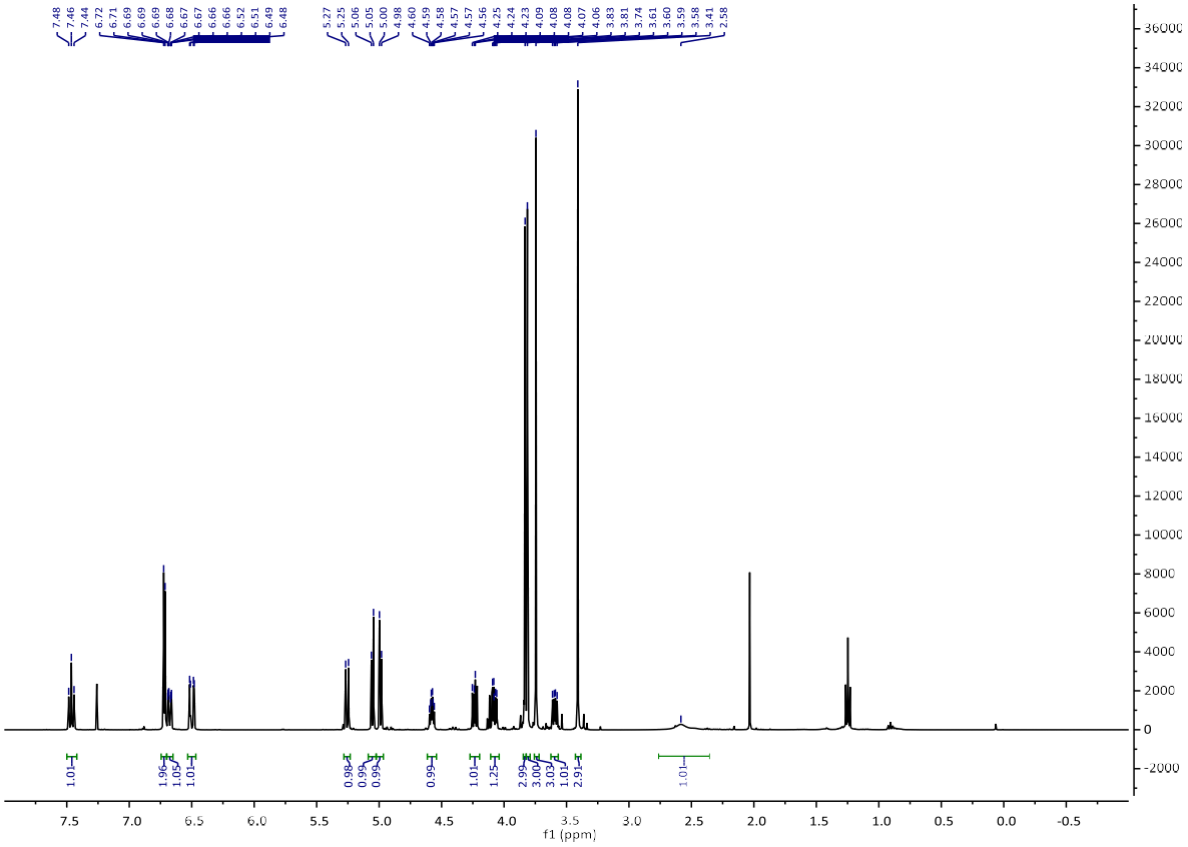


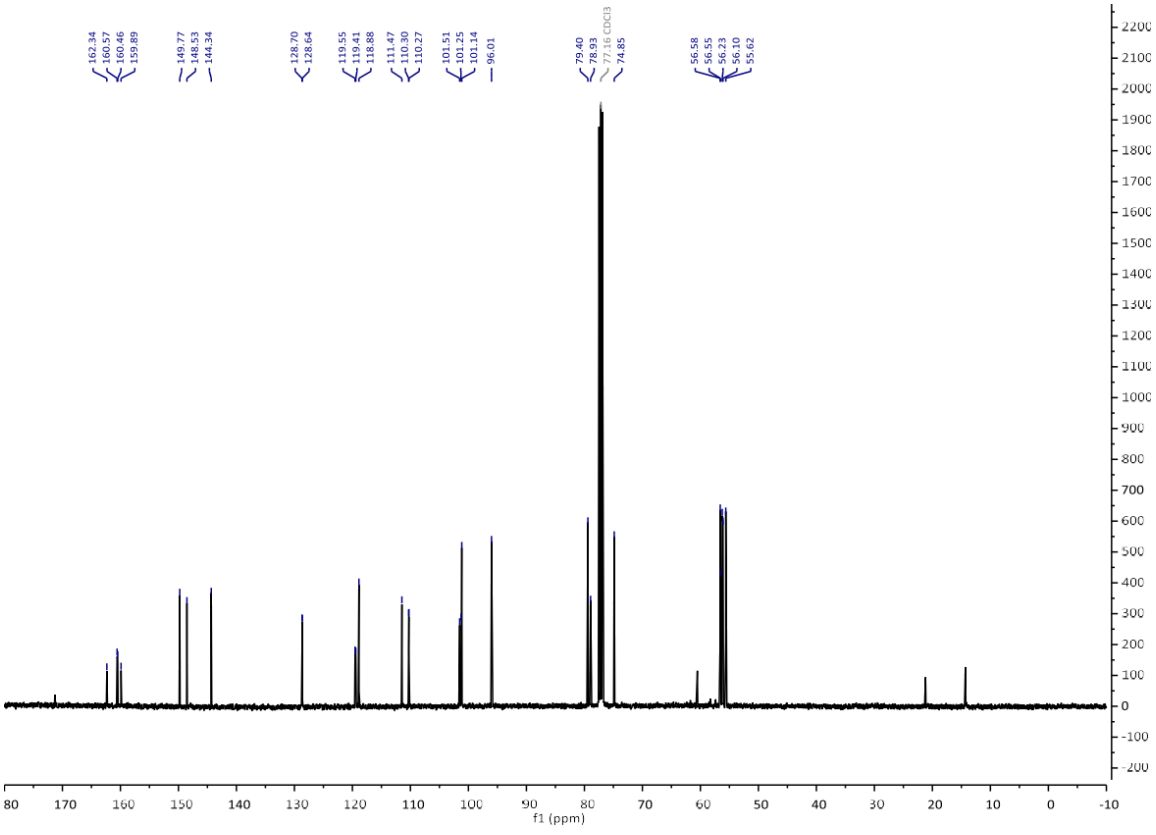
(*S*)-((3*S*,4*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-6,7-dimethoxychroman-4-yl)(2-fluoro-4-methoxyphenyl)methanol (83)



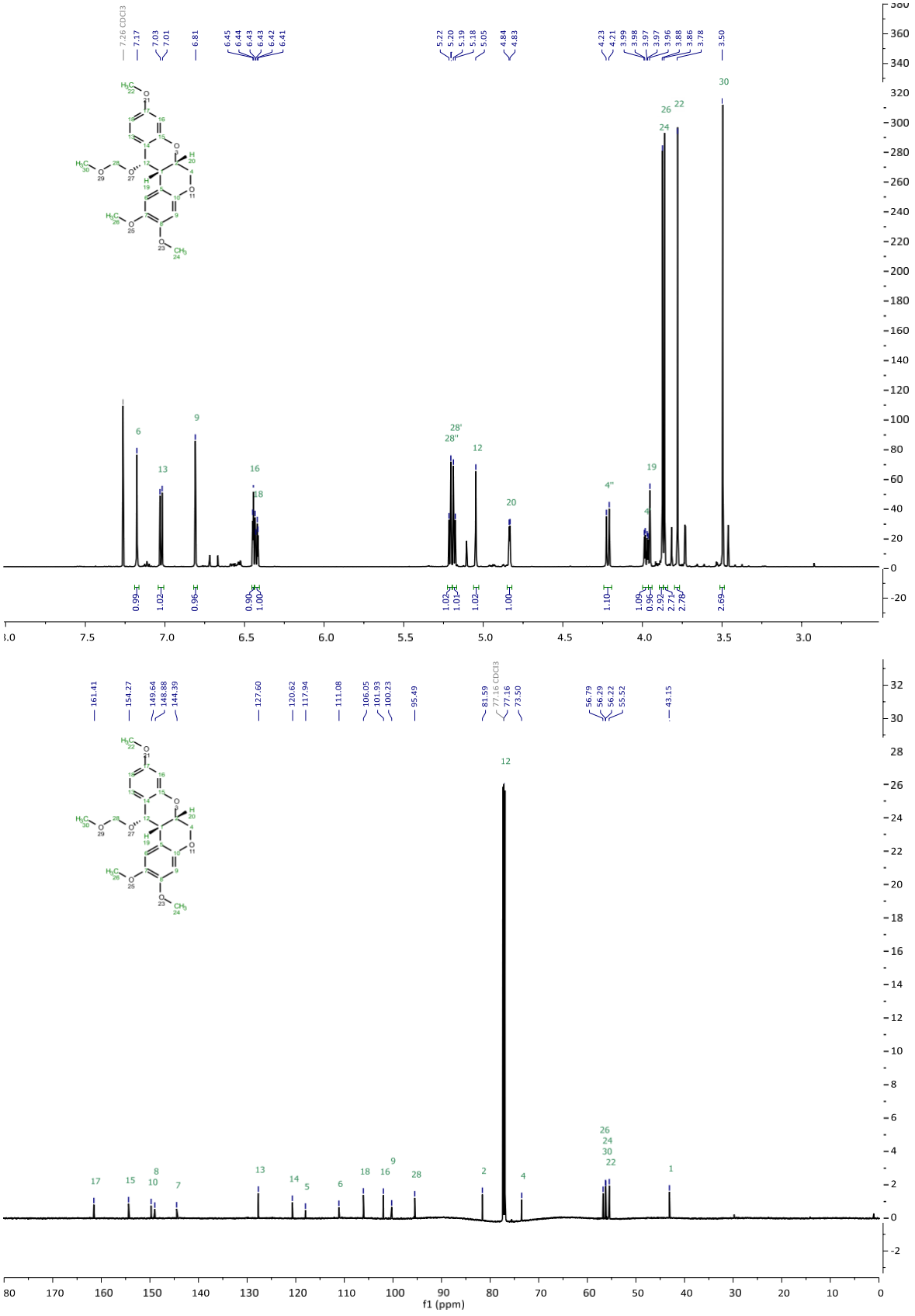


(3*S*,4*S*)-4-((*S*)-(2-fluoro-4-methoxyphenyl)(methoxymethoxy)methyl)-6,7-dimethoxychroman-3-ol (84)

