Dissertation zur Erlangung des Doktorgrades
der Fakultät für Chemie und Pharmazie
der Ludwig-Maximilians-Universität München

Stereo-Controlled Syntheses and Reactions of Secondary Alkyl Organometallics

von

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aus

Nara-Ken, Japan

2015

Erklärung

Diese Dissertation wurde im Sinne von § 7 der Promotionsordnung vom 28. November 2011 von Herrn Prof. Dr. Paul Knochel betreut.

Eidesstattliche Versicherung

Diese Dissertation wurde eigenständig und ohne unerlaubte Hilfe erarbeitet.

München, am 21. July 2015

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Kohei Moriya

Dissertation eingereicht am 27. July 2015

1. Gutachter: Prof. Dr. Paul Knochel
2. Gutachter: Prof. Dr. Herbert Mayr

Mündliche Prüfung am 18. September 2015

This work was carried out from April 2012 to July 2015 under the guidance of Prof. Dr. Paul Knochel at the Department Chemie und Pharmazie of the Ludwig-Maximilians-Universität München.

First, I would like to thank Prof. Dr. Paul Knochel for the great opportunity to carry out my Ph.D. in his group and for his generous support and guidance in the course of my scientific research. I am also very grateful to Prof. Dr. Herbert Mayr for agreeing to be my second reviewer of this thesis as well as Prof. Dr. Hendrik Zipse, Prof. Dr. Konstantin Karaghiosoff, Dr. Henry Dube, Dr. Armin R. Ofial for their interest shown in my topics and for accepting to be referees. I appreciate Prof. Dr. Tamio Hayashi for his valuable support even after I graduated from his working group.

I really would like to thank Prof. Dr. Paul Knochel, Prof. Dr. Herbert Mayr, Prof. Dr. Hendrik Zipse, Varvara Morozova and Meike Simon for their careful correction on this thesis.

I thank all past and present co-workers I have met in the Knochel group for their kindness and their help. I really thank Dr. Tobias Thaler, Dr. Stephanie Seel, Dr. Guillaume Dagousset, Dr. Guillaume Berionni, Dr. Dorian Didier, Rasmus Mose, Jeffrey M. Hammann, Meike Simon, Varvara Morozova, Daniel Beck and Kuno Schwärzer, who tried this challenging chemistry with me. I also thank Prof. Dr. Hendrik Zipse for DFT calculations. I am grateful to Prof. Dr. Konstantin Karaghiosoff for X-ray measurements and NMR studies. Moreover, I appreciate Prof. Herbert Mayr for his valuable discussions and suggestions on my kinetic studies.

Special thanks to my actual and former lab mates in F.2017: Dr. John Markiewicz, Dr. Lydia Klier, Dr. Kraus Groll, Dr. Annette Frischmuth, Dr. Quan Chen, Dr. Trine Peterson, Mattias Becker, Jeffrey. M. Hammann, Dr. Chiara Marelli, Alicia Castello-Mico, Dr. Ilya Makarov, Meike Simon, Varvara Morozova, Dorotheé Ziegler.

I am grateful to Dr. Nadja Barl, Dr. Lydia Klier, Sarah Fernandez, Matthias Becker, Dr. Dorian Didier and Johannes Nickel for their support in my supervising Plaktikum, and also to Dr. Tobias Thaler, Dr. Andreas Steib, Dr. Christoph Sämman, Dr. Simon Herbert and Dr. Quan Chen for kind advices for my job searching.

I would like to thank Dr. Simon Herbert, Matthias Becker, Dr. Olesya Kuzumina, Dr. Ilya Makarov and Varvara Morozova for organizing nice dinner. Additional thanks go to Dr. Simon Herbert, Dr. Dorian Didier, Johannes Nickel and Michael Eisgold for organizing Friesbee games and to Zhi-Liang Shen and Dr. Vasudevan Dhayalan for organizing hiking trips. They make me much healthier than before.

I would also like to thank Renate Schröder, Simon Matthe, Dr. Vladimir Malakhov, Yulia Tsvik, Peter Dowling and Sophie Hansen for their kind help in organizing everyday's life in the lab and in the office, as well as the analytical team of the LMU for their invaluable help.

Very special thanks go to my family for their deep understanding of my challenge in Germany and to my friends and baseball mates, especially Kiyoshige Takeuchi and Prof. Dr. Eiichiro Komatsu, for very nice weekends.

Part of this Ph. D. thesis:

1. Diastereoselective Synthesis of Open-Chain Secondary Alkyllithium Compounds and Trapping Reactions with Electrophiles

   Guillaume Dagousset, Kohei Moriya, Rasmus Mose, Guillaume Berionni, Konstantin Karaghiosoff, Paul Knochel
   Angew. Chem. **2014**, *126*, 1449–1453; *Angew. Chem. Int. Ed.* **2014**, *53*, 1425–1429.

2. Diastereoconvergent Negishi Cross-Coupling Using Functionalized Cyclohexylzinc Reagents

   Kohei Moriya, Paul Knochel
   Org. Lett. **2014**, *16*, 924–927.

3. Stereoselective Synthesis and Reactions of Secondary Alkyllithium Reagents Functionalized at the 3-Position

   Kohei Moriya, Dorian Didier, Meike Simon, Jeffrey M. Hammann, Guillaume Berionni, Konstantin Karaghiosoff, Hendrik Zipse, Herbert Mayr, Paul Knochel
   Angew. Chem. **2015**, *127*, 2793–2796; *Angew. Chem. Int. Ed.* **2015**, *54*, 2754–2757.

4. Stereoselective Domino-Transmetalation of Secondary Alkyllithiums

   Kohei Moriya, Meike Simon, Rasmus Mose, Konstantin Karaghiosoff, Paul Knochel
   Angew. Chem. **2015**, *127*, 11113–11117; *Angew. Chem. Int. Ed.* **2015**, *54,* 10963–10967.

5. *Title is not decided yet*

   Varvara Morozova, Kohei Moriya, Dorian Didier, Paul Knochel
   Manuscript in prepration. **2015**.

6. *Title is not decided yet*

   Meike Simon, Kohei Moriya, Kuno Schwärzer, Dorian Didier, Paul Knochel
   Manuscript in prepration. **2015**.

"If you dream it, you can do it."

Walt Disney (1901-1966)

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Abbreviation

Ac	acetyl
AcOH	acetic acid
Ar	aryl
Ar	argon
ax	axial
Boc	*tert*-butoxycarbonyl
br	broad
Bn	benzyl
Bpin	boronic acid pinacol ester
Bu, ^{n}Bu	*n*-butyl
^{s}Bu	*s*-butyl
^{t}Bu	*t*-butyl
calc	calculated
cat.	catalytic amount
d	doublet
d	deuterated
D	deuterium
δ	chemical shifts in parts per million
dba	*trans,trans*-dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0] undec-7-ene
DCC	*N,N'*-dicyclohexylcarbodiimide
DEI	desorption electrospray ionization
DFT	density functional theory
DMF	*N,N*-dimethylformamide
d.r.	diastereoselectivity (It is defined in each sections.)
E	electrophile

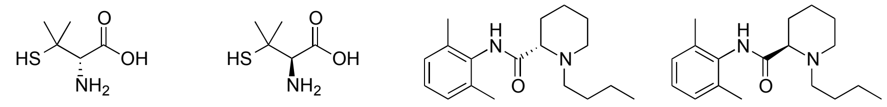
EI	electron ionization
ESI	electrospray ionization
Eth	ether
eq	equatorial
eq	equilibrium
equiv	equivalent
Et	ethyl
FG	functional group
G	Gibbs energy
GC	gas chromatography
h	hour
h	sextet
h	Planck's constant
H	enthalpy
HRMS	high resolution mass spectroscopy
i	iso
Ipc	diisopinocampheyl
^{i}Pr	isopropyl
IR	infra-red
J	coupling constant
K, k	kinetic constant
k_B	Boltzmann constant
LDA	lithium diisopropylamide
LRMS	low resolution mass spectroscopy
m	multiplet
M	molarity
Me	methyl
Met	metal
min	minute
mmol	millimole
m.p.	melting point
MS	mass spectroscopy

MTBE	methyl *tert*-butyl ether
NMI	*N*-methylimidazole
NEP	*N*-ethylpyrrolidone
NMR	nuclear magnetic resonance
Ph	phenyl
PMB	*para*-methoxybenzyl
PMDTA	*N*,*N*,*N’*,*N’*,*N’’*-pentamethyldiethylenetriamine
q	quartet
quint	quintet
R	organic group
R-Phos	2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl
RT	room temperature
RuPhos	2-dicyclohexylphophino-2’,6’-diisopoxybiphenyl
s	singlet (NMR)
s	strong (IR)
S	entropy
SPhos	2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl
t	triplet
T	time
T	temperature
TBAF	tetrabutylammonium fluoride
Tf	trifluoromethylsulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TBS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
TMEDA	*N*,*N*,*N’*,*N’*-tetramethylethylenediamine
TMS	trimethylsilyl
Ts	4-toluenesulfonyl

1 Introduction

1.1 Overview

The development of new synthetic strategies is one of the most important objectives in organic chemistry, particularly for a class of compounds that cannot be easily accessed by existing methods. Recently, lots of new stereoselective reactions have been reported to approach stereodefined molecules especially in terms of pharmaceutical and agrochemical applications.[1] This control of the stereoselectivity is highly important in order to fully ensure the bioactivity of chiral molecules and to avoid side effects. Thus, while one of the enantiomers is useful and, on the other hand, the other sometimes may show adverse effects. (Figure 1-1) In fact, 60% of drugs with Food and Drug Administration approval in USA contain stereoinformation.[2]



(*S*)-Penicillamine
rheumatoid arthritis drug

(*R*)-Penicillamine
inhibitor for vitamin B_6

(*S*)-Ropivacaine
local anaesthetic drug

(*R*)-Ropivacaine
cardiac toxicity

Figure 1-1. Difference of properties between two stereoisomers.

In order to fulfill these synthetic challenges, many possibilities have been offered so far. They are categorized in the next section.

1.2 Access to stereodefined molecules

1.2.1 Isolation from natural sources

Historically, isolation from natural sources is a common way to obtain stereodefined molecules. Usually they are treated as basic building blocks[3] and converted to more complex structures using organic synthesis procedures. Stereocontrol of several stereocenters are often

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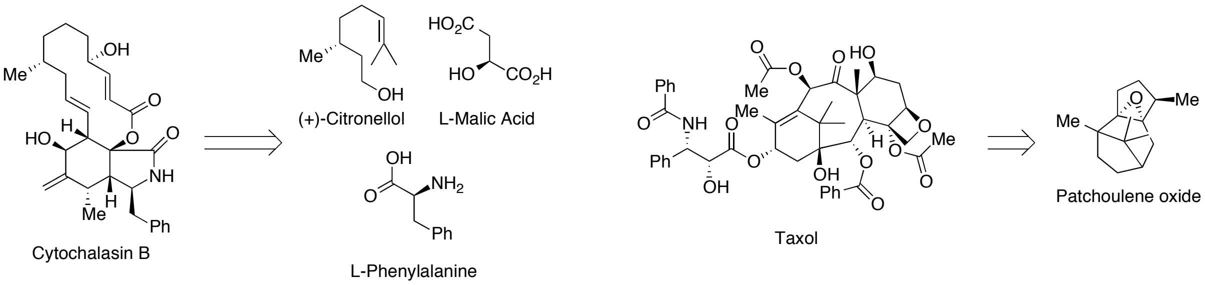
[1] a) *Asymmetric synthesis - The Essentials* (Eds.: M. Christmann, S. Bräse), Wiley-VCH, **2007**; b) A. G. O'Brien, *Tetrahedron* **2011**, *67*, 9639.

[2] *Drug Discovery Today* **2004**, *9*, 105.

[3] S. Hanessians, J. Franco, B. Larouce, *Pure. Appl. Chem.* **1990**, *62*, 1887.

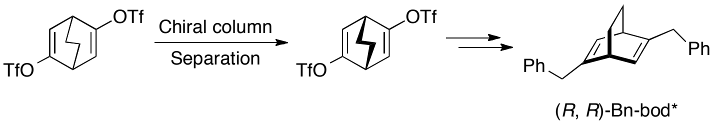
needed during these procedures (section 1.2.5). For example, Cytochalasin B and Taxol were synthesized with chiral building blocks from natural sources (Scheme 1-1).[4]



Scheme 1-1. Total synthesis from chiral building blocks.

1.2.2 Separation of racemic mixture

Classical approaches to separate racemic mixtures are recrystallization or chromatography (in the case of chiral products with a chiral column). These methods sometimes have the advantage that several stereoisomers can be controlled at the same time. Hayashi *et al.* reported the separation of mixture of a racemic precursor to prepare a diene ligand Bn-bod (Scheme 1-2).[5]



Scheme 1-2. Separation of mixture of a racemic precursor to prepare a ligand (Bn-bod*).

1.2.3 Resolution

Kinetic resolution represents a further alternative. In this method, the racemic mixture is subjected to a stereoselective reaction and only one stereoisomer is being selectively transformed. In all cases, the highest possible yield for one stereoisomer cannot exceed 50%. Jacobsen *et al.* have reported the hydrolytic kinetic resolution of a terminal epoxide in the presence of a cobalt-salen complex (Scheme 1-3).[6]

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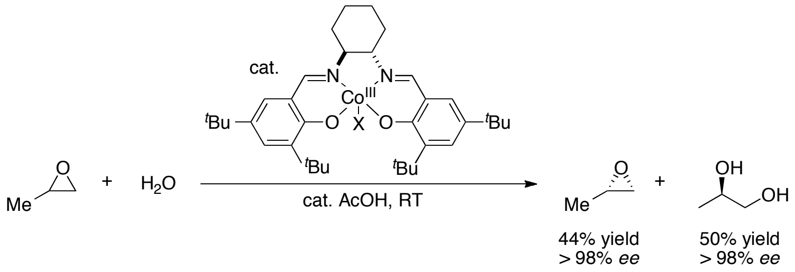
[4] a) R. A. Holton, C. Somoza, H. B. Kim, F, Liang, R. J. Biediger, P. D. Boatman, M. Shindo, C. C. Smith, S. Kim, H. Nadizadeh, Y. Suzuki, C. Tao, P. Vu, S. Tang, P. Zhang, K. K. Murthi, L. N. Gentile, J. H. Liu, *J. Am. Soc. Chem.* **1994**, *116*, 1597; b) R. A. Holton, H. B. Kim, C. Somoza, F, Liang, R. J. Biediger, P. D. Boatman, M. Shindo, C. C. Smith, S. Kim, H. Nadizadeh, Y. Suzuki, C. Tao, P. Vu, S. Tang, P. Zhang, K. K. Murthi, L. N. Gentile, J. H. Liu, *J. Am. Soc. Chem.* **1994**, *116*, 1599.

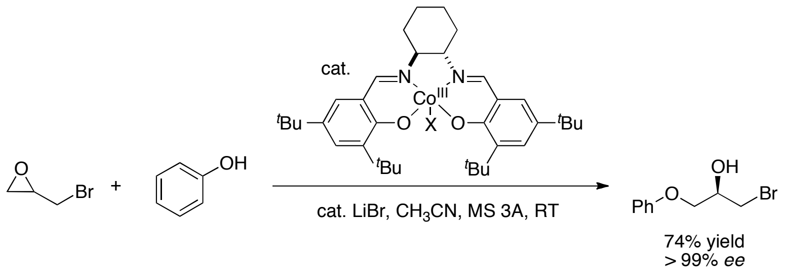
[5] Y. Otomaru, K. Okamoto, R. Shintani, T. Hayashi, *J. Org. Chem.* **2005**, *70*, 2503.