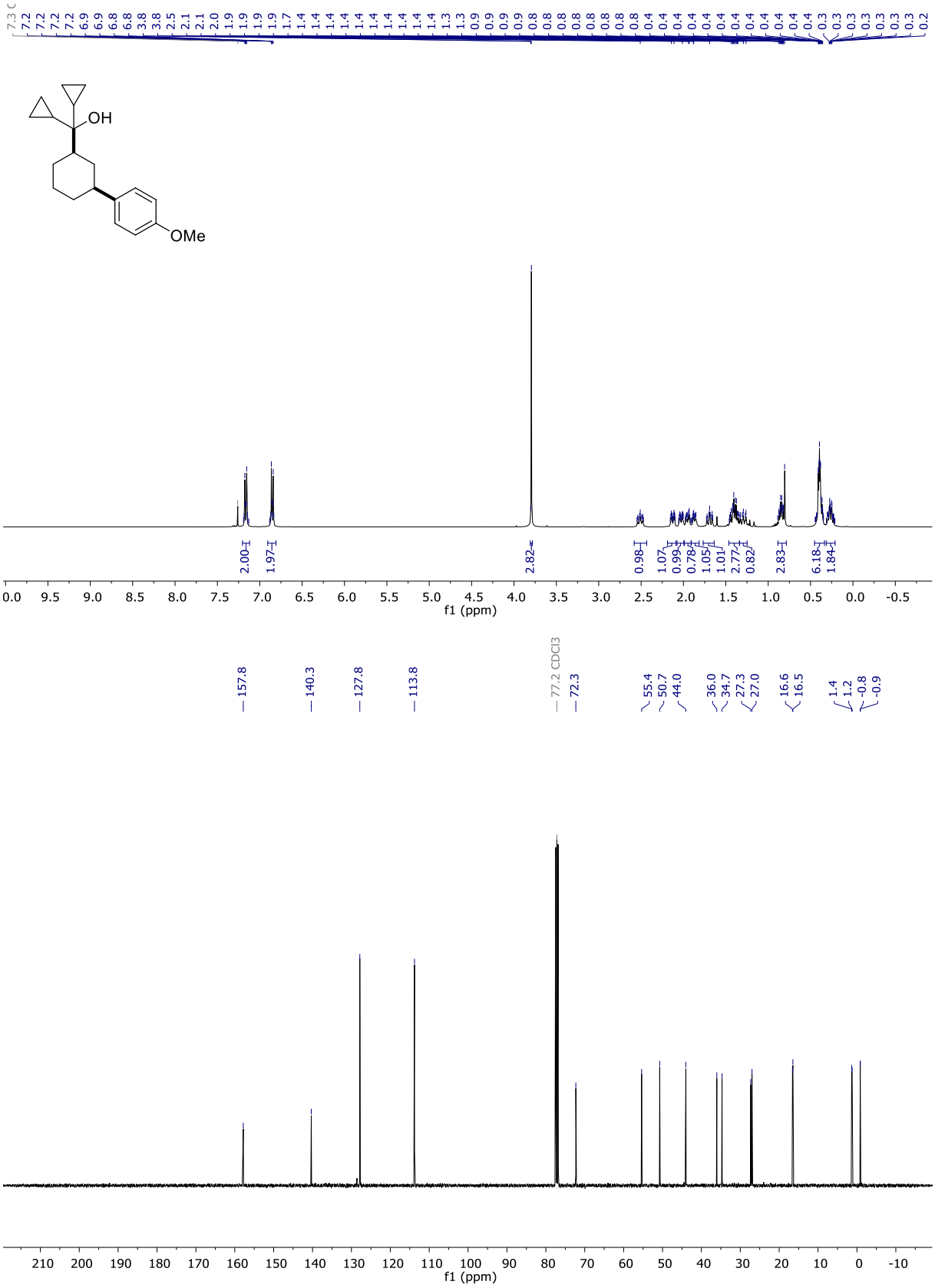




MOM-Protected Munduserol (80)



Dicyclopropyl(3-(4-methoxyphenyl)cyclohexyl)methanol (90b)