[6] M. Tokunaga, J. F. Larrow, F. Kakiuchi, E. N. Jacobsen, *Science* **1997**, *277*, 36.



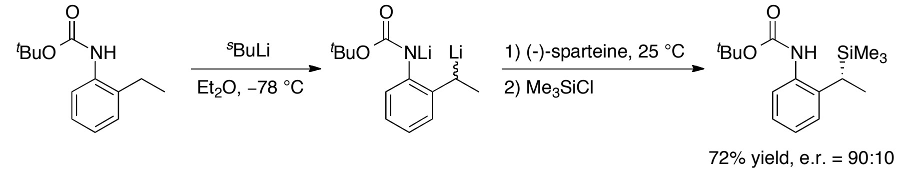
Scheme 1-3. Jacobsen hydrolytic kinetic resolution of a terminal expoxide.

Dynamic kinetic resolution (DKR) shows an important advance as it produces only one single stereoisomer from a racemic mixture since this process includes epimerization equilibrium between stereoisomers. Jacobsen *et al.* reported a cobalt-salen complex catalyzed dynamic kinetic resolution of a terminal epoxide in the presence of LiBr, which cause epimerization by opening epoxide with bromide anion (Scheme 1-4).[7]



Scheme 1-4. Jacobsen phenolytic dynamic kinetic resolution of a terminal expoxide.

Thermodynamic resolution is another type of a resolution reaction and depends on the configurational instability of the starting material or the reactive intermediate. Thus, one of the stereoisomers is converted to the other one via epimerization equilibrium. A diastereoisomer has to have a significantly higher thermodynamic stability. In the case below, the addition of (−)-sparteine shifted the equilibrium of the alkyllithium intermediate to obtain the product in good diastereoselectivity (Schem 1-5).[8]



Scheme 1-5. Generation of thermodynamically stable alkyllithium complex by the addition of a chiral ligand.

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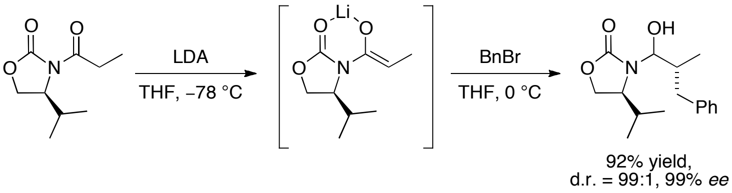
[7] a) J. M. Ready, E. N. Jacobsen, *J. Am. Chem. Soc.* **1999**, *121*, 6086; b) F. F. Juerta, A. B. E. Minidis, J. –E. Backvall, *Chem. Soc. Rev.* **2001**, *30*, 321.

[8] A. Basu, P. Beak, *J. Am. Chem. Soc.* **1982**, *104*, 1737.

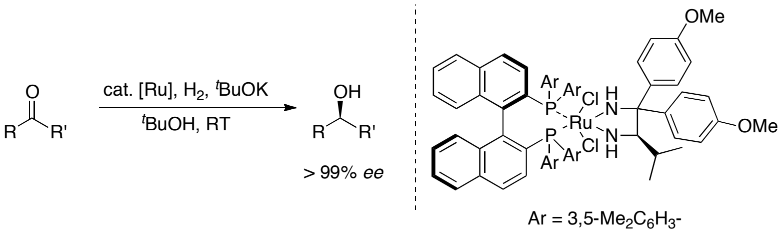
1.2.4 Asymmetric synthesis

Asymmetric synthesis is defined by IUPAC as a chemical reaction (or reaction sequence) where one or more chiral centers, axes or planes are formed in a substrate molecule and which produces stereoisomeric products in unequal amounts. These processes are based on energy difference between diastereomeric intermediates, which are caused by internal or external stereoinformation. The chiral auxiliaries are temporarily introduced chemical units to control the stereochemical outcome of such asymmetric syntheses. Evans *et al.* developed exazolidinone chiral auxiliary to access the aldol products enantioselectively (Scheme 1-6).[9]



Scheme 1-6. Evans oxazolidinone chiral auxiliary used to prepare enantioselectively aldol products.

Recently, various transition-metal catalyzed or organocatalyzed stereoselective reactions have been reported. The key point is the design of chiral ligands. They can be categorized as external stereoinformation. Noyori *et al.* produced the Ru(II)-BINAP-chiral diamine complex for the asymmetric reduction of simple ketones with very high turnover number (TON) (Scheme 1-7).[10]



Scheme 1-7. Ru-catalyzed Noyori asymmetric hydrogenation.

1.2.5 Stereodefined reaction

The development of stereo-control at a stereocenter is required for further transformations of chiral molecules. There are two types of stereoselective reaction pathways (Scheme 1-8).

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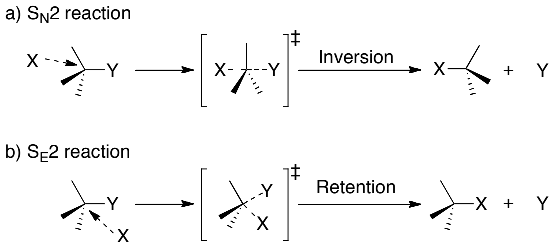
[9] D. A. Evans, M. D. Ennis, D. J. Mathre, *J. Am. Chem. Soc.* **1982**, *104*, 1737.

[10] R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, (Ed.: I, Ojima), John Wiley & Sons, New York, **1994**.



Scheme 1-8. Bimolecular inversion and retention reaction and transition states.

The S_N2 type reactions proceed with inversion of the configuration. In this case, the nucleophile approaches from the backside of the leaving group to form a tentatively pentacoordinate transition state. The S_E2 mechanism proceeds with retention of configuration. Sn/Li exchange[11] or I/Li exchange[12] are S_E2 mechanisms. Such reactions keep their stereoinformation retention during the transformation from the precursors.

1.3 Stereoselective generation of organometallics

1.3.1 Motivation

In the last two decades, transition-metal catalyzed chemistry has been developed very well (Table 1-1). This chemistry shows characteristic reactivities to enable transformations which cannot be achieved by existing methods.

Table 1-1. Number of publications with titles "~ catalyzed" in chemical journals (1995-2015).

	Pd	Rh	Ni	Cu	Fe
JACS	585	290	178	218	99
Angew. Chem.	643	332	127	335	126

Transition metal catalyzed reactions may allow inducing chirality from achiral starting materials by addition of chiral ligands as external chiral information. Some of transition metal-catalyzed reactions have already been applied in industrial production. On the other hand, they still have some drawbacks. For example, their efficiency and outcome

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[11] *Principles of Asymmetric Synthesis*, (Ed.: R. E. Gawley, J. Aubé), Elsevier Science, Oxford, **1996**.

[12] a) G. Wittig, U. Schöllkopf, *Tetrahedron* **1958**, *3*, 91; b) M. Newcomb, W. G. Willams, E. L. Crumpacker, *Tetrahedron* 1985, 26, 1183; c) M. Newcomb, W. G. Willams, *Tetrahdron Lett.* **1985**, *26*, 1179; d) E. C. Ashby, T. N. Pham, *J. Org. Chem.* **1987**, *52*, 1291; e) P. Beak, D. J. Allen, *J. Am. Chem. Soc.* **1992**, *114*, 3420.

usually depend on the structure of the substrates. Moreover, the availability of transition metals is also point of a matter. To compensate these weak points, easily accessible abundant main group metals such as Li, Mg and Zn can be good alternatives. The stereoselective generation of such main group metal organometallics is a very general approach because their substrate patterns and trapping reactions with various electrophiles lead to a wide diversity of products (Figure 1-2).

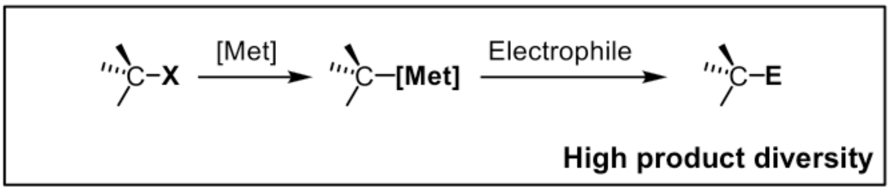

Figure 1-2. Stereoselective generation of organometallics with a main group metal and their reactions.

The properties of organometallics, especially their reactivity and stability, largely depend on the nature of the metal center as shown below. Thus, the reactivity generally increases and the stability decreases with the increasing ionic nature of the carbon-metal bond caused by the difference of electronegativity between the metal center and the carbon atom (Figure 1-3).

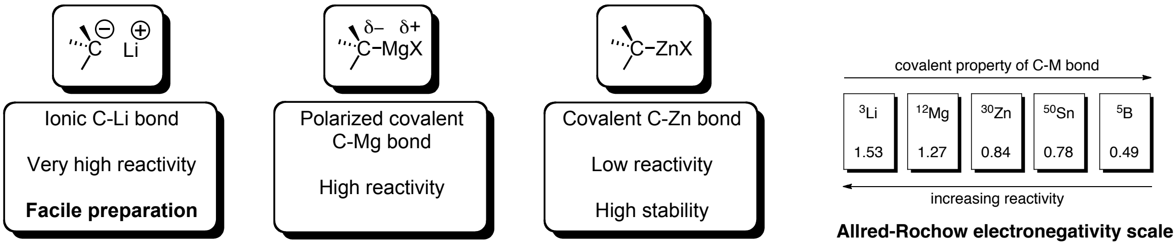

Figure 1-3. Differences of organometallic properties with various metal centers due to the difference of electronegativity between the metal center and the carbon atom.

1.3.2 Stereodefined organolithium reagents

Organolithium reagents are the most widely used organometallics in contemporary organic chemistry[13] due to their high reactivity combined with their availability based on practical preparation methods.[14] Indeed, many secondary alkyllithium reagents are chiral but their use

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[13] a) J. Clayden, *Organolithiums: Selectivity for Synthesis* (Eds.; J. E. Baldwin, R. M. Williams), Pergamon: Oxford, **2002**; b) M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem. Int. Ed.* **2004**, *43*, 2206; c) D. B. Collum, A. J. McNeil, A. Ramirez, *Angew. Chem. Int. Ed.* **2007**, *46*, 3002.

[14] *The Chemistry of Organolithium Compounds*. (Eds. Z. Rappoport, I. Marek), John Wiley & Sons, Chichester, **2004**; b) E. Negishi, D. R. Swanson, C. J. Rousset, *J. Org. Chem.* **1990**, *55*, 5406; c) W. F. Bailey, E. R. Punzalan, *J. Org. Chem.* **1990**, *55*, 5404; d) A. Basu, S. Thayumanavan, *Angew. Chem. Int. Ed.* **2002**, *41*, 716; e) F. Foubelo, M. Yus, *Chem. Soc. Rev.* **2008**, *37*, 2620.

in stereoselective synthesis is limited because some stabilizing groups are usually required (Figure 1-4).[15,16,17] On the other hand, secondary alkyllithium reagents without such a stabilizing effect (unstabilized alkyllithium reagents) have not been fully investigated so far. Early attempts to prepare unstabilized secondary alkyllithium reagents stereoselectively were usually not successful due to their low configurational stability and low yield. For example,

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[15] Stereoselective synthesis of α-heteroatom substituted alkyllithiums: a) T. Cohen, M.-T. Lin, *J. Am. Chem. Soc.* **1984**, *106*, 1130; b) S. D. Rychnovsky, D. E. Mickus, *Tetrahedron Lett.* **1989**, *30*, 3011; c) D. Hoppe, F. Hintze, P. Tebben, *Angew.Chem. Int. Ed.* **1990**, *29*, 1422; d) R. W. Hoffmann, T. Ruhland, M. Bewersdorf, *J. Chem. Soc., Chem. Commun.* **1991**, 195; e) R. E. Gawley, Q. Zhang, *J. Am. Chem. Soc.* **1993**, *115*, 7515; f) P. O'Brien, S. Warren, *J. Chem. Soc., Perkin Trans. 1*, **1996**, 2567; g) F. Hammerschmidt, A. Hanninger, H. Völlenkle, *Chem. Eur. J.* **1997**, *3*, 1728; h) D. Hoppe, T. Hense, *Angew. Chem. Int. Ed.* **1997**, *36*, 2282; i) S. C. Hume, N. S. Simpkins, *J. Org. Chem.* **1998**, *63*, 912; j) S. D. Rychnovsky, A. J. Buckmelter, V. H. Dahanukar, D. J. Skalitzky, *J. Org. Chem.* **1999**, *64*, 6849; k) C. Serino, N. Stehle, Y. S. Park, S. Florio, P. Beak, *J. Org. Chem.* **1999**, *64*, 1160; l) V. Selvamurugan, I. S. Aidhen, *Synthesis* **2001**, 2239; m) S. D. Rychnovsky, L. R. Takaoka, *Angew. Chem. Int. Ed.* **2003**, *42*, 818; n) S. A. Wolckenhauer, S. D. Rychnovsky, *Org. Lett.* **2004**, *6*, 2745; o) P. O'Brien, K. B. Wiberg, W. F. Bailey, J.-P. R. Hermet, M. J. McGrath, *J. Am. Chem. Soc.* **2004**, *126*, 15480; p) I. Coldham, S. Dufour, T. F. N. Haxell, J. J. Patel, G. Sanchez-Jimenez, *J. Am. Chem. Soc.* **2006**, *128*, 10943; q) D. C. Kapeller, L. Brecker, F. Hammerschmidt, *Chem. Eur. J.* **2007**, *13*, 9582; r) R. Luisi, V. Capriati, S. Florio, B. Musio, *Org. Lett.* **2007**, *9*, 1263; s) R. Klein, R. E. Gawley, *J. Am. Chem. Soc.* **2007**, *129*, 4126; t) D. C. Kapeller, F. Hammerschmidt, *J. Am. Chem. Soc.* **2008**, *130*, 2329; u) R. J. Bahde, S. D. Rychnovsky. *Org. Lett.* **2008**, *10*, 4017-4020; v) F. Foubelo, M. Yus, *Chem. Soc. Rev.* **2008**, *37*, 2620; w) D. C. Kapeller, F. Hammerschmidt, *J. Org. Chem.* **2009**, *74*, 2380; x) D. C. Kapeller, F. Hammerschmidt, *Chem. Eur. J.* **2009**, *15*, 5729; y) V. Capriati, S. Florio, F. M. Perna, A. Salomone, *Chem. Eur. J.* **2010**, *16*, 9778; z) J. J. Gammon, V. H. Gessner, G. R. Barker, J. Granander, A. C. Whitwood, C. Strohmann, P. O'Brien, B. Kelly, *J. Am. Chem. Soc.* **2010**, *132*, 13922-13927; aa) V. H. Gessner, S. Dilsky, C. Strohmann, *Chem. Commun.* **2010**, *46*, 4719; ab) G. Carbone, P. O'Brien, G. Hilmersson, *J. Am. Chem. Soc.* **2010**, *132*, 15445; ac) V. H. Gessner, S. Dilsky, C. Strohmann, *Chem. Commun.* **2010**, *47*, 4719; ad) G. Carbone, P. O'Brien, G. Hilmersson, *J. Am. Chem. Soc.* **2010**, *132*, 15445; ae) S. Roesner, J. M. Casatejada, T. G. Elford, R. P. Sonawane, V. K. Aggarwal, *Org. Lett.* **2011**, *13*, 5740; af) T. K. Beng, J. S. Woo, R. E. Gawley, *J. Am. Chem. Soc.* **2012**, *134*, 14764; ag) A. Wieczorek, F. Hammerschmidt, *J. Org. Chem.* **2012**, *77*, 10021; ah) K. N. Baryal, D. Zhu, X. Li, J. Zhu, *Angew. Chem. Int. Ed.* **2013**, *52*, 8012; ai) T. Boultwood, J. A. Bull. *Org. Lett.* **2014**, *16,* 2740; aj) A. Salomone, F. M. Perna, A. Falcicchio, S. O. N. Lill, A. Moliterni, R. Michel, S. Florio, D. Stalke, V. Capriati, *Chem. Sci.* **2014**, *5*, 528; ak) X. Li, I. Coldham, *J. Am. Chem. Soc.* **2014**, *136*, 5551; al) A. Salomone, F. M. Perna, A. Falcicchio, S. O. N. Lill, A. Moliterni, R. Michel, S. Florio, D. Stalke, V. Capriati, *Chem. Sci.* **2014**, *5*, 528; am) X. Li, I. Coldham, *J. Am. Chem. Soc.* **2014**, *136*, 5551; an) S. G. Koller, U. Kroesen, C. Strohmann, *Chem. Eur. J.* **2015**, *21*, 641; ao) D. M. Hodgson, C. L. Mortimer, J. M. Mckenna, *Org. Lett*, **2015**, *17*, 330.