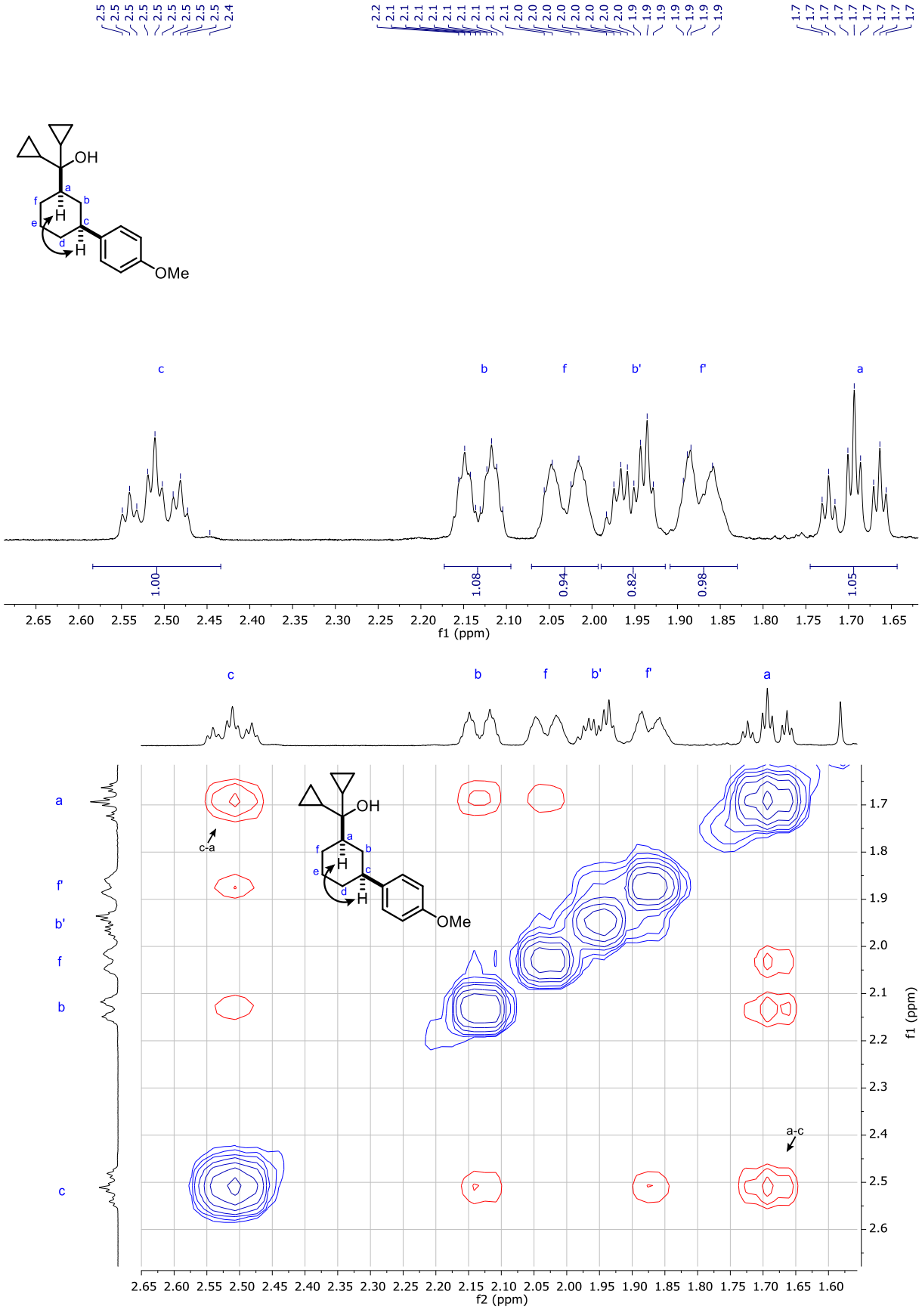
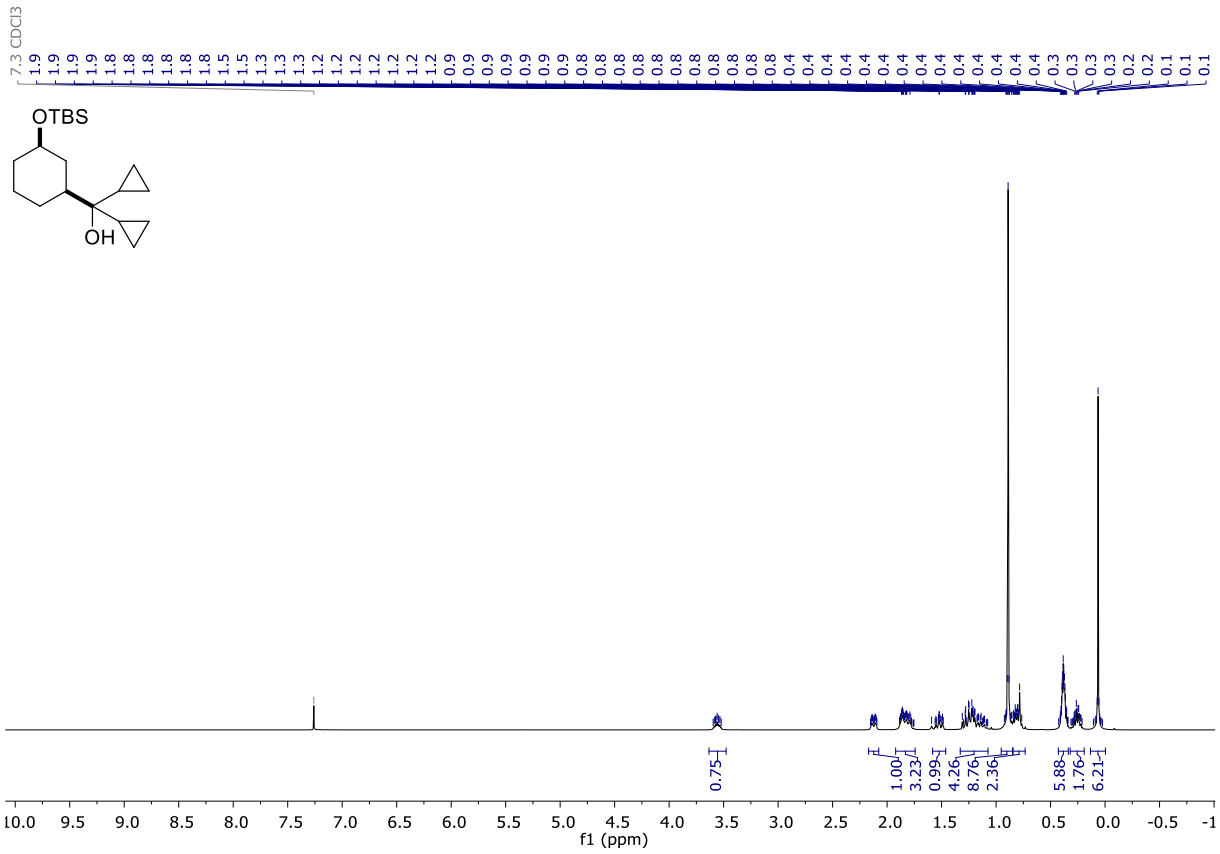
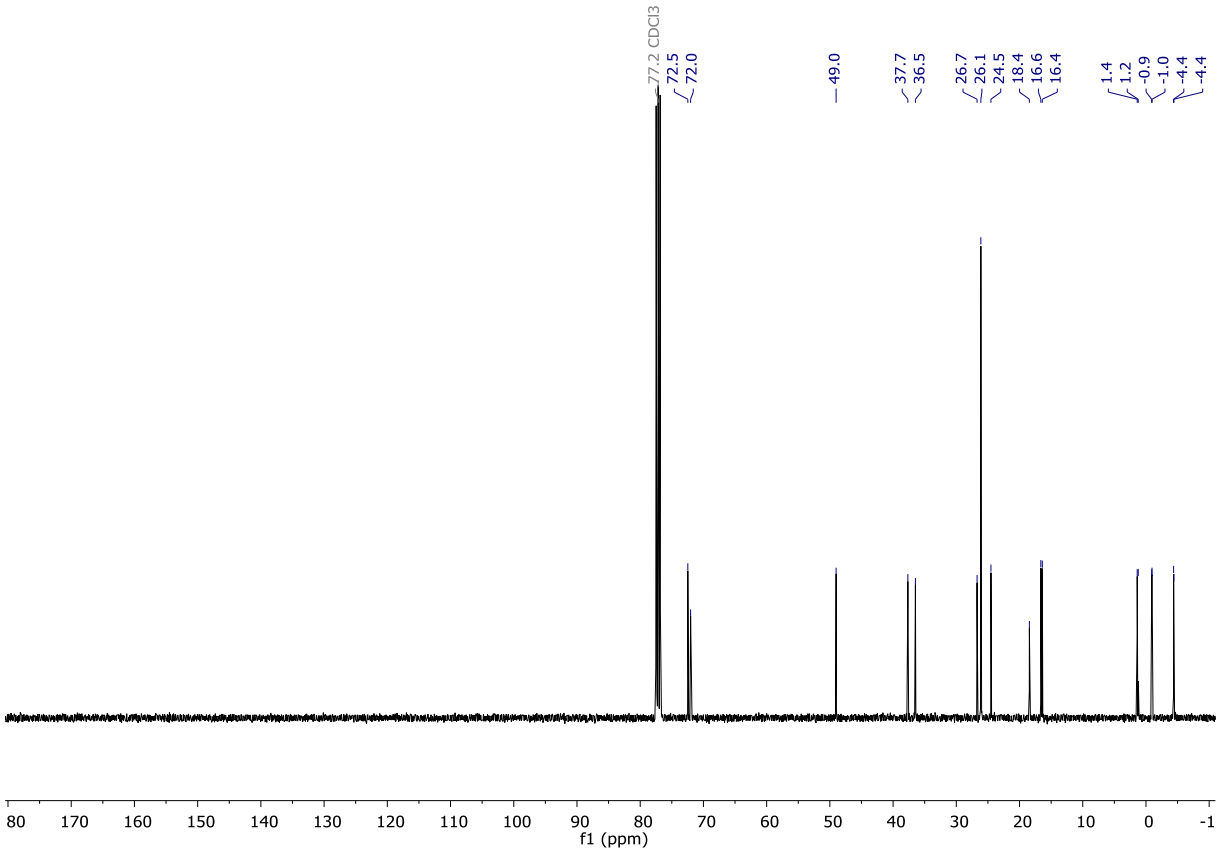


Figure S1. Selected ^{1}H and NOESY spectrum of **90b** (400 MHz, $CDCl_3$).

(3-((*Tert*-butyldimethylsilyl)oxy)cyclohexyl)dicyclopropylmethanol (90c)





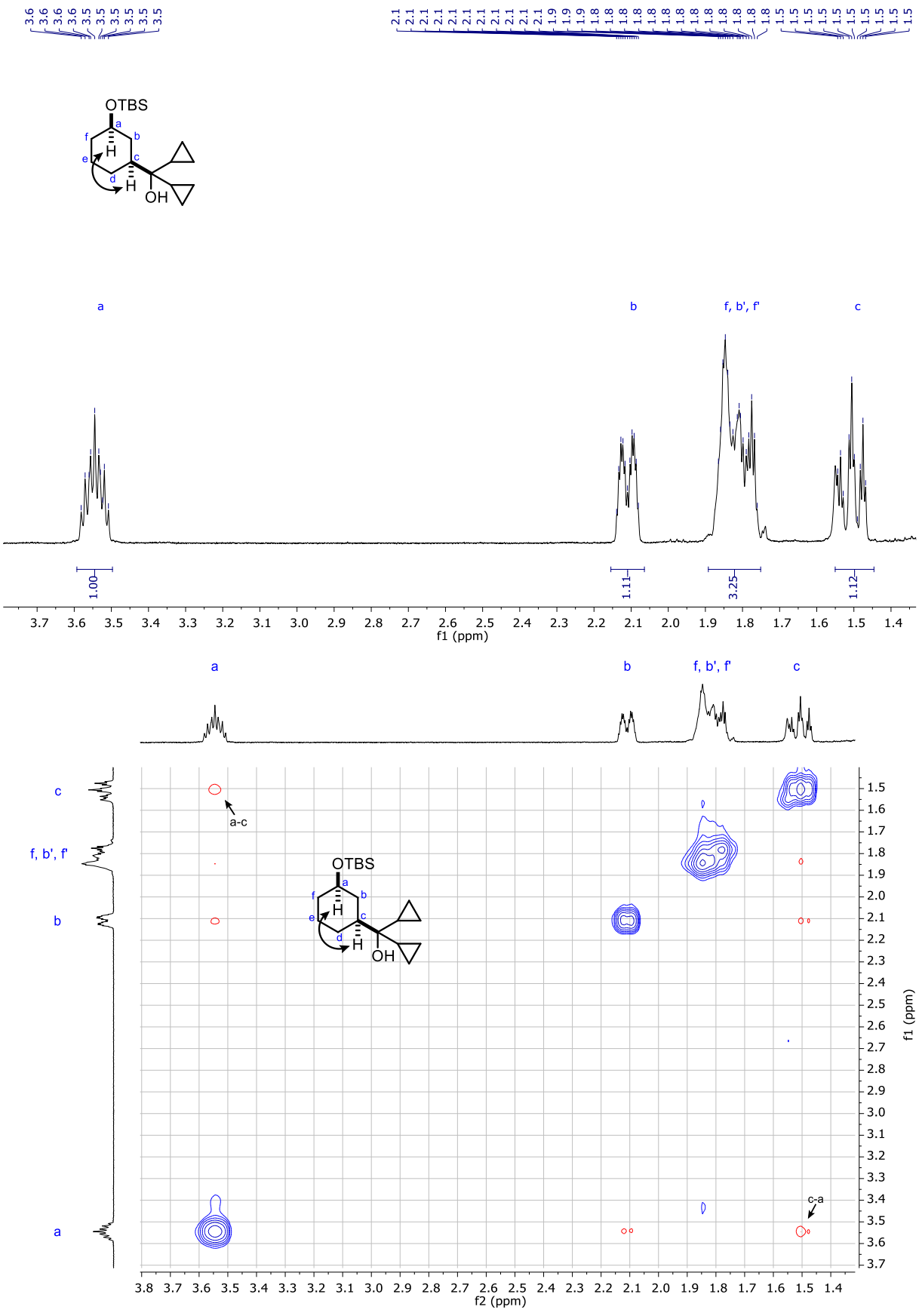
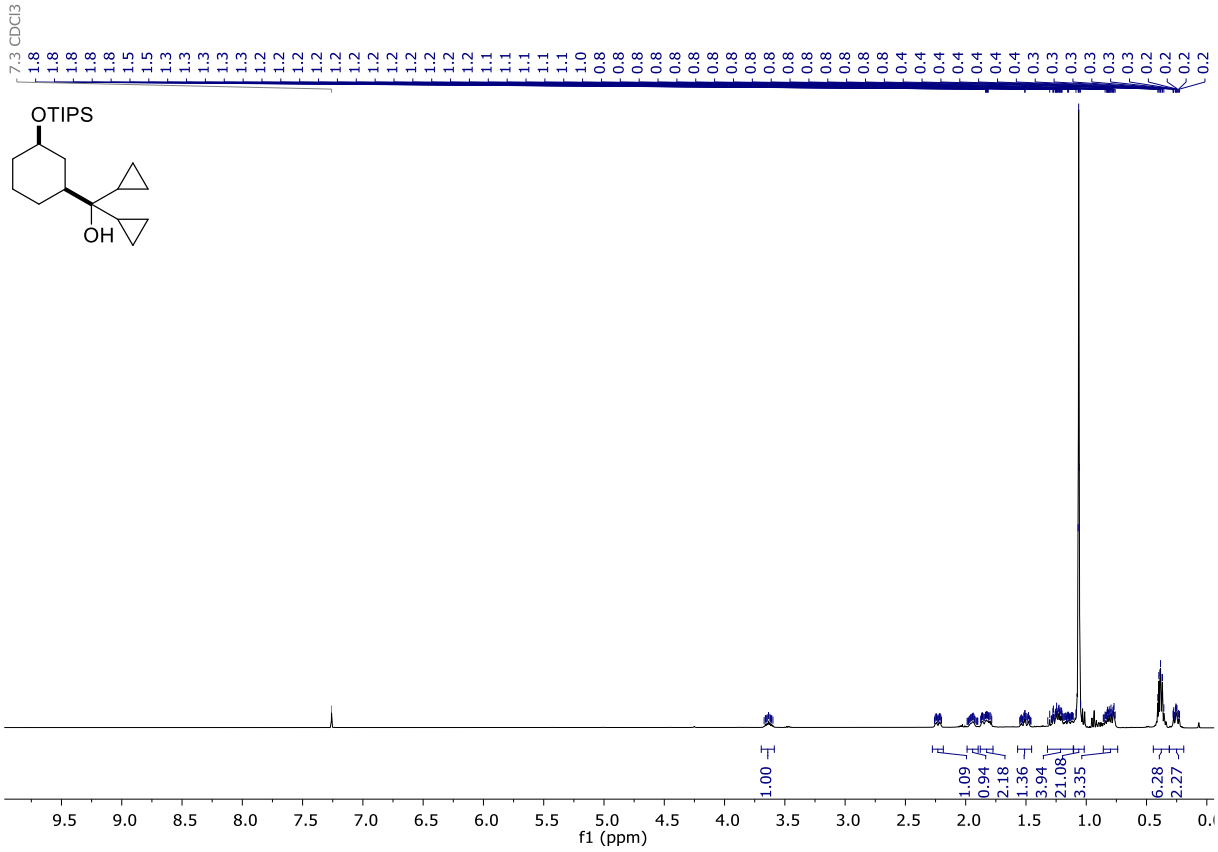
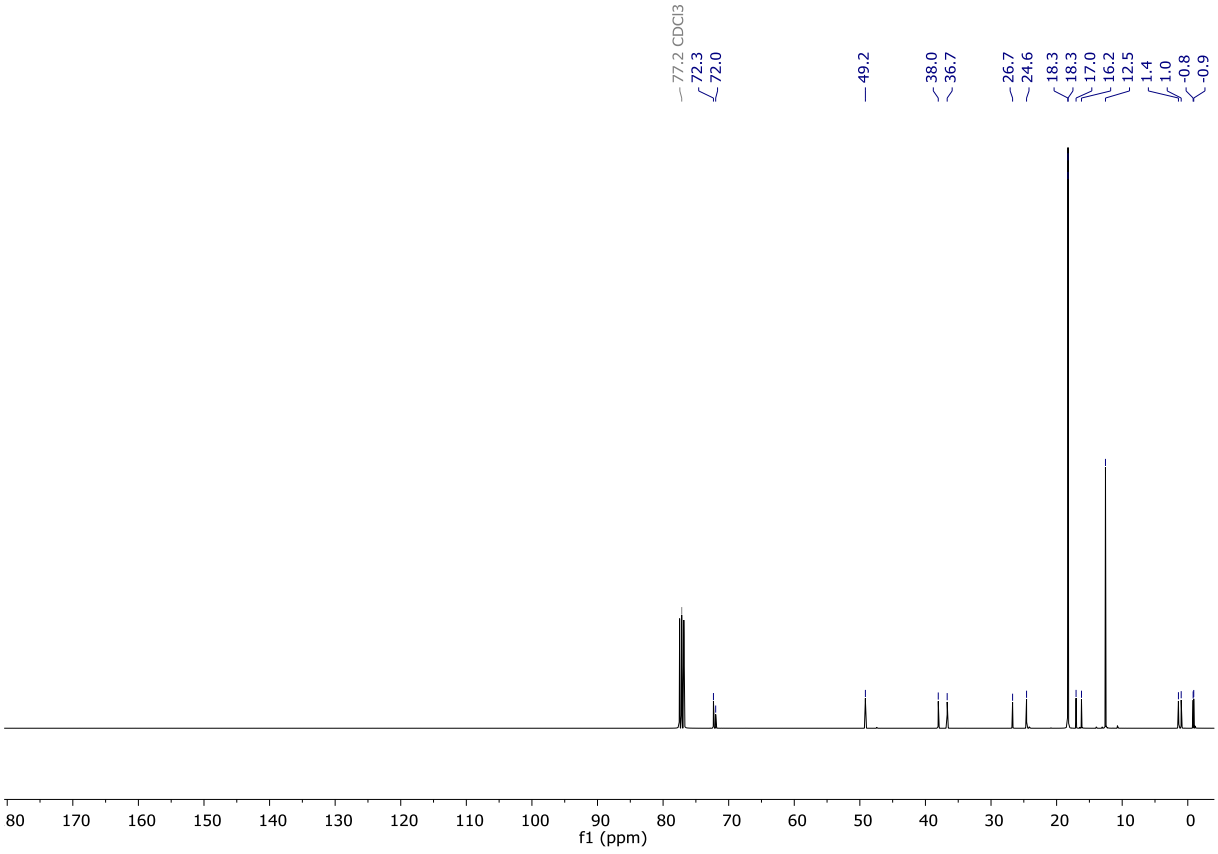


Figure S2. Selected ^{1}H and NOESY spectrum of **90c** (400 MHz, $CDCl_3$).

Dicyclopropyl(3-((triisopropylsilyl)oxy)cyclohexyl)methanol (90d)