[16] Stereoselective synthesis of α-heteroatom substituted alkyllithiums stabilized by hyperconjugation: a) P. v. R. Schleyer, T. Clark, A. J. Kos, G. W. Spitznagel, C. Rohde, D. Arad, K. N. Houk, N. G. Rondan, *J Am. Chem. Soc.* **1984**, *106*, 6467; b) H. J. Reich, M. D. Bowe, *J. Am. Chem. Soc.* **1990**, *112*, 8994; c) R. W. Hoffmann, R. K. Dress, T. Ruhland, A. Wenzel, *Chem. Ber.* **1995**, *128*, 861.

[17] Stereoselective synthesis of benzylic and allylic alkyllithiums: a) P. R. Peoples, J. B. Grutzner, *J. Am. Chem. Soc.* **1980**, *102*, 4709; b) D. Hoppe, A. Carstens, T. Krämer, *Angew. Chem. Int. Ed.* **1990**, *29* 1424; c) R. W. Hoffmann, T. Rühl, F. Chemla, T. Zahneisen, *Liebigs Ann. Chem.* **1992**, 719; d) S. Klein, I. Marek, J.-F. Normant, *J. Org. Chem.* **1994**, *59*, 2925; e) I. Hoppe, M. Marsch, K. Harms, G. Boche, D. Hoppe, *Angew. Chem. Int. Ed.* **1995**, *34*, 2158; f) S. Thayumanavan, A. Basu, P. Beak, *J. Am. Chem. Soc.* **1997**, *119*, 8209; g) L. Prat, L. Mojovic, V. Levacher, G. Dupas, G. Quéguiner, J. Bourguignon, *Tetrahedron: Asymmetry* **1998**, *9*, 2509; h) M. D. Curtis, P. Beak, *J. Org. Chem.* **1999**, *64*, 2996; i) J. Clayden, M. Helliwell, J. H. Pink, N. Westlund, *J. Am. Chem. Soc.* **2001**, *123*, 12449; j) J. Clayden, F. E. Knowles, C. J. Menet, *Synlett* **2003**, 1701; k) P. O. Burgos, I. Fernández, M. J. Iglesias, S. García-Granda, F. L. Ortiz, *Org. Lett.* **2008**, *10*, 537; l) S. Roesner, J. M. Casatejada, T. G. Elford, R. P. Sonawane, V. K. Aggarwal, *Org. Lett.* **2011**, *13*, 5740; m) F. M. Perna, A. Salomone, M. Dammacco, S. Florio, V. Capriati, *Chem Eur. J.* **2011**, *17*, 8216; n) S. Roesner, J. M. Casatejada, T. G. Elford, R. P. Sonawane, V. K. Aggarwal, *Org. Lett.* **2011**, *13*, 5740; o) J. Lefranc, A. M. Fournier, G. Mingat, S. Herbert, T. Marcelli, J. Clayden, *J. Am. Chem. Soc.* **2012**, *134*, 7286; p) J. Lefranc, A. M. Fournier, G. Mingat, S. Herbert, T. Marcelli, J. Clayden, *J. Am. Chem. Soc.* **2012**, *134*, 7286; q) R. Mansueto, F. M. Perna, A. Salomone, S. Florio, V. Capriati, *Chem. Commun.* **2013**, *49*, 4911.

early reports showed that I/Li exchange on (-)-2-iodooctane **1-1** at −70 °C in petroleum ether resulted in the formation of the desired alkyllithium **1-2** in low yield with loss of stereoinformation, judged by trapping reaction with CO_2 to obtain the corresponding acid **1-3** (Scheme 1-9).[18]

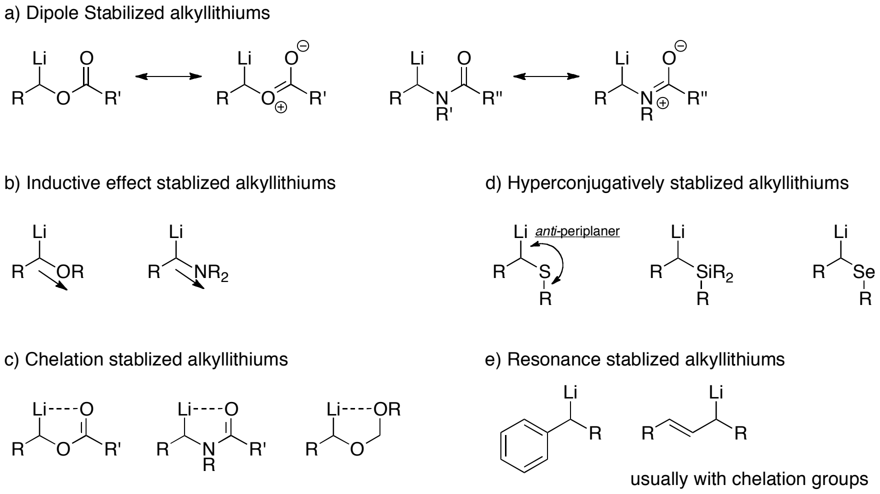
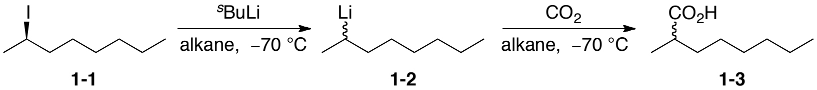


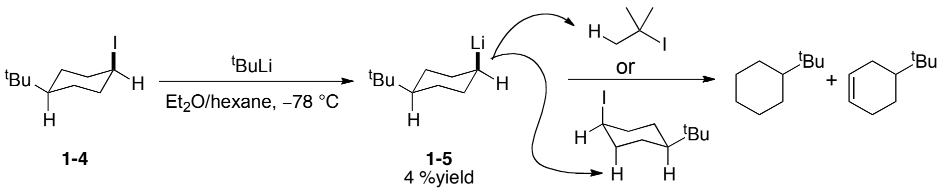
Figure 1-4. Overview of stabilized secondary alkyllithium reagents.



1-1 **1-2** **1-3**
80% racemization

Scheme 1-9. I/Li exchange on stereodefined 2-iodooctane **1-1**.

An I/Li exchange on cyclohexyl iodide **1-4** was used to obtain cyclohexyllithium reagent **1-5**, but the yield was still very low due to the important side reactions to produce hydrolysis or elimination products (Scheme 1-10).[19]



1-4 **1-5**
4 %yield

Scheme 1-10. I/Li exchange on stereodefined cyclohexyl iodide **1-4**.

Reich *et al.* offered a solution using a Te/Li exchange in the presence of the coordinating additive PMDTA to avoid those side reactions and to generate a pair of diastereomers of

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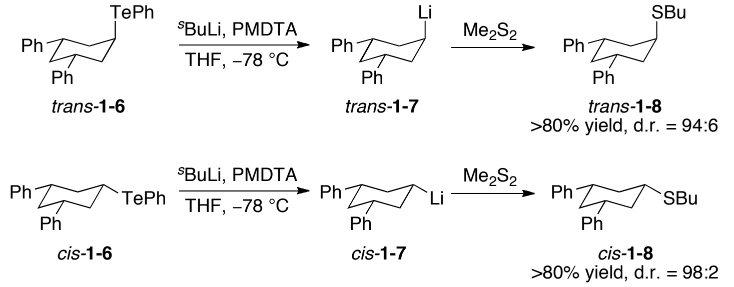
[18] R. L. Letsinger, *J. Am. Chem. Soc.* **1950**, *72*, 4842.
[19] W. F. Bailey, J. D. Brubaker, K. P. Jordan, *J. Organomet. Chem.* **2003**, *681*, 210.

cyclohexyllithium reagents in good yield (Scheme 1-11).[20] Thus, *trans*-**1-6** was treated with ^{s}BuLi at −78 °C in THF and PMDTA to form cyclohexyllithium reagent *trans*-**1-7** selectively, and immediate trapping reaction led to *trans*-product *trans*-**1-8** in more than 80% yield with retention of the configuration (d.r. = 94:6). Cyclohexyl iodide *cis*-**1-6** was transformed into the *cis*-product *cis*-**1-8** (>80% yield, d.r. = 98:2) via the cyclohexyllithium reagent *cis*-**1-7** in the same way.



Scheme 1-11. Stereoselective Te/Li exchange on cyclohexy iodides **1-6**.

It was found that cyclohexyllithium reagent *trans*-**1-7** was thermodynamically unfavored due to the axial position of the lithium atom and was epimerized to *cis*-cyclohexyllithium reagent *cis*-**1-7** with a half life time of 9 min at −78 °C, reaching the equilibrium mixture of *cis*:*trans* = 92:8 in 1 h. This suggested that the aggregation of these cyclohexyllithium reagents is critical, and that inverting the free carbanion **1-9** and **1-10** were key intermediates for the epimerization process (Figure 1-5).[21]

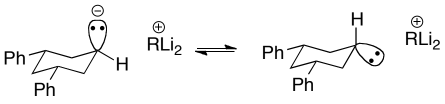


Figure 1-5. Proposed key intermediates **1-9** and **1-10** for the epimerization of cyclohexylithium reagents.

Recently Knochel *et al.* have reevaluated an inverse-addition[14b,c] method for generation of alkyllithium reagents (Scheme 1-12).[22] Thus, the addition of stereodefined cyclohexyl iodide *cis*-**1-11** to a solution of ^{t}BuLi (inverse addition) instantaneously produced cyclohexyllithium *cis*-**1-12**, and immediate quenching with Bu_2S_2 led to thioether *cis*-**1-13** with retention of the configuration (*cis*:*trans* = 90:10) in 59% yield. The Li atom occupied the axial position. For

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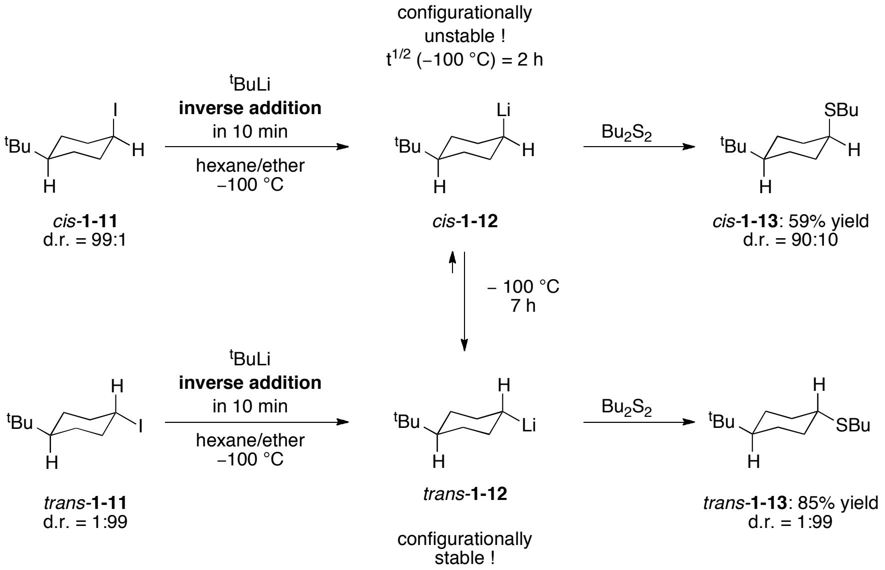
[20] H. J. Reich, M. A. Marco, M. D. Bowe, *J. Am. Chem. Soc.* **1992**, *114*, 11003.
[21] H. J. Reich, *J. Org. Chem.* **2012**, *77*, 5471.
[22] S. Seel, G. Dagousset, T. Thaler, A. Frischmuth, K. Karaghiosoff, H. Zipse, P. Knochel, *Chem. Eur. J.* **2013**, *19*, 4614.

that reason, the lithium reagent *cis*-**1-12** displayed low thermodynamic stability and fully equilibrated into the more stable all-equatorially substituted *trans*-**1-12** within 7 h at −100 °C (*cis*:*trans* = 3:97). On the other hand, subjecting *trans*-**1-11** to the same conditions produced the equatorially substituted lithium reagent *trans*-**1-12**. Quenching with Bu_2S_2 gave the corresponding thioether *trans*-**1-13** (85% yield, *cis*:*trans* = 1:99).



Scheme 1-12. Stereoselective syntheses of cyclohexylithium reagents via I/Li exchange by inverse addition.

The energy difference of these two configuration of cyclohexyllithium reagents **1-12** was evaluated by theoretical calculations (the geometries were optimized at the B3LYP/6-31+G(d) level and the energies were determined at MP2(FC)/6-311+G(2d,p) level; Figure 1-7). Interestingly, comparison of the gas-phase stabilities of monomeric *trans*- and *cis*-compounds indicated no thermodynamic preference. However, the large energy difference in favor of *trans*-compounds was observed in hexameric alkyllithium species. The hexameric structures of cyclohexyllithium were known in less-polar solvents. So the experimentally observed strong preference for *trans*-compounds can be explained by the energy difference caused by the aggregation of alkyllithium compounds.