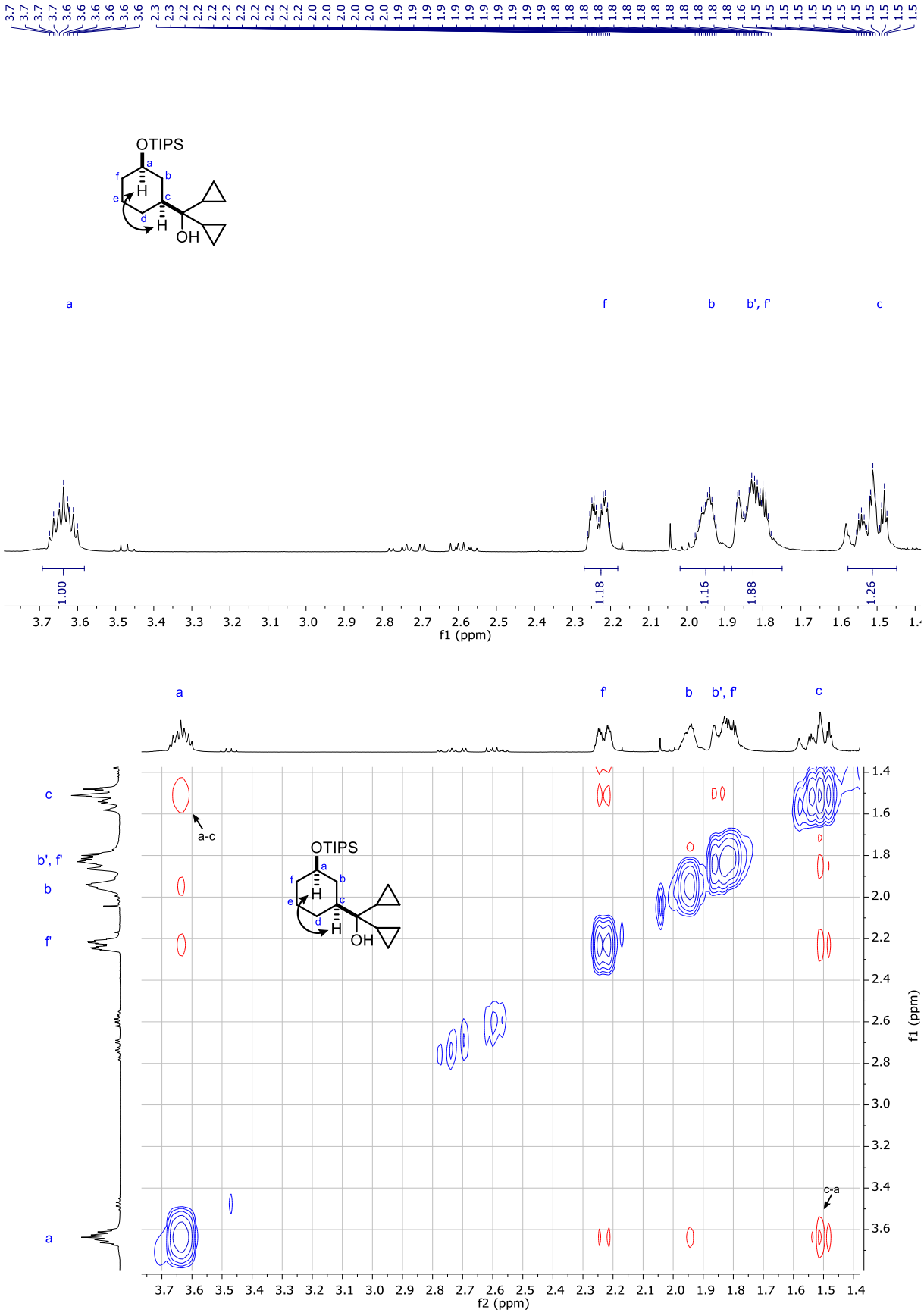
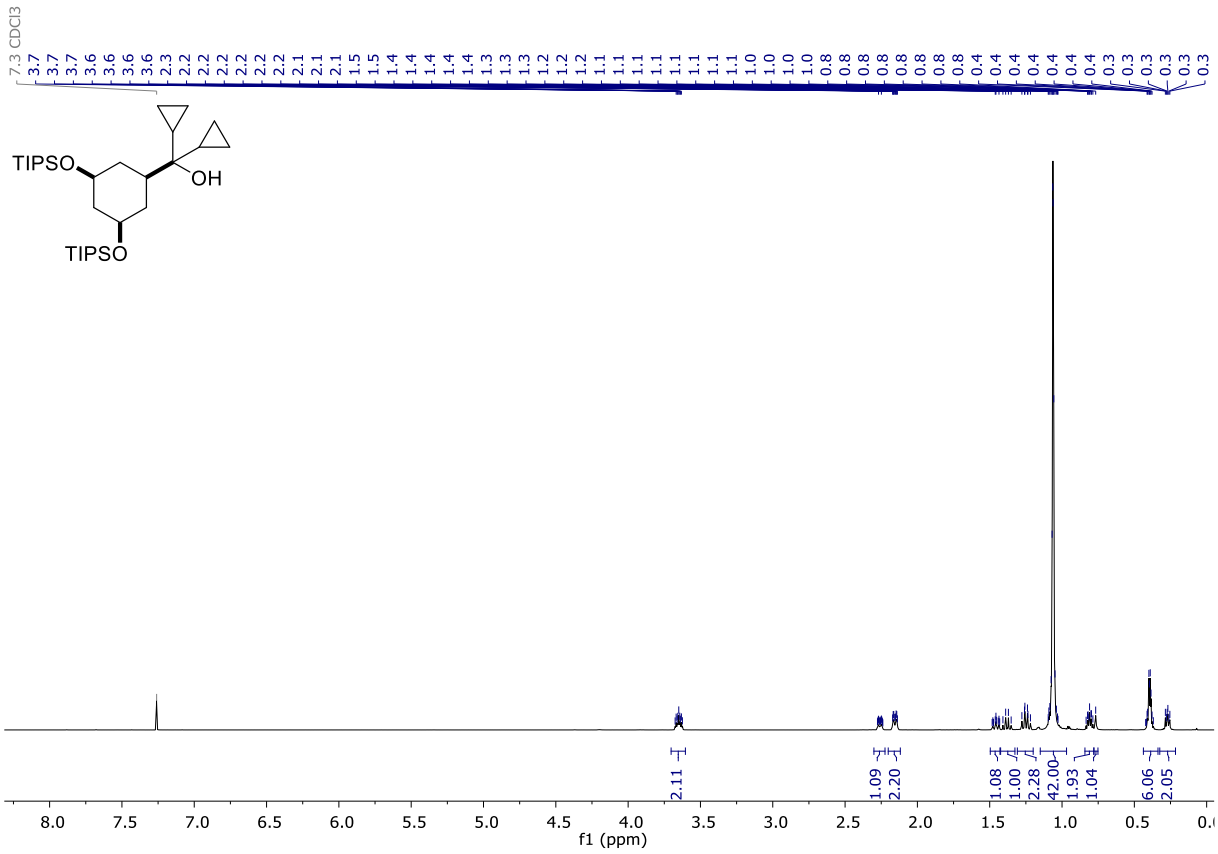
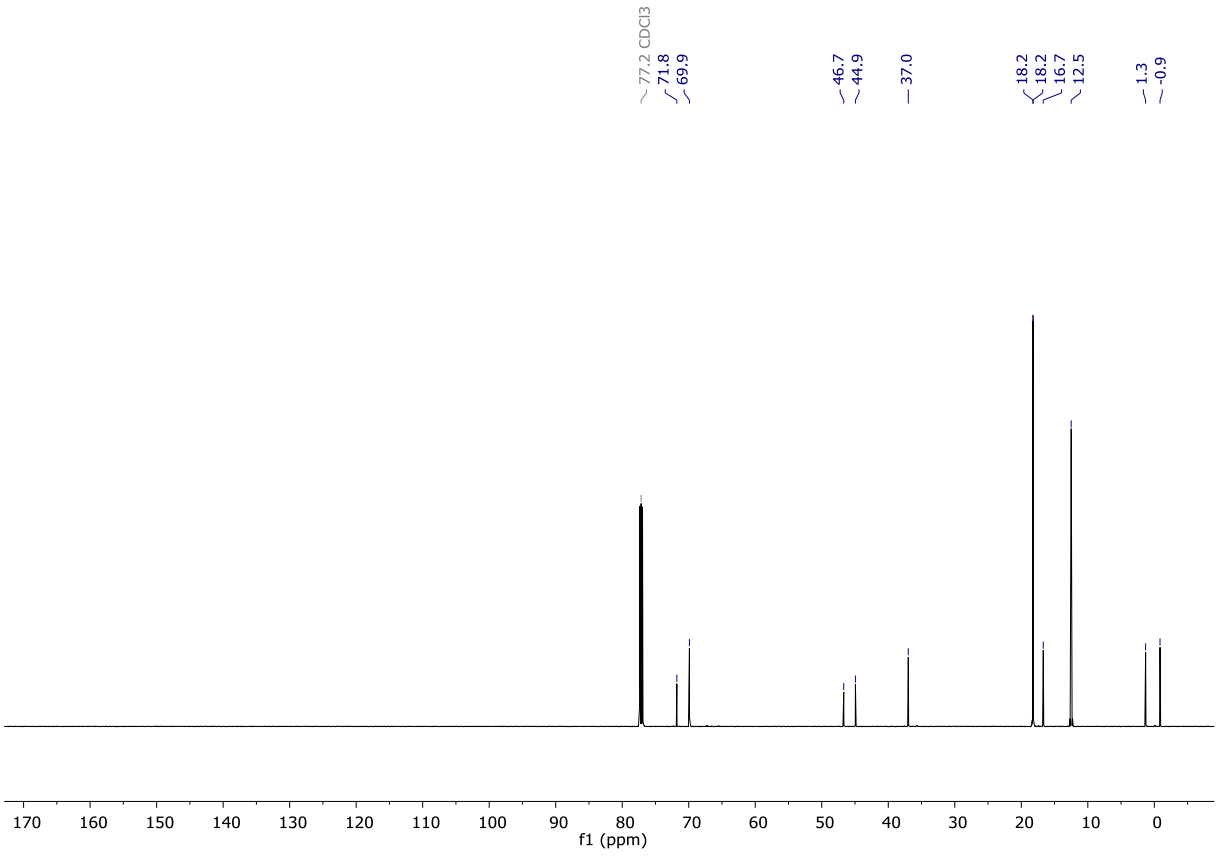


Figure S3. Selected ^{1}H and NOESY spectrum of **90d** (400 MHz, $CDCl_3$).

(3,5-Bis((triisopropylsilyl)oxy)cyclohexyl)dicyclopropylmethanol (90e)





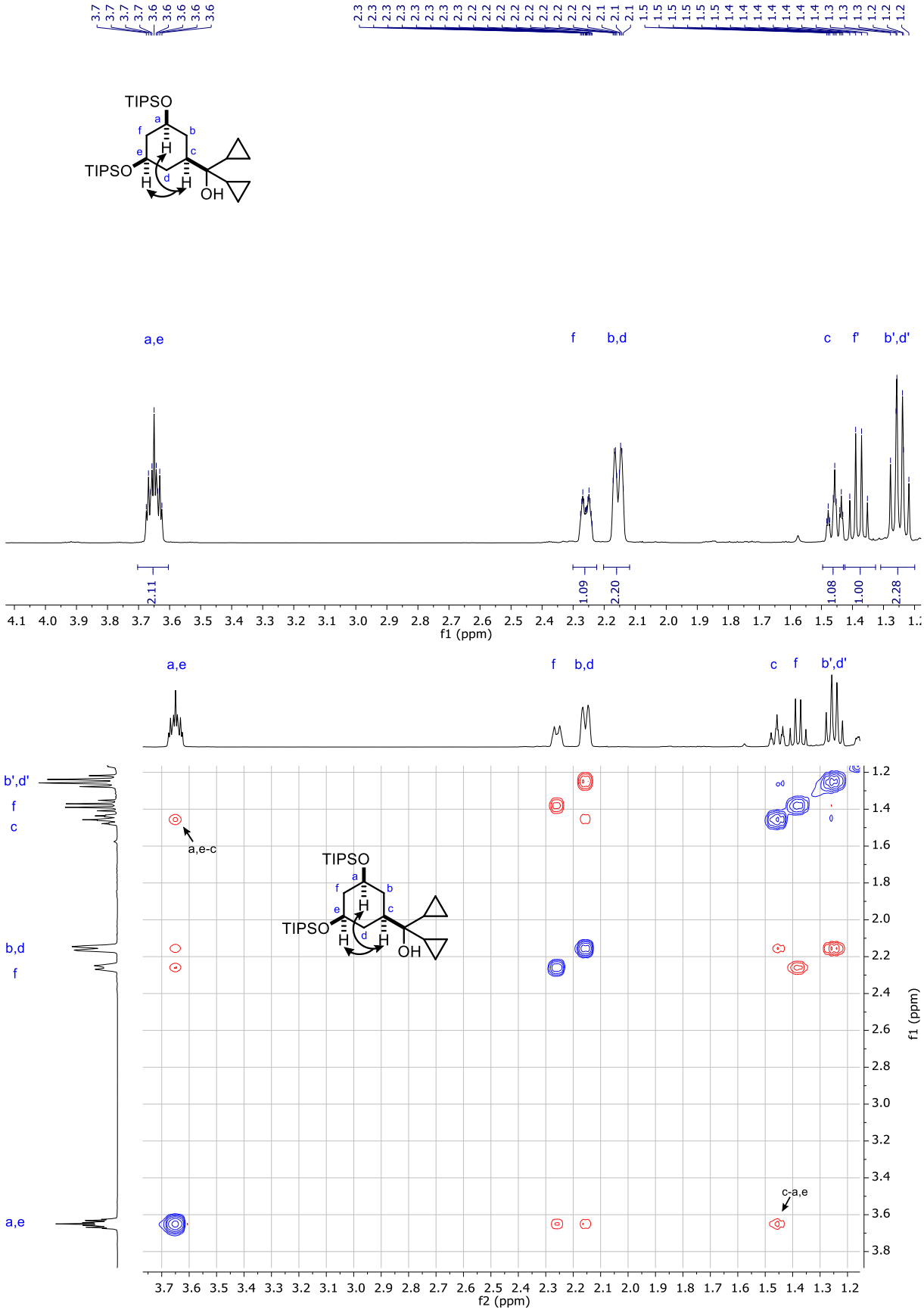
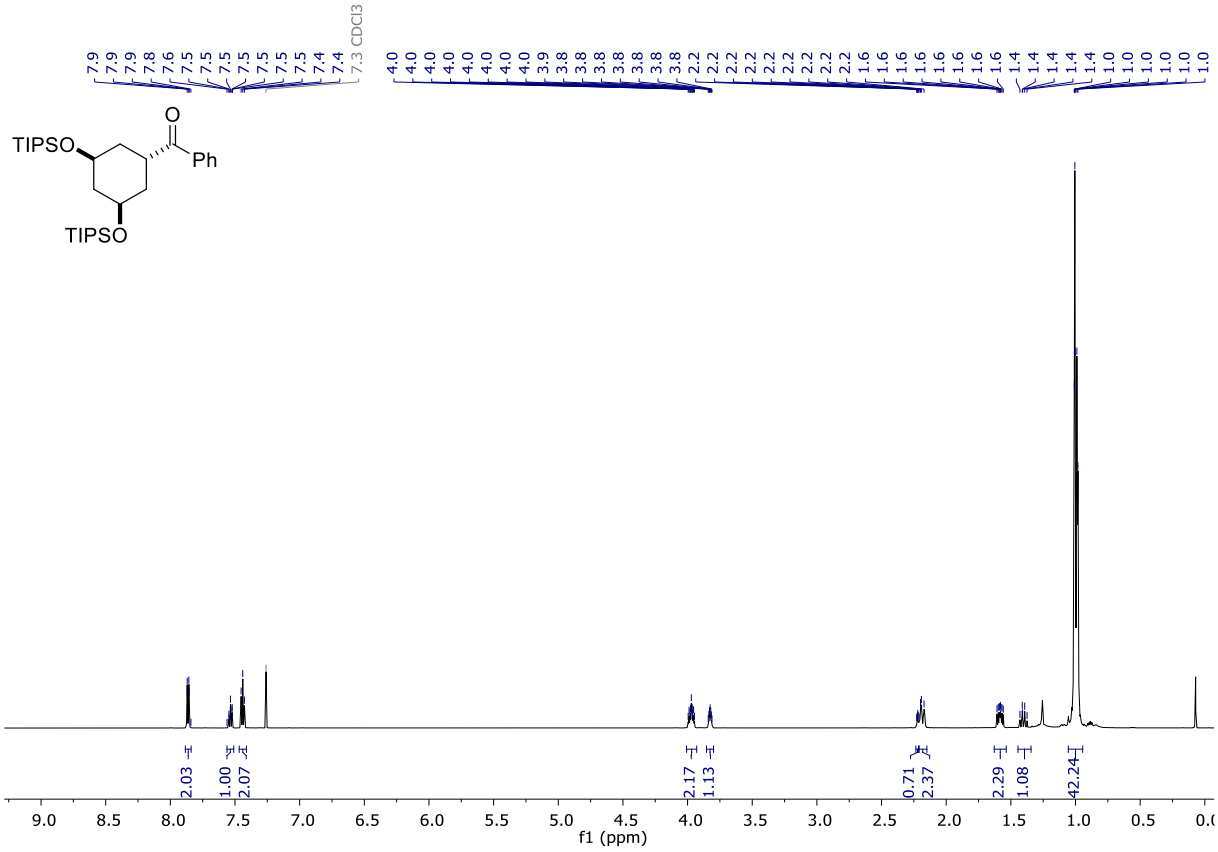
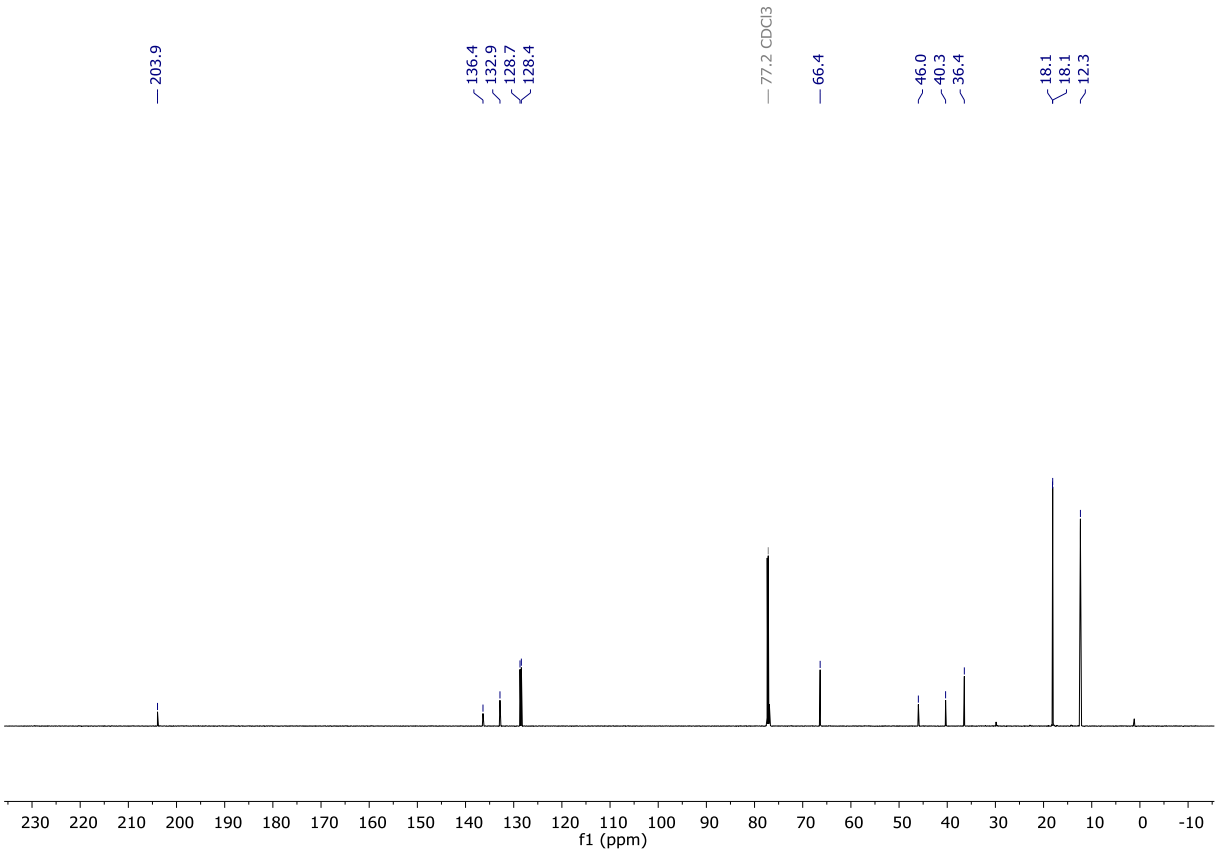


Figure S4. Selected 1H and NOESY spectrum of **90e** (400 MHz, $CDCl_3$).

(3,5-Bis((triisopropylsilyl)oxy)cyclohexyl)(phenyl)methanone (90f)