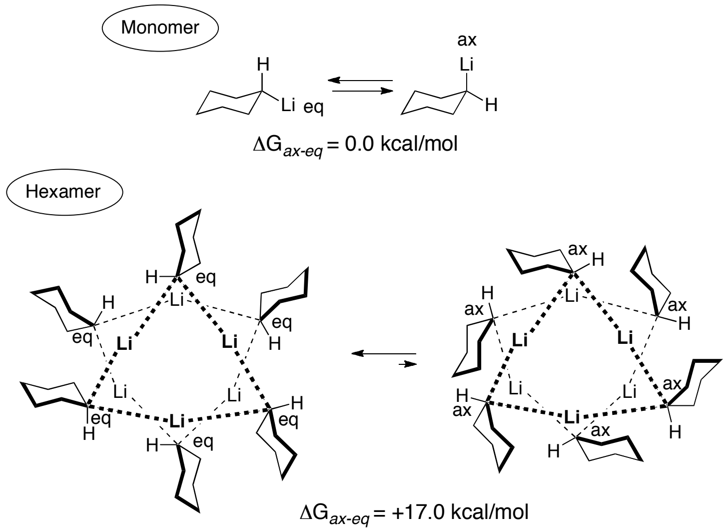
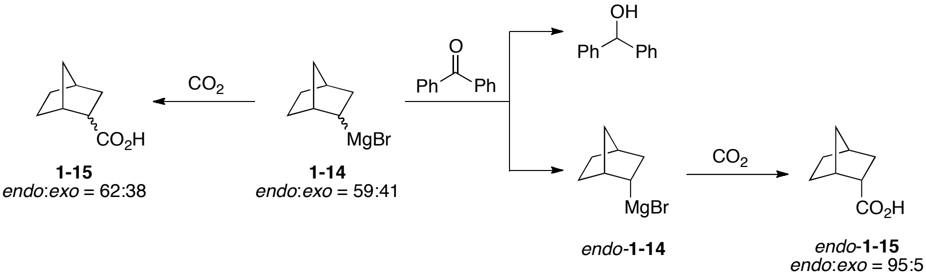


Figure 1-7. Relative gas-phase stabilities of monomer and hexamer of **1-12**.

1.3.3 Stereodefined organomagnesium reagents

The stereoselective preparation of organomagnesium reagents has not been investigated so well compared to organolithium reagents probably because both direct insertion of magnesium to a carbon-halogen bond and halogen-metal exchange reaction tend to proceed under single-electron-transfer (SET) mechanism, losing stereoinfomation. An early report from Jensen and Nakamaye shows the kinetic resolution provided the stereoselective generation of *endo*-norbornylmagnesium bromide (Scheme 1-13).[23] Benzophenone was reduced by more reactive Grignard reagent *exo*-**1-14** selectively to yield diphenylmethanol and pure *endo*-**1-14**. The following trapping reaction with CO_2 led to the selective formation of the corresponding carboxylic acid *endo*-**1-15**. Slow interconversion between *endo*- and *exo*-**1-14** was also observed in NMR measurement[24] showing the relatively high configurational stability of these bicyclic secondary alkyl Grignard reagents.



Scheme 1-13. Kinetic resolution of the diastereomeric norbornylmagnesium reagents **1-14**.

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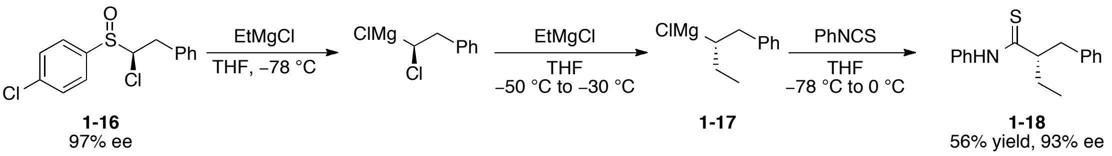
[23] F. R. Jensen, K. L. Nakamaye, *J. Am. Chem. Soc.* **1966**, *88*, 3437.

[24] G. M. Whitesides, J. D. Roberts, *J. Am. Chem. Soc.* **1965,** *87*, 4878.

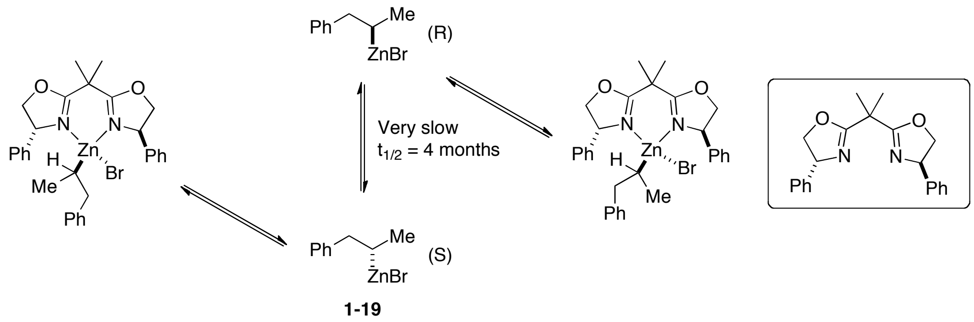
A more general approach to chiral secondary alkylmagnesium reagents was reported by Hoffmann *et al.*[25] by treating sulfoxide **1-16** with an excess of EtMgCl to form enantiomerically enriched magnesium reagent **1-17** via a sulfoxide/magnesium exchange and homologation sequence. The trapping reaction of **1-17** with phenyl isothiocyanate gave the desired thioamide **1-18** with retention of the configuration (Scheme 1-14).



Scheme 1-14. Hoffmann's method for enantioselective generation of secondary alkylmagnesium reagents.

1.3.4 Stereodefined organozinc reagents

The stereoselective preparation of organozinc reagents has not been studied so well, although organozinc compounds have advantages due to their higher stability and moderate reactivity. Rieke *et al.* demonstrated such a high stability by ^{1}H-NMR measurement.[26] They prepared the racemic secondary alkylzinc reagent **1-19** and made a complex with the bisoxazoline ligand. The newly formed complex epimerized very slowly to reach the new thermodynamic ratio after a long time (Scheme 1-15).



Scheme 1-15. Experiment to show the high configurational stability of bisoxazoline-complexed secondary alkylzinc reagents.

Actually, although the carbon-zinc bond is reported to be configurationally stable, it was also shown that the presence of metallic salts facilitates its epimerization[27] and the presence of PdX_2, MgX_2, ZnX_2 or LiCl in the reaction mixture may be responsible for this equilibration.

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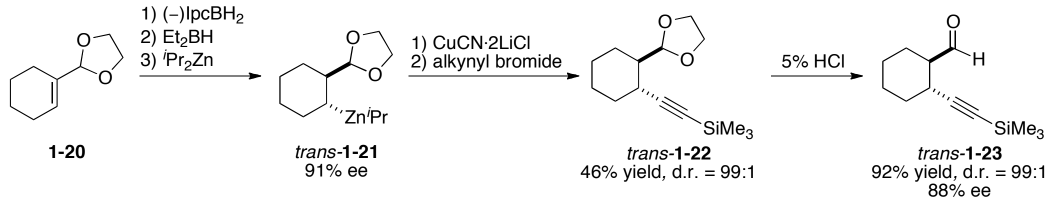
[25] R. W. Hoffmann, B. Hölzer, O. Knopff, K. Harms, *Angew. Chem. Int. Ed.* **2000**, *39*, 3072.

[26] A. Guijarro, R. D. Rieke, *Angew. Chem. Int. Ed.* **2000**, *39,* 1475.

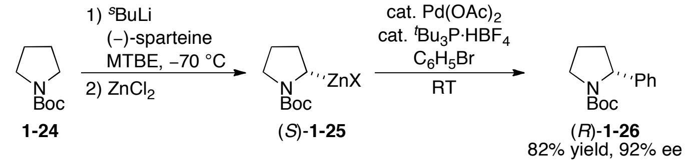
[27] A. Boudier, C. Darcel, F. Flachsmann, L. Micouin, M. Oestreich, P. Knochel, *Chem. Eur. J.* **2000**, *6*, 2748.

Therefore, zinc-boron exchange was used for the formation of stereo-defined secondary alkylzinc reagents.[28] As shown in Scheme 1-16, the *trans*-secondary alkylzinc reagent *trans*-**1-21** in 91% *ee* was produced after successive treatments of **1-20** with (−)-isopinocampheylborane, Et_2BH and ^{i}Pr$_2$Zn. Organozinc reagent *trans*-**1-21** reacted with alkynyl bromide affording the desired product *trans*-**1-22**, which was transformed to *trans*-**1-23** in 88% *ee* after deprotection.



Scheme 1-16. Enantioselective functionalization of the unsaturated acetal **1-20**.

Also α-heteroatom stabilized alkylzinc reagents have been synthesized stereoselectively (Scheme 1-17).[29] *N*-Boc pyrrolidine **1-24** was enantiomerically deprotonated by ^{s}BuLi in the presence of a chiral ligand to obtain a stereo-defined secondary alkylzinc reagent **1-25**. ^{t}Bu$_3$P·HBF$_4$ converted this alkylzinc reagent **1-25** to the arylated product **1-26** in good yield (82% yield) and diastereoselectivity (92% ee), which was established in the deprotonation step.



Scheme 1-17. Enantioselective arylation of *N*-Boc-pyrrolidine **1-24**.

1.4 Objectives

The aim of this work is the development of new methodologies to access stereoselectively secondary alkyl organometallics and their application to stereoselective organic synthesis.

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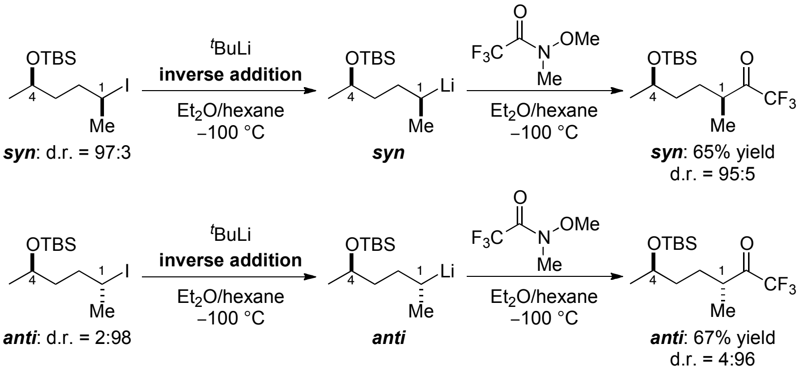
[28] a) A. Boudier, E, Hupe, P. Knochel, *Angew. Chem. Int. Ed.* **2000**, *39*, 2294; b) E. Hupe, P. Knochel, *Angew. Chem. Int. Ed.* **2001**, *40*, 3022; c) E. Hupe, I. Marek, P. Knochel, *Org. Lett.* **2002**, *4*, 2861; d) E. Hupe, M. I. Calaza, P. Knochel, *Chem. Eur. J.* **2003**, *9*, 2789.

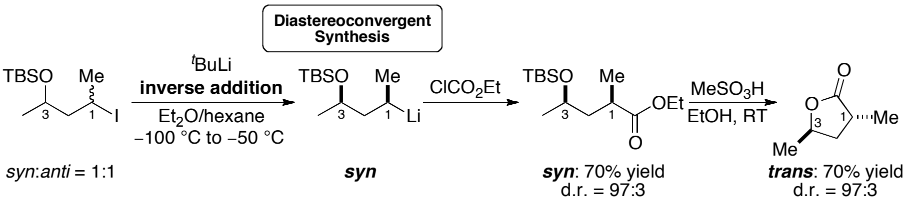
[29] a) K. R. Campos, A. Klapars, J. H. Waldman, P. G. Dormer, C. Chen, *J. Am. Chem. Soc.* **2006**, *128*, 3538; b) T. K. Beng, R. E. Gawley, *Org. Lett.* **2011**, *13*, 394.

1. Diastereoselective preparation of open-chain secondary alkyllithiums functionalized at the 4-position.[30]



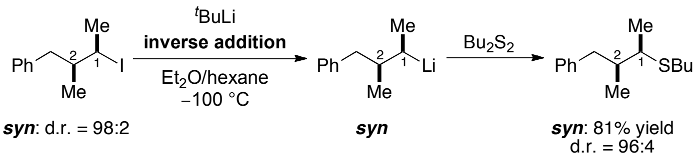
Scheme 1-18. Diastereoselective preparation of secondary alkyllithiums functionalized at the 4-position.

2. Diastereoconvergent preparation of open-chain secondary alkyllithiums functionalized at the 3-position.[31]



Scheme 1-19. Diastereoconvergent preparation of secondary alkyllithiums functionalized at the 3-position.

3. Diastereoselective preparation of open-chain secondary alkyllithiums functionalized at the 2-position.[32]



Scheme 1-20. Diastereoselective preparation of secondary alkyllithiums functionalized at the 2-position.

4. Intramolecular carbolithiation of secondary alkylithiums prepared by stereoselective I/Li exchange.[33]

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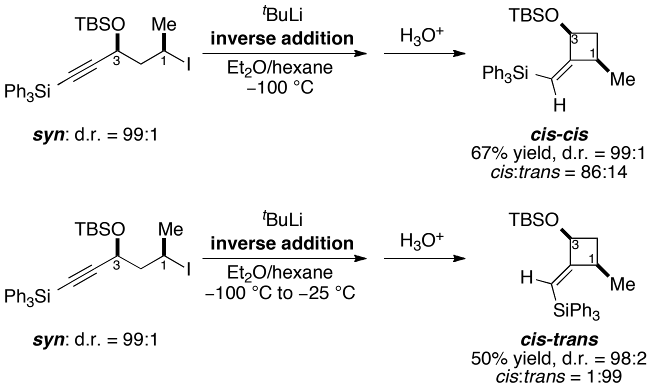
[30] G. Daggousset, K. Moriya, R. Mose, G. Berionni, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2014**, *53*, 1425.

[31] 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.

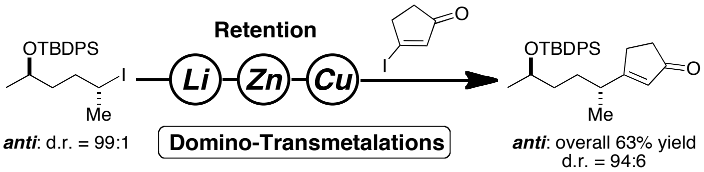
[32] V. Morozova, K. Moriya, D. Didier, P. Knochel, **2015**, *Manuscript in preparation.*

[33] M. Simon, K. Moriya, K. Schwärzer, D. Didier, P. Knochel, **2015**, *Manuscript in preparation.*



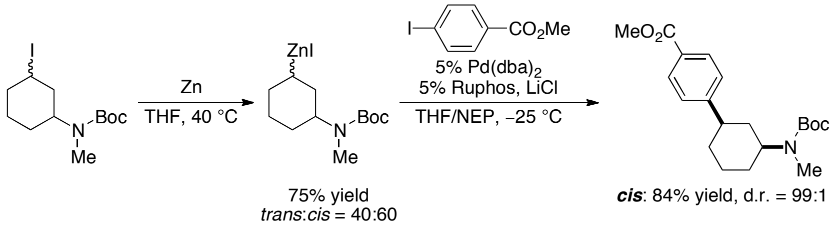
Scheme 1-21. Stereoselective carbolithiation of secondary alkyllithiums.

5. Stereoselective retentive domino-transmetalations of secondary alkyllithiums to functionalized secondary alkylcopper reagents.[34]



Scheme 1-22. Stereoselective retentive domino-transmetalation of secondary alkyllithiums.

6. Diastereoconvergent Negishi cross-coupling using functionalized cyclohexylzinc reagents.[35]



Scheme 1-23. Diastereoconvergent Negishi cross-coupling of cyclohexylzinc reagents.

---

[34] K. Moriya, M. Simon, R. Mose, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2015**, *54*, 10963.

[35] K. Moriya, P. Knochel, *Org. Lett.* **2014**, *16*, 924.

2 Diastereoretentive Preparation of Open-Chain Secondary Alkyllithiums Functionalized at the 4-Position

2.1 Introduction

Due to their high reactivity, organolithium compounds are important reagents in organic synthesis.[13] In particular, the stereoselective generation of stabilized alkyllithiums,[14] such as α-heteroatom-substituted alkyl-,[15,16] benzylic and allylic organolithium reagents[17] has been extensively studied as well as their subsequent trapping reactions with electrophiles. However, the preparation of non-stabilized alkyllithium compounds, especially acyclic secondary alkyllithiums and their stereoselective quenching reactions still remain a major synthetic challenge.[36]

Recently, we have shown that secondary cyclohexyllithium reagents can be generated stereoselectively by using an I/Li exchange reaction and the subsequent trapping with various electrophiles proceed in most cases with retention of the configuration.[22] Furthermore, these organolithiums have recently gained importance due to their direct use in Pd-catalyzed cross-coupling reactions.[37] Herein, we wish to report the first general preparation of stereodefined acyclic non-stabilized secondary alkyllithium reagents, followed by their quenching reactions with a range of electrophiles including carbon electrophiles.

2.2 Results

Alkyl iodide *syn*-**2-1a** was subjected to an I/Li exchange. Thus, adding *syn*-**2-1a** (d.r. (*syn*:*anti*) = 97:3) dropwise within 10 min to a solution of ^{t}BuLi at –100 °C (**inverse addition**) in Et_2O/hexane = 2/3 led to lithium reagent *syn*-**2-2a**, which was subsequently quenched with Me_2S_2 to afford thioether *syn*-**2-3a** in 74% yield with almost complete retention of the configuration (d.r. = 94:6; Scheme 2-1). Similarly, lithium reagent *anti*-**2-2a**

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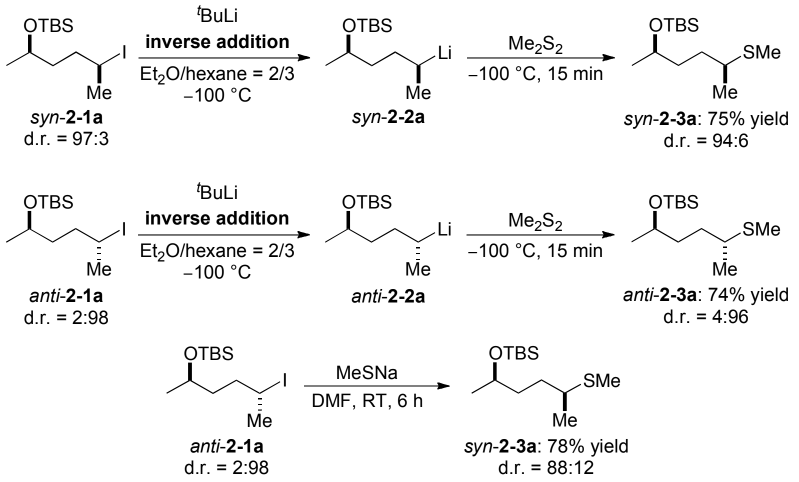
[36] a) D. Y. Curtin, W. J. Koehl, *J. Am. Chem. Soc.* **1962**, *84*, 1967; b) W. H. Glaze, C. M. Selman, *J. Organomet. Chem.* **1968**, *11*, P3; c) W. H. Glaze, C. M. Selman, A. L. Ball, Jr., L. E. Bray, *J. Org. Chem.* **1969**, *34*, 641; d) D. Seebach, H. Neumann, *Chem. Ber.* **1974**, *107*, 847; e) H. Neumann, D. Seebach, *Tetrahedron Lett.* **1976**, *17*, 4839; f) H. Neumann, D. Seebach, *Chem. Ber.* **1978**, *111*, 2785; g) W. F. Bailey, T. T. Nurmi, J. J. Patricia, W. Wang, *J. Am. Chem. Soc.* **1987**, *109*, 2442; h) W. F. Bailey, J. J. Patricia, *J. Organomet. Chem.* **1988**, *352*, 1; i) W. F. Bailey, E. R. Punzalan, *J. Org. Chem.* **1990**, *55*, 5404; j) H. J. Reich, M. A. Medina, M. D. Bowe, *J. Am. Chem Soc.* **1992**, *114*, 11003; k) W. F. Bailey, J. D. Brubaker, K. P. Jordan, *J. Organomet. Chem.* **2003**, *681*, 210; l) A. Sakakura, A. Ukai, K. Ishihara, *Nature* **2007**, *445*, 900.

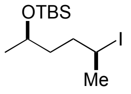
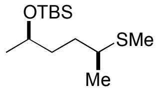
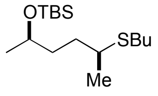
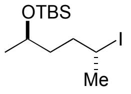
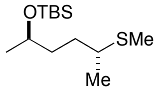
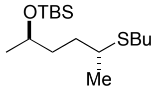
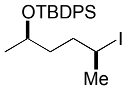
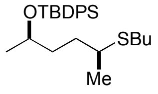
[37] a) M. Giannerini, M. Fañanás-Mastral, B. L. Feringa, *Nature Chem.* **2013**, *5*, 667; b) C. C. C. Johansson Seechurn, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem. Int. Ed.* **2012**, *51*, 5062.

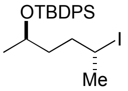
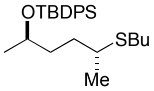
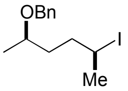
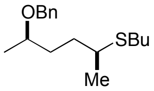
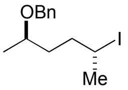
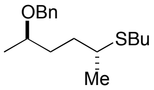
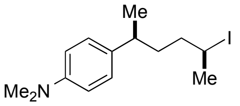
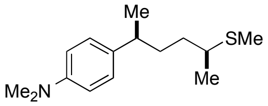
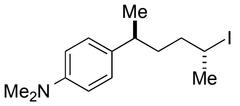
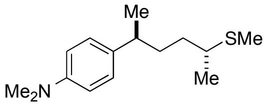
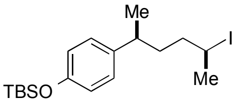
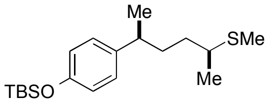
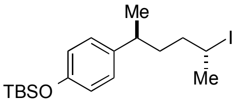
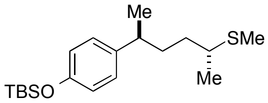
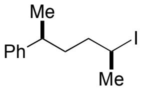
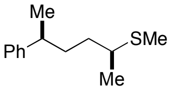
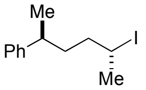
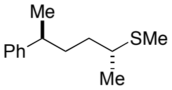
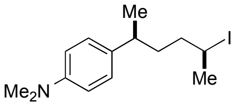
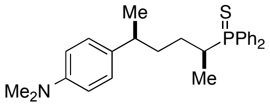
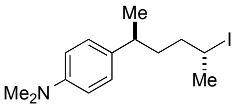
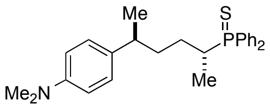
was prepared from alkyl iodide *anti*-**2-1a**, and was trapped with Me_2S_2 to afford *anti*-thioether *anti*-**2-3a** in 75% yield with excellent diastereoselectivity (d.r. = 4:96). Treatment of alkyl iodide *anti*-**2-1a** with sodium methanethiolate led to *syn*-thioether *syn*-**2-3a** in 78% yield (d.r. = 88:12) via S_N2 mechanism, which confirmed overall retention of the configuration during the I/Li exchange and quenching reaction sequence with Me_2S_2 (Scheme 2-1).



Scheme 2-1. Stereoselective preparation of *syn*- and *anti*- acyclic secondary alkyllithium **2-2a**.

Table 2-1. Stereoselective quenching reactions of acyclic secondary alkyllithiums with electrophiles.

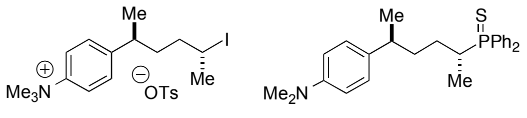
Entry	Substrate	Electrophile	Product	Yield[a], d.r.[b]
1	 *syn*-**2-1a** (d.r. = 97:3)	Me_2S_2	 *syn*-**2-3a**	75% 94:6
2	*syn*-**2-1a** (d.r. = 99:1)	Bu_2S_2	 *syn*-**2-4a**	73% 97:3
3	 *anti*-**2-1a** (d.r. = 2:98)	Me_2S_2	 *anti*-**2-3a**	74% 4:96
4	*anti*-**2-1a** (d.r. = 2:98)	Bu_2S_2	 *anti*-**2-4a**	74% 4:96
5	 *syn*-**2-1b** (d.r. = 97:3)	Bu_2S_2	 *syn*-**2-3b**	70% 95:5

6	 *anti*-**2-1b** (d.r. = 3:97)	Bu_2S_2	 *anti*-**2-3b**	71% 2:98
7	 *syn*-**2-1c** (d.r. = 97:3)	Bu_2S_2	 *syn*-**2-3c**	74% 89:11
8	 *anti*-**2-1c** (d.r. = 3:97)	Bu_2S_2	 *anti*-**2-3c**	77% 10:90
9	 *syn*-**2-1d** (d.r. = 92:8)	Me_2S_2	 *syn*-**2-3d**	70% 91:9
10	 *anti*-**2-1d** (d.r. = 4:96)	Me_2S_2	 *anti*-**2-3d**	65% 6:94
11	 *syn*-**2-1e** (d.r. = 98:2)	Me_2S_2	 *syn*-**2-3e**	73% 94:6
12	 *anti*-**2-1e** (d.r. = 2:98)	Me_2S_2	 *anti*-**2-3e**	75% 5:95
13	 *syn*-**2-1f** (d.r. = 92:8)	Me_2S_2	 *syn*-**2-3f**	73% 91:9
14	 *anti*-**2-1f** (d.r. = 2:98)	Me_2S_2	 *anti*-**2-3f**	73% 4:96
15	 *syn*-**2-1d** (d.r. = 92:8)	Ph_2PCl S_8	 *syn*-**2-4d**	70% 91:9
16	 *anti*-**2-1d** (d.r. = 4:96)	Ph_2PCl S_8	 *anti*-**2-4d**	76% 6:94

[a] Isolated yield. [b] d.r. (*syn*:*anti*) was determined by ^{13}C NMR spectroscopy.

By using these optimized conditions, we were able to stereospecifically access various new non-stabilized acyclic secondary alkyllithium compounds *syn*- and *anti*-**2-2a–f** from the corresponding acyclic *syn*- and *anti*-alkyl iodides **2-1a–f** through an I/Li exchange (Table 2-1).

As shown in scheme 2-1, alkyllithium reagents *syn*- and *anti*-**2-2a** were prepared from the corresponding alkyl iodide *syn*- and *anti*-**2-1a** and trapped with Bu_2S_2 to afford the desired product *syn*- and *anti*-**2-4a** with almost complete retention of configuration (*syn*-**2-4a**: d.r. = 97:3, *anti*-**2-4a**: d.r. = 4:96; entry 2, 4 in Table 2-1). Other protecting groups were also examined. Bulkier protecting group TBDPS were compatible to give the almost same results as a TBS group (entry 5, 6). However, benzyl protecting group caused faster epimerization probably due to moderate coordinating effect of the oxygen atom toward the lithium center (entry 7, 8). Various *syn*- and *anti*-aryl-substituted secondary iodides **2-1d–f** (**1d**: Ar = *p*-$Me_2NC_6H_4$, **1e**: Ar = *p*-$TBSOC_6H_4$ and **1f**: Ar = Ph) have been also prepared in excellent diastereomeric purity (up to d.r. = 98:2) and subjected to the I/Li exchange reaction (entries 9–14). These substituents (*p*-Me_2N; entries 5–8 and *p*-TBSO; entries 9, 10) are well tolerated and the I/Li exchange proceeds with high stereoselectivity in all cases. After quenching with Me_2S_2 the expected products *syn*- or *anti*-**2-3d–f** have been obtained in 65-77% yield with retention of the configuration (up to d.r. = 96:4 and 6:94 respectively; entries 9-14). Other heteroatom electrophiles also can be used.[38] The reaction of *syn*-**2-1d** with chlorodiphenylphosphine, followed by protection with sulphur, gave the expected alkyl diphenylphosphine sulfide *syn*-**2-4d** in 70% yield with retention of the configuration (d.r. = 91:9, entry 15), while the same reaction of *anti*-**2-1d** afforded *anti*-**2-4d** in similar yield and stereoselectivity (76% yield, d.r. = 6:94).



anti-**2-5d** *anti*-**2-4d**

Figure 2-1. Structure of *anti*-**2-5d** and *anti*-**2-4d** confirmed by X-ray crystallographic analyses.

In order to determine the relative stereochemistry of the secondary alkyl iodides **1d–f** and the products **2-3d–f** and **2-4d**, X-ray crystallographic analyses were performed.[39] Thus, the

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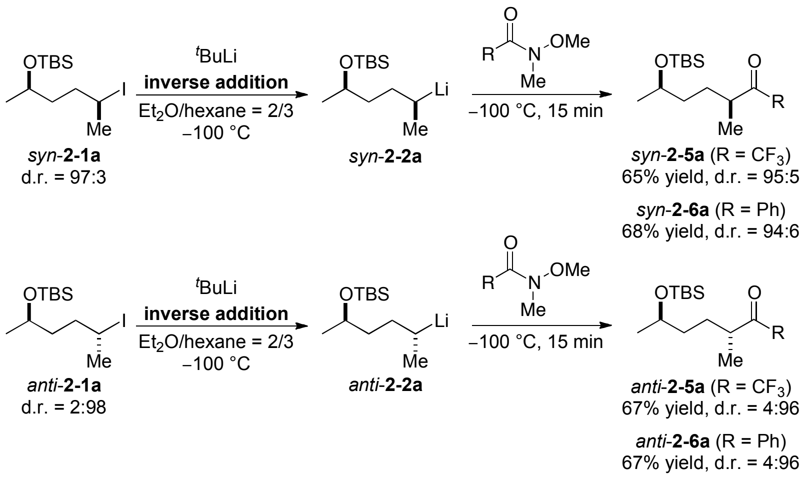
[38] The use of N- and O-centered electrophiles has not been successful at this point.

[39] CCDC/963930 (for *anti*-**2-4d**) and CCDC/963929 (for *anti*-**2-5d**) contain supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

quaternary ammonium tosylate *anti*-**2-5d** was prepared by the reaction of *anti*-**2-1d** with methyl tosylate in acetone. After recrystallization from chloroform, the relative stereochemistry of this salt was unambiguously determined by X-ray crystallographic analysis to be *anti*. Moreover, the *anti*-stereochemistry of the phosphorous compound *anti*-**2-4d** was also confirmed by X-ray crystallographic analysis, thus verifying the overall retention of the configuration for the I/Li exchange and quenching sequence.



Scheme 2-2. Stereoselective preparation of *syn*- and *anti*-acyclic ketone derivatives **2-5a** and **2-6a**.