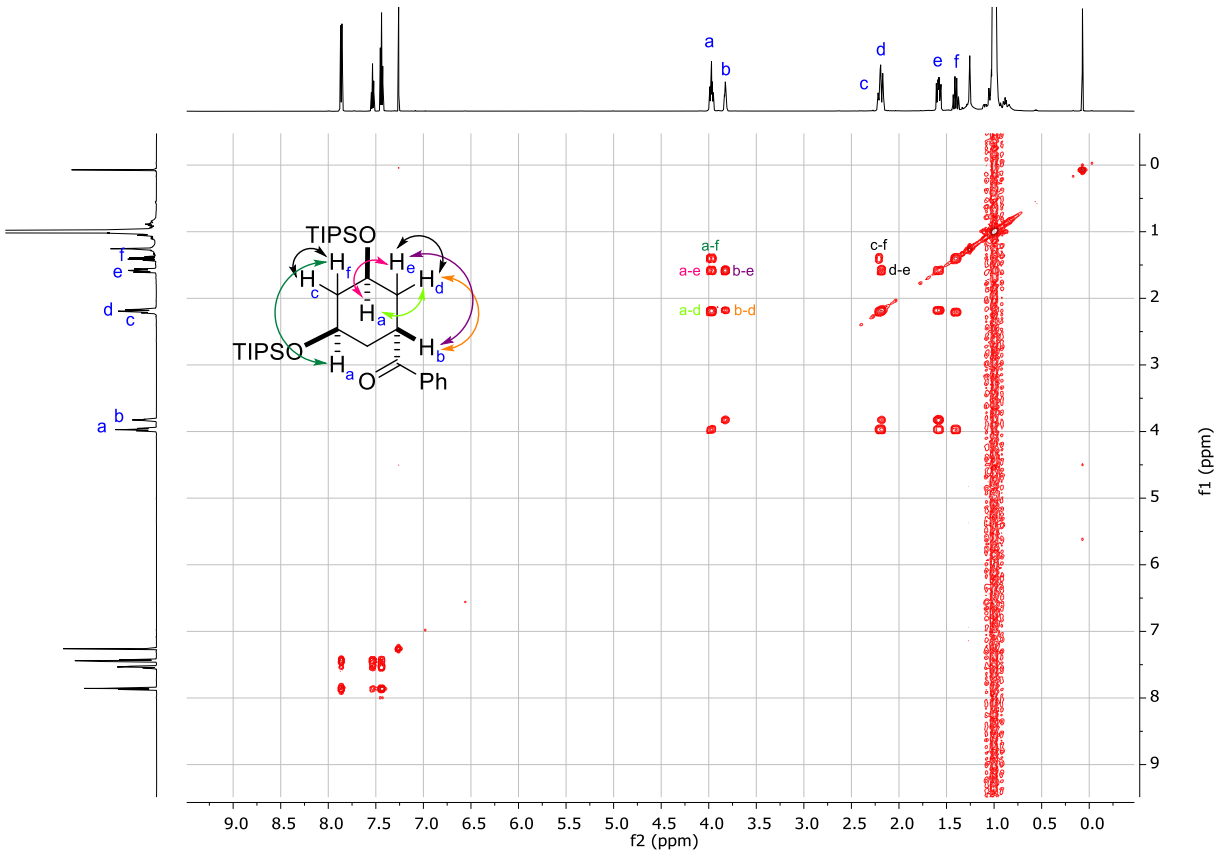


Figure S5. COSY spectrum of **90f** (400 MHz, $CDCl_3$).

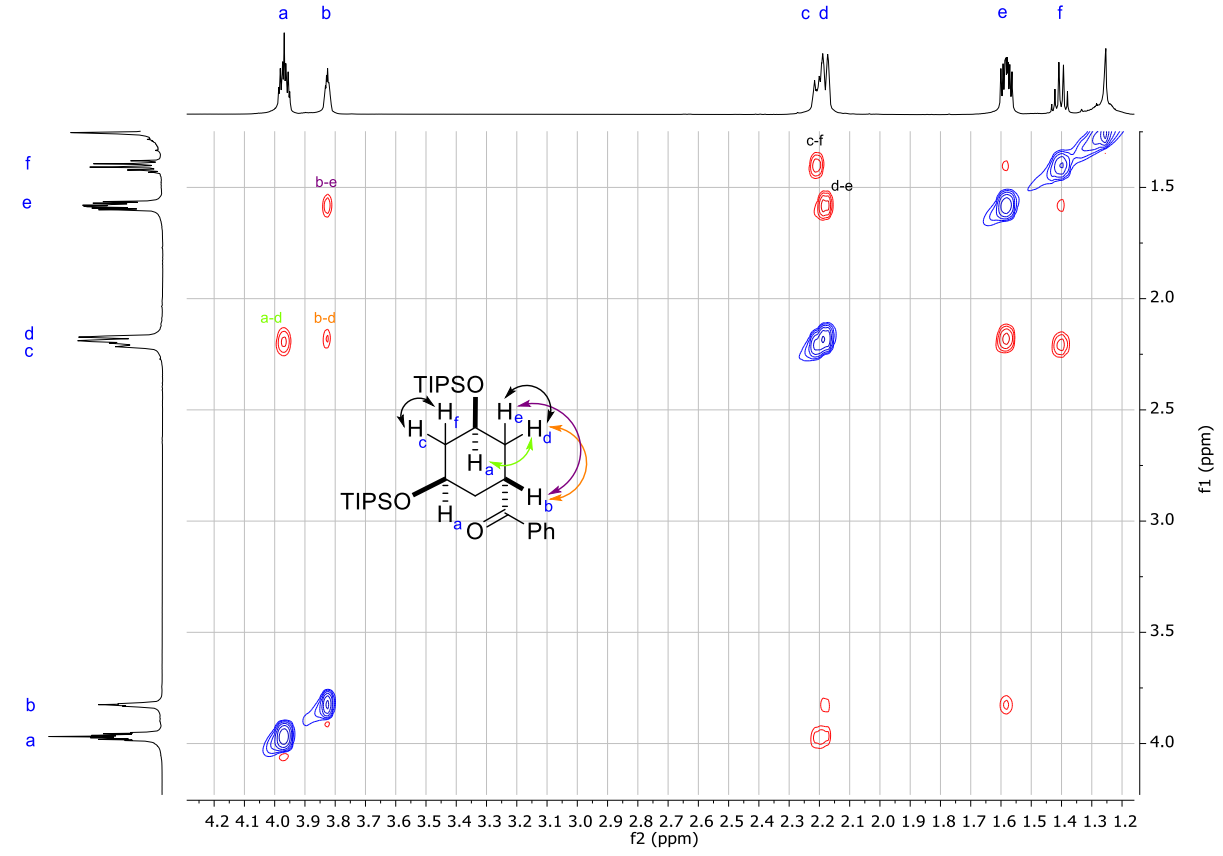


Figure S6. Selected NOESY spectrum of **90f** (800 MHz, $CDCl_3$).

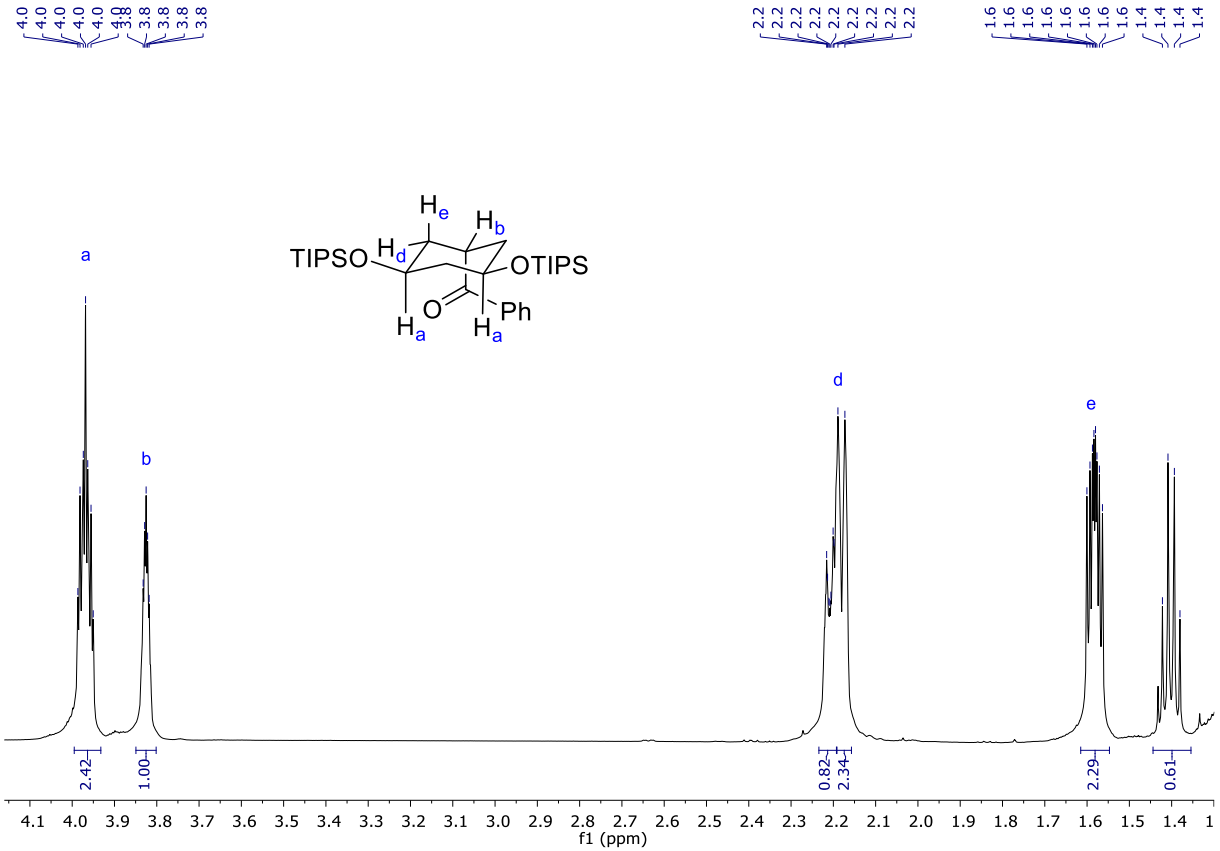


Figure S7. Selected ^{1}H spectrum of **90f** (800 MHz, $CDCl_3$).

Crystallographic Data

Single Crystal X-Ray Diffraction Studies

Single crystals of compound **105b**, suitable for X-ray diffraction, were obtained by slow evaporation of *i*hexane solution. 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.[157] Absorption correction using the multiscan method[163] was applied. The structures were solved with SHELXS-97,[158] refined with SHELXL-97[159] and finally checked using PLATON.[160] Details for data collection and structure refinement are summarized in Table S7.

CCDC-2201809 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.

[157] Program package 'CrysAlisPro 1.171.40.82a (Rigaku OD, 2020)'.
[158] G.M. Sheldrick, (1997) SHELXS-97: *Program for Crystal Structure Solution*, University of Göttingen, Germany.
[159] G.M. Sheldrick, (1997) SHELXL-97: *Program for the Refinement of Crystal Structures*, University of Göttingen, Germany.
[160] A.L. Spek, (1999) PLATON: *A Multipurpose Crystallographic Tool*, Utrecht University, Utrecht, The Netherlands.

Table S7. Details for X-ray data collection and structure refinement for compound **105b**.