The stereoselective formation of carbon-carbon bonds using these acyclic secondary alkyllithiums was successfully investigated (Scheme 2-2 and Table 2-2). Remarkably, the reaction of alkyllithiums *syn*- and *anti*-**2-1a** with Weinreb amides[40] (R = CF_3 or R = Ph) led to expected α-chiral trifluoromethyl ketone[41] **2-5a** and phenyl ketone **2-6a** in 65-68% yield with almost complete retention of the configuration[15l] (up to d.r. = 4:96 and 95:5; Scheme 2-2). Diastereoselective formylation[15af], carboxylation[15c,15n,36d] and amidation[15p,22] were also readily achieved by treating lithium reagents **2-2a, 2-2e–f** with DMF, CO_2 and PhNCO respectively (Table 2-2, entries 1-6).

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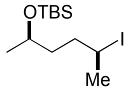
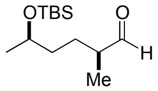
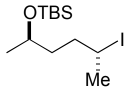
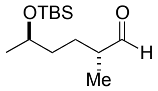
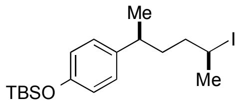
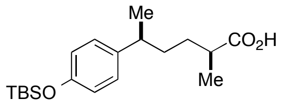
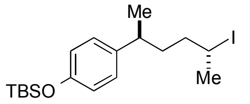
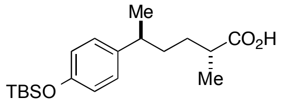
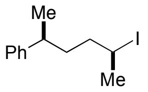
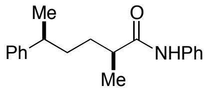
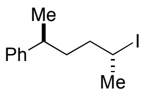
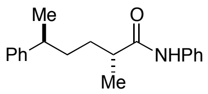
[40] a) S. Balasubramanian, I. S. Aidhen, *Synthesis* **2008**, 3707; b) V. Malathong, S. D. Rychnovsky, *Org. Lett.* **2009**, *11*, 4220.

[41] a) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.*, **2008**, *37*, 320; b) M. Tredwell, V. Gouverneur, *Angew. Chem. Int. Ed.* **2012**, 51, 11426.

Table 2-2. Stereoselective formylation, carboxylation and amidation of secondary alkyllithiums.

Entry	Substrate	Electrophile	Product	Yield[a], d.r.[b]
1	 *syn*-**2-1a** (d.r. = 97:3)	DMF	 *syn*-**2-7a**	70% 91:9
2	 *anti*-**2-1a** (d.r. = 2:98)	DMF	 *anti*-**2-7a**	80% 8:92
3	 *syn*-**2-1e** (d.r. = 98:2)	CO_2	 *syn*-**2-4e**	77% 95:5
4	 *anti*-**2-1e** (d.r. = 2:98)	CO_2	 *anti*-**2-4e**	79% 6:94
5	 *syn*-**2-1f** (d.r. = 92:8)	PhNCO	 *syn*-**2-4f**	80% 92:8
6	 *anti*-**2-1f** (d.r. = 2:98)	PhNCO	 *anti*-**2-4f**	73% 4:96

[a] Isolated yield. [b] d.r. (*syn*:*anti*) was determined by ^{13}C NMR spectroscopy.

2.3 Kinetic study

Recently, we have shown that *cis*-4-*tert*-butylcyclohexyllithium reagent *cis*-(*ax*)-**2-8** epimerizes very rapidly at –100 °C (Scheme 2-3a).[22] Now, we have examined the epimerization kinetics of the lithium compounds *syn*-**2-2a** and *anti*-**2-2a** under standard conditions at –100 °C (●, ♦) and –90 °C (▲, ■) as shown in Scheme 2-3b by retentive quenching with Me_2S_2 after different times. The plot of the epimerization percentage for *syn*-**2-2a** versus time resulted in mono-exponential decays, showing that the epimerizations proceed via first-order reversible reactions. The rate constants for the epimerization of *syn*-**2-2a** and *anti*-**2-2a** at –90 °C (■) were calculated from Equation (1).[42] The slopes of the resulting straight lines provided the value of (k_1 + k_{-1}) and the individual rate constants k_1 and k_{-1} were readily determined from the equilibrium concentrations at t = 7 h, when the equilibrium *syn*:*anti* = 40:60 was reached ($k_{-1}/k_1 = 1.5$). We found that at –90 °C the rate

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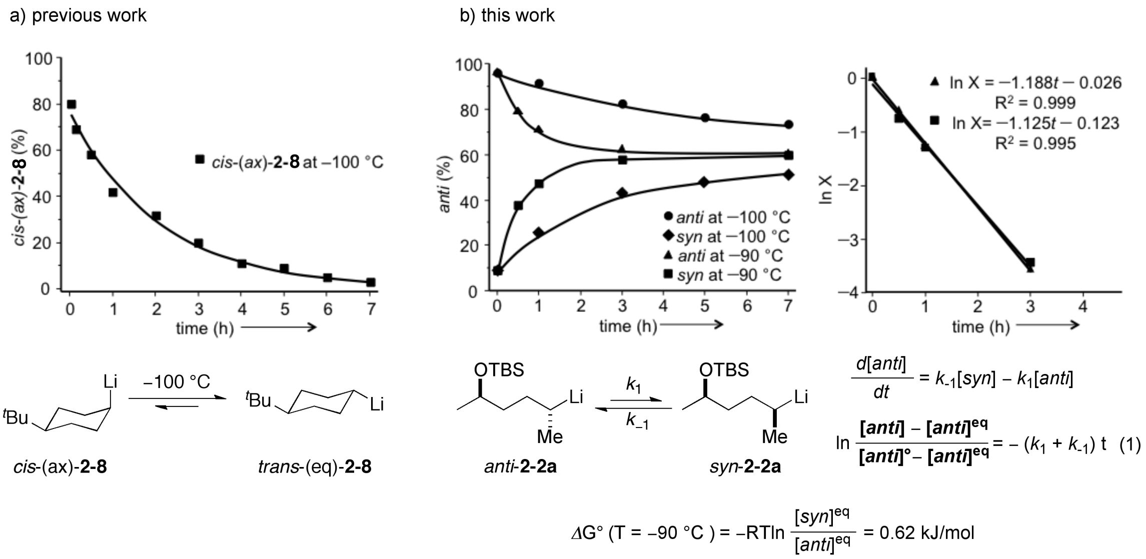
[42] K. A. Connors, *Chemical Kinetics: The Study of Reaction Rates in Solution*, Wiley-VCH, Weinheim, **2010**.

constants k_1 and k_{-1} of epimerization of *syn*-**2-2a** and *anti*-**2-2a** were equal to 1.28×10^{-4} s^{-1} and 1.92×10^{-4} s^{-1} respectively. The Gibbs free energy ΔG° (0.62 kJ/mol at –90 °C) indicated that *syn*-**2-2a** and *anti*-**2-2a** have almost the same configurational stability.[22] Interestingly, epimerization of *syn*-**2-2a** at –100 °C was much slower than in the case of *cis*-(*ax*)-**2-8** (1,3-diaxial interactions may destabilize this lithium reagent),[22] explaining the higher configurational stability of these acyclic secondary alkyllithium reagents. In the case of *syn*-**2-2a**, even after 1 h at –100 °C, the *syn*:*anti* ratio was still remaining high (8:92), confirming the experimental observation that the iodides **2-1a–f** can be added dropwise within 10 min to the solution of ^{t}BuLi without any significant loss of diastereoselectivity.



Scheme 2-3. Kinetic investigation of the equilibration between *syn*- and *anti*-**2-2a** and determination of the Gibbs free energy ΔG° of this equilibrium.

2.4 Summary

In summary, we have developed the first practical preparation of stereodefined acyclic secondary alkyllithium reagents with a functional group in a remote position from their corresponding secondary alkyl iodides. Some functionalities were tolerated during this I/Li exchange reaction, and the corresponding lithium derivatives were quenched with a range of electrophiles. In particular, several classes of carbon electrophiles have been successfully used, thus allowing the access to various carbonyl compounds, carboxylic acids and amides bearing a stereocenter in α-position with excellent diastereoselectivities and overall retention of the configuration. This methodology opens new possibilities for construction of chiral open-chain molecules. Thus, new chiral synthons[43] are now available to form new carbon-carbon bonds with high stereoselectivities since the required optically pure starting secondary alkyl iodides can be prepared from the corresponding chiral alcohols.[44]

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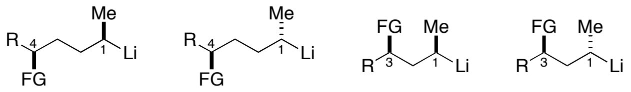
[43] D. Seebach, *Angew. Chem. Int. Ed.* **1979**, *18*, 239.

[44] K. Burgess, L. D. Jennings, *J. Am. Chem. Soc.* **1991**, *113,* 6129.

3 Stereoconvergent Preparation of Open-Chain Secondary Alkyllithiums Functionalized at the 3-Position

3.1 Introduction

Organolithium reagents occupy a central position in organic synthesis.[13] Their exceptionally high reactivity combined with the availability of a range of practical preparations has led to an increasing use of these organometallics in organic synthesis.[14] However, despite several reports,[45] the stereoselective preparation of non-heteroatom stabilized secondary alkyllithiums has been a difficult task.[15,16,17] Recently, we have shown that an I/Li exchange can be used for preparing stereoselectively various substituted cyclohexyllithiums[22] as well as acyclic secondary alkyllithiums bearing a functional group (FG = OTBS, Ph) at a remote position.[30] This study demonstrated the high synthetic potential of functionalized secondary alkyllithiums of type **3-1** and led us to investigate the stereoselective synthesis of 3-functionalized secondary alkyllithiums of type **3-2** (Figure 3-1).



syn-**3-1** *anti*-**3-1** *syn*-**3-2** *anti*-**3-2**

Figure 3-1. 1,4- and 1,3-fuctionalized secondary alkyllithium reagents.

We anticipated that the close proximity of the functional group (FG = OTBS, Ph) to the carbon-lithium bond might influence the preparation of those secondary lithium reagents. Herein, we report a stereoselective synthesis of various secondary alkyllithium reagents of type **3-2**. We demonstrate the importance of the nature of the protecting groups on the stereoconvergence occurring during the I/Li exchange and show that these lithium reagents react with retention of the configuration with various electrophiles including carbon electrophiles.

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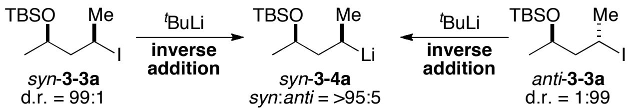
[45] a) *Stereochemical Aspects of Organolithium Compounds*. (Eds. R. E. Gawley, J. S. Siegel), VHCA; Zürich, **2010**; b) R. L. Letsinger, *J. Am. Chem. Soc.* **1950**, *72*, 4842; b) R. W. Hoffmann, M. Bewersdorf, M. Krüger, W. Mikolaiski, R. Stürmer, *Chem. Ber.* **1991**, *124*, 1243; c) H. J. Reich, M. A. Medina, M. D. Bowe, *J. Am. Chem. Soc.* **1992**, *114*, 11003; d) R. W. Hoffmann, K. Brumm, M. Bewersdorf, W. Mikolaiski, A. Kusche. *Chem. Ber.* **1992**, *125*, 2741; e) S. Yamato, G. Yamamura, M. Komatsu, M. Arai, T. Fukuyama, I. Ryu, *Org. Lett.* **2005**, *7*, 2489.

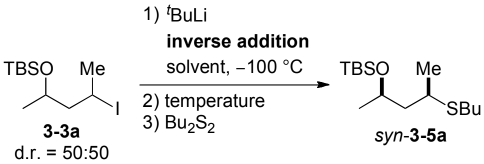
3.2 Results

As preliminary results, we found that the addition (**inverse addition**: **3-3a** was added to ^{t}BuLi)[19] of *syn*-alkyl iodide *syn*-**3-3a** to ^{t}BuLi (2.5 equiv, –100 °C to –50 °C, Et_2O/hexane = 1/3) led to the *syn*-lithium species *syn*-**3-4a** with a diastereoselectivity of ca. 95:5 as determined by subsequent quenching with Bu_2S_2.[22] Interestingly, the *anti*-iodide *anti*-**3-3a** also yielded the *syn*-lithium species *syn*-**3-4a** with the same diastereoselectivity by this procedure. This stereoconvergence implies that stereocontrol of the C-I bond is not required. Thus we have used a mixture of *syn*- and *anti*-**3-3a** in all further experiments (Scheme 3-1).



Scheme 3-1. Diastereoconvergent preparation of a secondary alkyllithium reagents *syn*-**3-4a** from **3-3a**.

Table 3-1. Effects of solvent ratio and temperature on stereoconvergent generation of 3-alkoxyalkyllithiums.



Entry	Solvents	Temperature	Yield	d.r.[a]
1	Et_2O only	−100 °C	35% (GC)	86:14
2	Et_2O/hexane = 2/3	−100 °C	42% (GC)	90:10
3	Et_2O/hexane = 1/3	−100 °C	60% (GC)	87:13
4	Et_2O/hexane = 1/3	−100 °C to −50 °C	73% (isolated)	93:7
5	Et_2O/hexane = 1/3	−100 °C to 0 °C	decomposition	-
6	hexane only	−100 °C	no reaction	-
7	THF only	−100 °C	0% (GC)	-

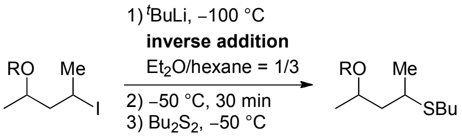
[a] d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis.

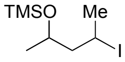
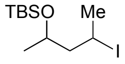
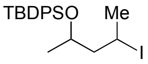
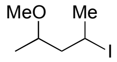
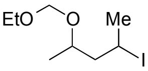
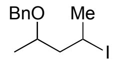
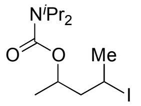
For further optimization, reaction conditions were examined in detail (Table 3-1). The highest yield was obtained in Et_2O/hexane = 1/3 mixture at −100 °C (entries 1-3). Further improvement of both yield and diastereoselectivity was observed when the temperature was increased to −50 °C after the generation of the alkyllithium reagents and the reaction mixture was stirred at this temperature for additional 30 min, followed by quenching the reaction with an electrophile (Bu_2S_2) at −50 °C. If the reaction mixture was warmed up to 0 °C, *retro*-[1,4]-

Brook rearrangement products were observed instead of the desired product (entry 5). We also found an I/Li exchange definitely needs some amount of Et_2O (entries 6, 7).[46]

We have next prepared various secondary alkyl iodides bearing a protected hydroxyl group in position 3 and examined the effect of protecting groups. (Table 3-2)

Table 3-2. Effects of the protecting groups of the hydroxyl groups on stereoconvergence.



Entry		Substrates	Product	Yield[a]	d.r.[b]
1		*syn*-**3-3b** (d.r. = 99:1)	**3-6a**	64%	85:15
		anti-**3-3b** (d.r. = 1:99)		63%	84:16
2		*syn*-**3-3a** (d.r. = 99:1)	**3-5a**	75%	92:8
		anti-**3-3a** (d.r. = 1:99)		73%	92:8
3		*syn*-**3-3c** (d.r. = 99:1)	-	trace	-
		anti-**3-3c** (d.r. = 1:99)		trace	-
4		*syn*-**3-3d** (d.r. = 99:1)	**3-7a**	77%	56:44
		anti-**3-3d** (d.r. = 1:99)		65%	52:48
5		*syn*-**3-3e** (d.r. = 99:1)	**3-8a**	61%	64:36
		anti-**3-3e** (d.r. = 1:99)		61%	64:36
6		*syn*-**3-3f** (d.r. = 99:1)	**3-9a**	56%	66:34
		anti-**3-3f** (d.r. = 1:99)		56%	66:34
7		*syn*-**3-3g** (d.r. = 99:1)	-	trace	-
		anti-**3-3g** (d.r. = 1:99)		trace	-

[a] Isolated yield. [b] d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis.

Alkyl iodide with TMS protected alcohol *syn*-**3-3b** was converted to the desired product **3-6a** in d.r. (*syn*:*anti*) = 85:15 after trapping with Bu_2S_2. The other diastereomer *anti*-**3-3b** was also transformed to the same product **3-6a** (d.r. = 84:16; entry 1). Interestingly, this diastereoselectivity was improved with TBS protected alcohol (d.r. = 92:8; entry 2). However, bulkier TBDPS group disturbed the reaction and almost no product was observed (entry 3). With other protecting groups besides silyl protected groups, generated alkyllithium reagents

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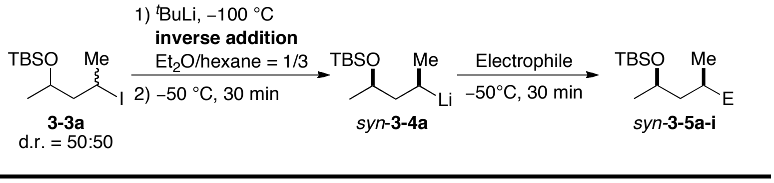
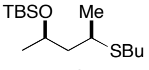
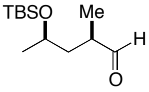
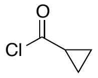
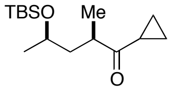
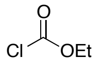
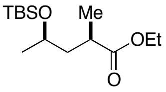
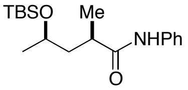
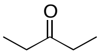
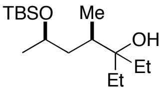
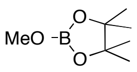
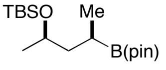
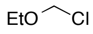
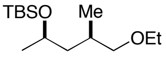
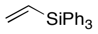
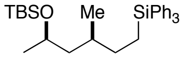
[46] The addition of additives (TMEDA, PMDTA and THF) resulted in dominant hydrolysis reaction.

was converted to 1:1 to 1:2 mixture of the diastereomers, judged by trapping with Bu_2S_2 (entry 4–6). Moreover, a bulky carbamate group also interrupted the reaction (entry 7). In fact, proper bulkiness on silyl protecting group was necessary for this stereoconvergent formation of the secondary alkyllithium reagents.

Table 3-3. Stereoconvergent I/Li exchange on 3-silyloxy substituted secondary alkyl iodide **3-3a**.



Entry	Electrophile	Product	Yield[a]	d.r.[b]
1	Bu_2S_2	 *syn*-**3-5a**	75%	93:7
2	DMF	 *syn*-**3-5b**	74%	92:8
3		 *syn*-**3-5c**	67%	96:4
4		 *syn*-**3-5d**	70%[c]	97:3
5	Ph−N=C=O	 *syn*-**3-5e**	69%[d]	96:4
6		 *syn*-**3-5f**	55%	99:1
7		 *syn*-**3-5g**	73%	97:3
8		 *syn*-**3-5h**	60%[c]	99:1
9		 *syn*-**3-5i**	65%[c]	99:1

[a] Isolated yield. [b] d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis. [c] Gram-scale reaction. [d] Yield after deprotection with TBAF·$3H_2O$.

As mentioned above, the generation of the alkyllithium *syn*-**3-4a** from 1:1 = *syn*:*anti* mixture of **3-3a** and trapping with Bu_2S_2 led to the thioether *syn*-**3-5a** in 75% yield and d.r. = 93:7 (entry 1). Remarkably, a range of carbon electrophiles reacted successfully with the lithium reagent *syn*-**3-4a**. Quenching *syn*-**3-4a** with DMF[30], an acid chloride[47], ethyl chloroformate, or PhNCO[30] led to the expected carbonyl derivatives *syn*-**3-5b–e** in 67-74% yield and *syn*:*anti* ratios up to 97:3 (entries 2–5). Moreover, diethyl ketone reacted with *syn*-**3-4a** to provide the tertiary alcohol *syn*-**3-5f** in 55% yield and d.r. = 99:1 (entry 6).[48] Trapping of *syn*-**3-4a** with methoxy boronic acid pinacol ester led to the boronic acid pinacol ester *syn*-**3-5g** in 73% yield (d.r. = 97:3; entry 7).[49] Alkylation of *syn*-**3-4a** with ethoxy methyl chloride furnished the ether *syn*-**3-5h** in 60% yield (d.r. = 99:1; entry 8).[50] Finally, *syn*-**3-4a** underwent a carbolithiation-reaction with triphenylvinylsilane to form the silane *syn*-**3-5i** in 65% yield and d.r. = 99:1 (entry 9).[51] In addition, the scale-up to gram-scale of our procedure is straightforward (entries 4, 8, 9).

In order to evaluate the substrate scope, we have prepared various 3-siloxy substituted secondary alkyl iodides (Table 3-4). First, we have replaced the 3-methyl substituent in **3-3a** by a propyl (**3-3g**) or a phenethyl group (**3-3h**). In both cases, the same high stereoconvergence was observed and quenching reactions with electrophiles such as Bu_2S_2, DMF, MeOB(pin) or $ClCO_2Et$ gave **3-10a–c** and **3-11a–c** in 58-69% yield and d.r. ≥ 91:9 (entries 1–6). The 3-methyl group was also replaced by an alkynyl (**3-3i**) or alkenyl group (**3-3j**) to produce the expected *syn*-products **3-12a–b** and **3-13a–c** in 57–77% yield and diastereoselectivities up to 99:1 (entries 7–11). Finally, we have also prepared the secondary alkyl iodide **3-3k** bearing two OTBS groups, which may be relevant for the construction of carbon-chains of natural products with 1,3-functionality.[52] The corresponding lithium reagent reacted with Bu_2S_2 or $ClCO_2Et$ in 69–71% yield and d.r. ≥ 91:9 (entries 12–13). In all these examples (Table 3-3, 3-4) the products were obtained in high diastereoselectivity, showing that the nature of the substituents has strongly favored the lithium reagent *syn*-**3-4**. The last two substrates **3-3l–m** show that replacement of 1-methyl substituent in **3-3a** by an ethyl

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[47] I. Hoppe, M. Marsch, K. Harms, G. Boche, D. Hoppe, *Angew. Chem. Int. Ed.* **1995**, *34*, 2158.

[48] a) D. M. Hodgson, P. G. Humphreys, J. G. Ward, *Org. Lett.* **2005**, *7*, 1153; b) J. Huang, S. P. Moore, P. O'Brian, A. C. Whitwood, J. Gilday, *Org. Biomol. Chem.* **2009**, *7*, 335; c) T. Boultwood, J. A. Bull. *Org. Lett.* **2014**, *16,* 2740.

[49] E. Vedrenne, O. A. Wallner, M. Vitale, F. Schmidt, V. K. Aggarwal, *Org. Lett.* **2009**, *11*, 165.

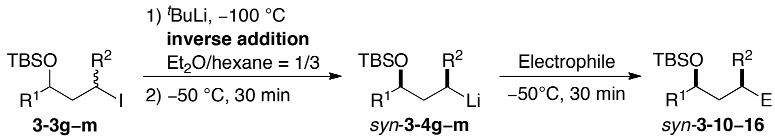
[50] N. Sheikh, D. Leonori, G. Barker, J. D. Firth, K. R. Campos, A. J. H. M. Meijer, P. O'Brien, I. Coldham, *J. Am. Chem. Soc.* **2012**, *134*, 5300.

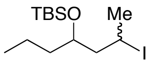
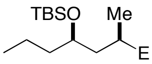
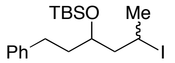
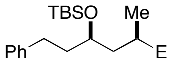
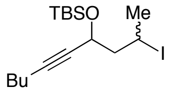
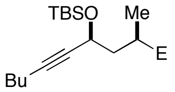
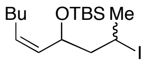
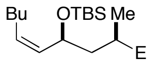
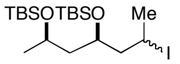
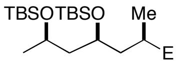
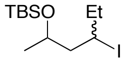
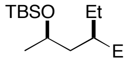
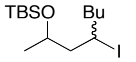
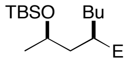
[51] a) L. F. Cason, H. G. Brooks, *J. Am. Chem. Soc,* **1952**, *74*, 4582; b) L. F. Cason, H. G. Brooks, *J. Org. Chem.* **1954**, *19*, 1278.

[52] T. Iwai, T. Kubota, J. Kobayashi, *J. Nat. Prod.* **2014**, *77*, 1541.

(**3-3l**) or butyl group (**3-3m**) led to lower diastereoselectivities (86:14, compared to 93:7 for **3-5a**).

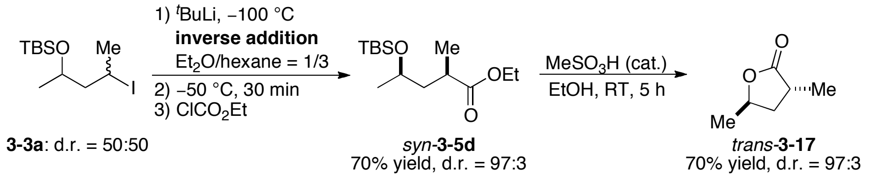
Table 3-3. Stereoconvergent I/Li exchange on 3-silyloxy substituted secondary alkyl iodides **3-3g**–**m**.



Entry	Substrate	Product	Yield[a]	d.r.[b]
1	 **3-3g** (d.r. = 66:34)	 *syn*-**3-10a** E = SBu	58%	94:6
2		*syn*-**3-10b** E = CHO	61%	91:9
3		*syn*-**3-10c** E = B(pin)	65%	97:3
4	 **3-3h** (d.r. = 62:38)	 *syn*-**3-11a** E = SBu	62%	93:7
5		*syn*-**3-11b** E = CO_2Et	64%	93:7
6		*syn*-**3-11c** E = B(pin)	69%	97:3
7	 **3-3i** (d.r. = 50:50)	 *syn*-**3-12a** E = SBu	58%	90:10
8		*syn*-**3-12b** E = CO_2Et	57%	98:2
9	 **3-3j** (d.r. = 50:50)	 *syn*-**3-13a** E = SBu	67%	95:5
10		*syn*-**3-13b** E = CO_2Et	77%	97:3
11		*syn*-**3-13c** E = B(pin)	60%	99:1
12	 **3-3k** (d.r. = 63:37)	 *syn*-**3-14a** E = SBu	69%	91:9
13		*syn*-**3-14b** E = CO_2Et	71%	96:4
14	 **3-3l** (d.r. = 50:50)	 *syn*-**3-15a** E = SBu	65%	86:14
15	 **3-3m** (d.r. = 50:50)	 *syn*-**3-16a** E = SBu	63%	86:14

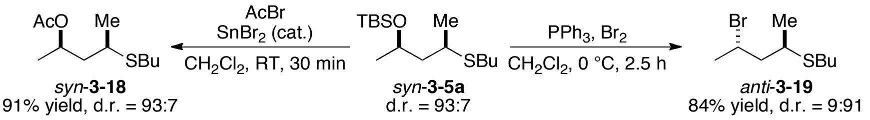
[a] Isolated yield. [b] d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis.

We have applied this method for the stereoselective synthesis of the disubstituted butyrolactone *trans*-**3-17**.[53] Thus, treatment of *syn*-**3-5d** with $MeSO_3H$ (10 mol%) produced the *trans*-lactone *trans*-**3-17** in 70% yield (d.r. = 97:3).

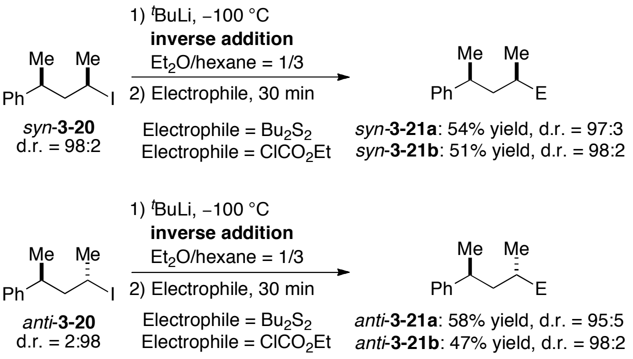


Scheme 3-2. Stereoselective synthesis of trans-2,4-dimethylbutyrolactone *trans*-**3-17**.

Further transformation of OTBS group to other functional groups was also examined (Scheme 3-3). Thus, treatment of *syn*-**3-5a** with acetyl bromide in the presence of $SnBr_2$ gave directly the corresponding acetate *syn*-**3-18** without loss of diastereoselectivity (91% yield, d.r. = 93:7). Reaction of *syn*-**3-5a** with triphenylphosphine and bromine led to the corresponding secondary alkylbromide *anti*-**3-19** with inversion of the configuration (84% yield, d.r. = 9:91).



Scheme 3-3. Transformation of OTBS group to other functional groups.



Scheme 3-4. Stereoselective I/Li exchange on 3-phenyl substituted secondary alkyl iodides *syn*- and *anti*-**3-20**.

Having established that 3-siloxy-substituted alkyl iodides underwent a stereoconvergent conversion to the corresponding alkyllithium reagents, we have also examined the lithiation of the 3-phenyl substituted iodide **3-20**. Therefore, both *syn*- and *anti*-**3-20** were treated with ^{t}BuLi at –100 °C in Et_2O/hexane = 1/3. At this low temperature little epimerization of C–Li

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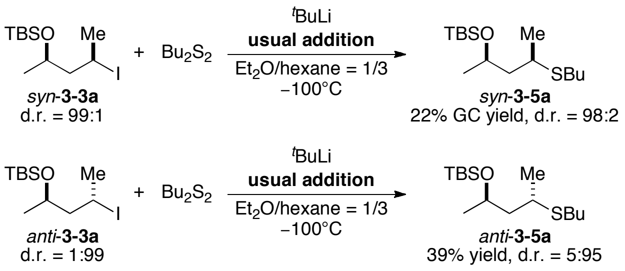
[53] S. Wada, A. Iida, R. Tanaka, *J. Nat. Prod.* **2002**, *65*, 1657.

bond was observed, and quenching with either Bu_2S_2 or $ClCO_2Et$ gave *syn*- and *anti*-**3-21a–b** in 47–58% yield with retention of the configuration (Scheme 3-3). This result contrasts the behavior of 3-siloxy substituted alkyllithium reagents.