	1
Empirical formula	$C_{10}H_{17}IO_2$
Formula mass	296.13
T[K]	123(2)
Crystal size [mm]	0.35 × 0.20 × 0.10
Crystal description	colorless block
Crystal system	monoclinic
Space group	*P*21/*n*
a [Å]	10.7844(4)
b [Å]	13.0081(3)
c [Å]	16.3505(4)
α [°]	90.0
β [°]	98.842(3)
γ [°]	90.0
V [Å^3]	2266.46(11)
Z	8
$\rho_{calcd.}$ [g cm^{-3}]	1.736
μ [mm^{-1}]	2.796
F(000)	1168
Θ range [°]	2.01 – 25.24
Index ranges	-13 ≤ *h* ≤ 13
	-16 ≤ *k* ≤ 16
	-20 ≤ *l* ≤ 20
Reflns. collected	34926
Reflns. obsd.	3577
Reflns. unique	4601 (R_{int} = 0.0459)
R_1, wR_2 (2σ data)	0.0296, 0.0714
R_1, wR_2 (all data)	0.0435, 0.0787
GOOF on F^2	1.034
Peak/hole [e Å^{-3}]	1.014 / -0.439

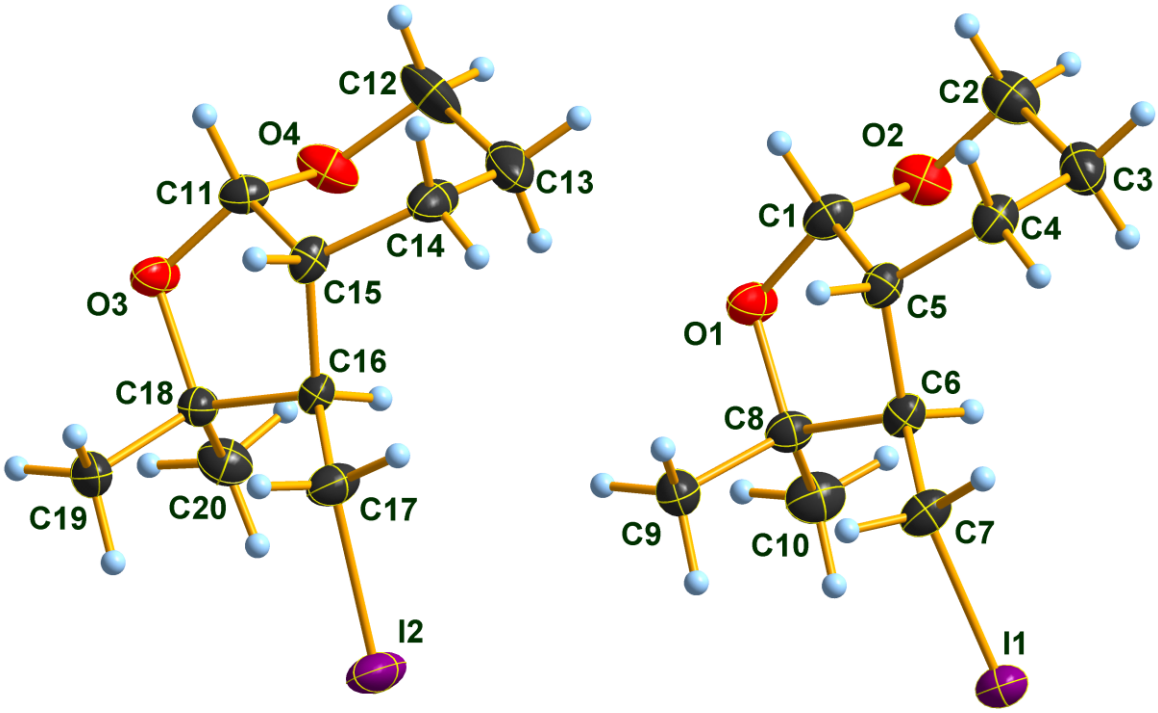


Figure S8. Molecular structure of compound **105b** in the crystal. View of the two crystallographically independent molecules. DIAMOND[161] representation; thermal ellipsoids are drawn at 50 % probability level.

Table S8. Selected bond lengths (Å) of compound **105b**.

I1 – C7	2.171(3)	C11 – C15	1.516(4)
O1 – C1	1.405(4)	C15 – C14	1.534(5)
O1 – C8	1.467(4)	C15 – C16	1.535(4)
C1 – O2	1.431(4)	C14 – C13	1.514(6)
C1 – C5	1.516(4)	C13 – C12	1.511(6)
I2 – C17	2.163(3)	C20 – C18	1.514(5)
O2 – C2	1.447(4)	C19 – C18	1.524(4)
C2 – C3	1.523(5)	C18 – C16	1.556(4)
C3 – C4	1.513(5)	C17 – C16	1.507(5)
O3 – C11	1.386(4)	C6 – C7	1.519(4)
O3 – C18	1.477(4)	C6 – C8	1.543(4)
C4 – C5	1.542(5)	C8 – C10	1.524(5)
O4 – C11	1.429(4)	C8 – C9	1.538(5)
O4 – C12	1.438(4)	C5 – C6	1.538(4)

[161] DIAMOND, Crystal Impact GbR., Version 3.2i.

Table S9. Selected bond angles (°) of compound **105b**.

C1 – O1 – C8	110.5(2)	C13 – C14 – C15	111.4(3)
O1 – C1 – O2	107.2(3)	C12 – C13 – C14	109.5(3)
O1 – C1 – C5	105.8(3)	C6 – C7 – I1	113.2(2)
O2 – C1 – C5	112.1(3)	O3 – C18 – C20	108.2(3)
C1 – O2 – C2	110.7(3)	O3 – C18 – C19	105.6(3)
O2 – C2 – C3	109.6(3)	C20 – C18 – C19	110.9(3)
C4 – C3 – C2	110.2(3)	O3 – C18 – C16	104.4(2)
C11 – O3 – C18	109.6(2)	C20 – C18 – C16	112.9(3)
C3 – C4 – C5	112.3(3)	C19 – C18 – C16	114.2(3)
C11 – O4 – C12	111.4(3)	C16 – C17 – I2	113.9(2)
C1 – C5 – C6	100.3(3)	C17 – C16 – C15	110.0(3)
C1 – C5 – C4	113.3(3)	C17 – C16 – C18	117.8(3)
C6 – C5 – C4	117.2(3)	C15 – C16 – C18	103.8(2)
C7 – C6 – C5	111.1(3)	O4 – C12 – C13	110.1(3)
C7 – C6 – C8	117.3(3)	C9 – C8 – C6	113.8(3)
C5 – C6 – C8	102.4(3)	O3 – C11 – O4	107.7(3)
O1 – C8 – C10	106.7(3)	O3 – C11 – C15	106.3(3)
O1 – C8 – C9	106.6(3)	O4 – C11 – C15	111.6(3)
C10 – C8 – C9	110.4(3)	C11 – C15 – C14	114.2(3)
O1 – C8 – C6	104.2(3)	C11 – C15 – C16	100.8(2)
C10 – C8 – C6	114.3(3)	C14 – C15 – C16	115.5(3)

Table S10. Selected torsion angles (°) of compound **105b**.

C8 – O1 – C1 – O2	97.0(3)	C12 – O4 – C11 – O3	-174.0(3)
C8 – O1 – C1 – C5	-22.8(3)	C12 – O4 – C11 – C15	-57.6(4)
O1 – C1 – O2 – C2	-175.7(3)	O3 – C11 – C15 – C14	163.8(3)
C5 – C1 – O2 – C2	-60.0(4)	O4 – C11 – C15 – C14	46.7(4)
C1 – O2 – C2 – C3	66.5(4)	O3 – C11 – C15 – C16	39.4(3)
O2 – C2 – C3 – C4	-59.9(4)	O4 – C11 – C15 – C16	-77.8(3)
C2 – C3 – C4 – C5	47.7(4)	C11 – C15 – C14 – C13	-43.5(4)
O1 – C1 – C5 – C6	38.4(3)	C16 – C15 – C14 – C13	72.7(4)
O2 – C1 – C5 – C6	-78.2(3)	C15 – C14 – C13 – C12	49.6(4)
O1 – C1 – C5 – C4	164.1(3)	C5 – C6 – C7 – I1	-165.7(2)
O2 – C1 – C5 – C4	47.6(4)	C8 – C6 – C7 – I1	77.0(3)
C3 – C4 – C5 – C1	-42.1(4)	C11 – O3 – C18 – C20	-111.0(3)
C3 – C4 – C5 – C6	74.0(4)	C11 – O3 – C18 – C19	130.3(3)

C1 – C5 – C6 – C7	-164.7(3)	C11 – O3 – C18 – C16	9.5(3)
C4 – C5 – C6 – C7	72.2(4)	I2 – C17 – C16 – C15	-170.3(2)
C1 – C5 – C6 – C8	-38.7(3)	I2 – C17 – C16 – C18	71.1(3)
C4 – C5 – C6 – C8	-161.8(3)	C11 – C15 – C16 – C17	-158.9(3)
C1 – O1 – C8 – C10	-124.0(3)	C14 – C15 – C16 – C17	77.6(4)
C1 – O1 – C8 – C9	118.0(3)	C11 – C15 – C16 – C18	-31.9(3)
C1 – O1 – C8 – C6	-2.7(3)	C14 – C15 – C16 – C18	-155.5(3)
C7 – C6 – C8 – O1	148.3(3)	O3 – C18 – C16 – C17	137.1(3)
C5 – C6 – C8 – O1	26.4(3)	C20 – C18 – C16 – C17	-105.6(3)
C7 – C6 – C8 – C10	-95.6(4)	C19 – C18 – C16 – C17	22.3(4)
C5 – C6 – C8 – C10	142.5(3)	O3 – C18 – C16 – C15	15.3(3)
C7 – C6 – C8 – C9	32.6(4)	C20 – C18 – C16 – C15	132.6(3)
C5 – C6 – C8 – C9	-89.4(3)	C19 – C18 – C16 – C15	-99.6(3)
C18 – O3 – C11 – O4	88.6(3)	C11 – O4 – C12 – C13	66.0(4)
C18 – O3 – C11 – C15	-31.2(3)	C14 – C13 – C12 – O4	-61.2(4)