3.3 Mechanistic consideration

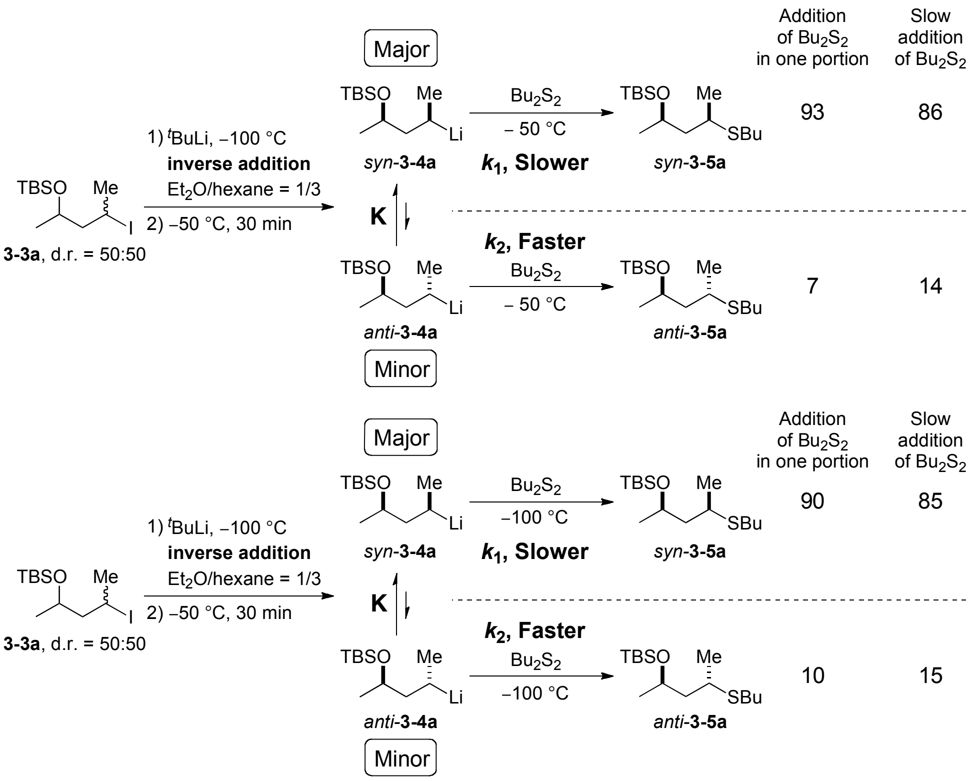
We carried out mechanistic studies to get insight on this stereoconvergence. We tried first *in-situ* trapping reactions[16b] of secondary alkyllithium reagents **3-4a** to ensure the retentive initial formation of these lithium reagents, followed by stereoconvergence to reach finally *syn*-**3-4a**. Thus, *syn*-**3-3a** and Bu_2S_2 were premixed and ^{t}BuLi (5 equiv) was added to this mixture at −100 °C to obtain *syn*-**3-5a** in d.r. = 98:2. On the other hand, *in-situ* trapping reaction with *anti*-**3-3a** led to *anti*-**3-5a**, which was the opposite result to the usual sequence of an I/Li exchange with inverse addition method and trapping with electrophiles. It means alkyllithium reagents were generated with retention of the configuration and then epimerized to the more thermodynamically favored diastereoisomer.[36h]



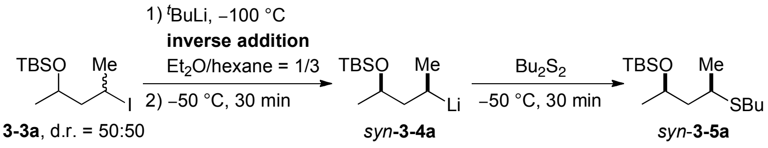
Scheme 3-5. *In-situ* trapping reactions with secondary alkyl iodides **3-3a**.

Slow addition of the electrophile was also tested to check the kinetic resolution effect during trapping reaction (Scheme 3-6). Thus, secondary alkyllithium reagents **3-4a** were generated from alkyl iodides **3-3a** and they were reacted with Bu_2S_2 with slow addition at −100 °C and −50 °C. At −50 °C slow addition of Bu_2S_2 resulted in lower diastereoselectivity of *syn*-**3-5a** (d.r. = 86:14) compared to the addition in one portion (d.r. = 93:7). Moreover, the ratio of product *syn*-**3-5a** provided with the addition in one portion at −100 °C got even lower (d.r. = 90:10). Having these results we can conclude that when the electrophile addition is very slow, the electrophile concentration is always low, and the following trapping reaction becomes slower than the equilibration between the alkyllithiums reagents *syn*-**3-4a** and *anti*-**3-4a**. Therefore, a *Curtin-Hammett* situation is obtained, and the ratio of the trapping products is determined by the ratio of the rate constants for the reaction of *syn*-**3-4a** and *anti*-**3-4a** with

Bu_2S_2 (k_1 and k_2) multiplied with the equilibrium constant K. The observed product ratio under these conditions (d.r. = 86:14) indicates that *anti*-**3-4a** is more reactive than *syn*-**3-4a**.[42]

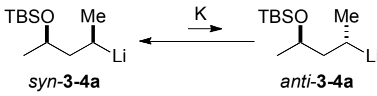


Scheme 3-6. The effect of the slow addition at −50 and −100 °C on the diastereoselectivity of the products.



Entry	Bu_2S_2	Yield[a]	d.r.[b]
1	2.0 equiv	75%	93:7
2	10.0 equiv	73%	95:5
3	20.0 equiv	70%	95:5

[a] GC yield. [b] d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis.



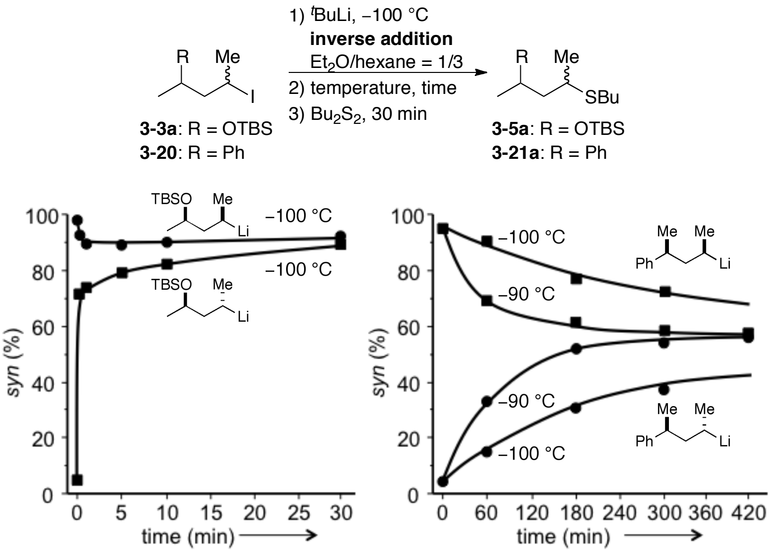
K: Equilibrium constant $K = \frac{[anti]^{eq}}{[syn]^{eq}} = 0.052$

$\Delta G° = -RT\ln K$ (Gibbs free energy) $\Delta G° = 5.5$ kJ/mol at −50 °C

Scheme 3-7. The effect of the concentration of the electrophile on the diastereoselectivity of the products.

When the electrophile is added in one portion, trapping of the alkyllithium reagents *syn*-**3-4a** and *anti*-**3-4a** appears to be faster than the equilibration of these alkyllithium reagents. As supported by the fact that an increase of the concentration of Bu_2S_2 has almost no effect on the product ratio, the observed product ratio obtained by using excess amount of Bu_2S_2 (d.r. = 95:5) is assumed to correspond to the equilibrium ratio of *anti*-**3-4a**/*syn*-**3-4a** allowing us to determine an equilibrium constant of $K = 0.052$, corresponding to $\Delta G^o = 5.5$ kJ/mol at –50 °C. Accidentally, this value is the same as the one obtained by the quantum chemical calculations shown later.

To obtain more information of the stereoconvergent generation of alkyllithium reagents *syn*-**3-4a**, we have studied the epimerization kinetics of the alkyllithium derivatives of *syn*- and *anti*-isomers of **3-3a** and **3-20** (Figure 3-3).[54,55] We found that the epimerization rates of the 3-siloxy substituted alkyllithium reagents are much greater than those of the 3-phenyl substituted alkyllithium reagents.[56]



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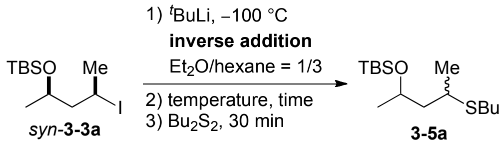
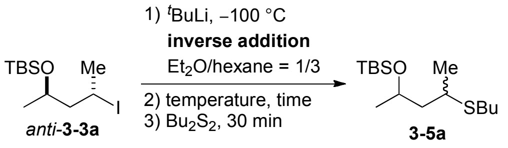
[54] Ligand assisted dynamic thermodynamic resolution of alkyllithiums: a) A. Basu, D. J. Gallagher, P. Beak, *J. Org. Chem.* **1996**, *61*, 5718; b) S. Nakamura, R. Nakagawa, Y. Watanabe, T. Toru, *J. Am. Chem. Soc.* **2000**, *122*, 11340; c) S. Nakamura, R. Nakagawa, Y. Watanabe, T. Toru, *Angew. Chem. Int. Ed.* **2000**, *39*, 353; d) J. A. Wilkinson, S. B. Rossington, S. Ducki, J. Leonard, N. Hussain, *Tetrahedron* **2006**, *62*, 1833; e) I. Coldham, S. Raimbault, D. T. E. Whittaker, P. T. Chovatia, D. Leonori, J. J. Patel, N. S. Sheikh, *Chem. Eur. J.* **2010**, *16*, 4082.

[55] Ligand assisted dynamic kinetic resolution of alkyllithiums: a) I. Coldham, J. J. Patel, G. Sanchez-Jimenez, *Chem. Commun.* **2005**, 3083; b) J. J. Gammon, V. H. Gessner, G. R. Barker, J. Granander, A. C. Whitwood, C. Strohmann, P. O'Brien, B. Kelly, *J. Am. Chem. Soc.* **2010**, *132*, 13922.

[56] The retentive generation of 3-siloxy-substituted alkyllithiums at the initial phase was confirmed by *in-situ* trapping. Furthermore, the thermodynamic ratio observed for lithium reagents **3-4a** at −100 °C in Figure 3-2 (ca. 90:10) is lower than the product ratios reported in Table 3-2. This may be a result of a kinetic resolution.

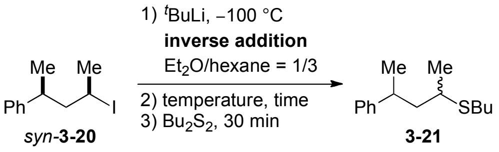


Time	Temperature	d.r. (*syn*:*anti*)
0 min	−100 °C	97.8:2.2
10 sec	−100 °C	92.7:7.3
1 min	−100 °C	88.9:11.1
5 min	−100 °C	91.1:8.9
10 min	−100 °C	91.2:8.8
30 min	−100 °C	92.4:7.6



Time	Temperature	d.r. (*syn*:*anti*)
0 min	−100 °C	5.5:94.5
10 sec	−100 °C	71.8:28.2
1 min	−100 °C	74.0:26.0
5 min	−100 °C	81.5:18.5
10 min	−100 °C	82.6:17.4
30 min	−100 °C	88.8:11.2

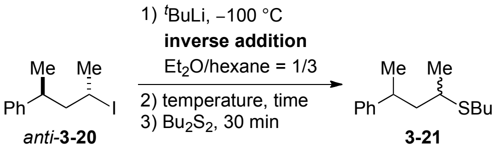
d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis



Time	Temperature	d.r. (*syn*:*anti*)
0 h	−100 °C	97.0:3.0
1 h	−100 °C	90.5:9.5
3 h	−100 °C	77.2:22.8
5 h	−100 °C	73.0:27.0

Time	Temperature	d.r. (*syn*:*anti*)
0 h	−90 °C	97.0:3.0
1 h	−90 °C	69.5:30.5
3 h	−90 °C	61.5:38.5
5 h	−90 °C	59.1:40.9
7 h	−90 °C	57.9:42.1

d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis



Time	Temperature	d.r. (*syn*:*anti*)
0 h	−100 °C	5.3:94.7
1 h	−100 °C	14.7:85.3
3 h	−100 °C	30.5:69.5
5 h	−100 °C	36.7:63.3

Time	Temperature	d.r. (*syn*:*anti*)
0 h	−90 °C	5.3:94.7
1 h	−90 °C	33.0:67.0
3 h	−90 °C	52.6:47.4
5 h	−90 °C	54.1:45.9
7 h	−90 °C	56.3:43.7

d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis

Figure 3-2. Kinetic studies of the epimerization of alkyllithiums generated from *syn*- and *anti*-**3-3a** and **3-20**.

As shown in the quantum chemically calculated[57] free energy diagram in Figure 3-3, the highly *syn*-selective transformations observed under equilibrating conditions at –100 °C for alkyllithium intermediate **3-4a** could be explained by assuming a higher stability of *syn*-**3-4a** compared to *anti*-**3-4a**.[16c,21] The relative free energies of these two species in their monomeric form complexed to one diethyl ether molecule have therefore been calculated at the MP2(FC)/6-311+G(2d,p)//B3LYP/6-31+G(d) level of theory. Solvent effects for hexane have been included through the single point calculations with the SMD/B3LYP/6-31+G(d) solvation model. In the energetically more favorable isomer *syn*-**3-4a** the lithium coordinates to the oxygen atom of the OTBS substituent to form a 5-membered ring system. In the most favorable conformation *syn*-**3-4a** (e,a), the methyl group at C1 position occupies an equatorial and the methyl group at C3 occupies an axial position. The latter orientation is the most effective way for the C3 methyl group to avoid a collision with the large TBS substituent. The inversion of the 5-membered ring through flipping leads to *syn*-**3-4a** (a,e) located 10.8 kJ/mol higher than *syn*-**3-4a** (e,a). The less favorable isomer *anti*-**3-4a** also exists in two major conformational families. The more stable *anti*-**3-4a** (a,a) is located 5.5 kJ/mol higher than *syn*-**3-4a** (e,a). The inversion of the 5-membered ring leads to the less stable *anti*-**3-4a** (e,e) conformer, in which the methyl substituent at C3 again occupies an equatorial position and thus causes some strain with the OTBS substituent. The free energy difference of 5.5 kJ/mol between *anti*-**3-4a** and *syn*-**3-4a** translates into an equilibrium ratio of 1:45 at 173.15 K.

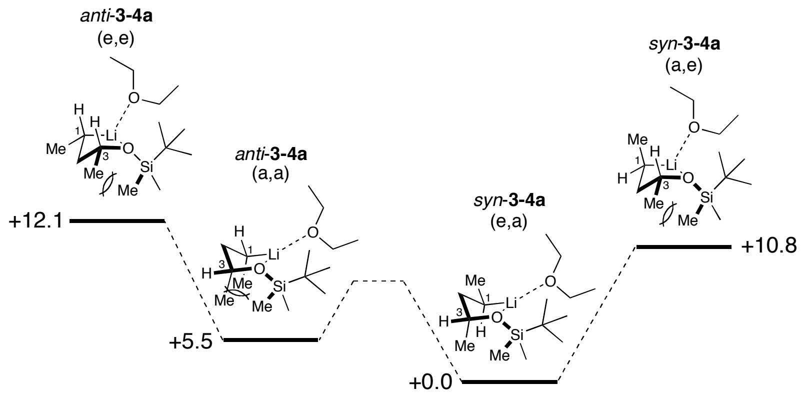


Figure 3-3. Relative free energies at −100 °C [ΔG_{173}, in kJ/mol] for *syn*- and *anti*-**3-4a** (complexed to one diethyl ether molecule)

Replacing the OTBS substituent in *syn*- and *anti*-**3-4a** by a phenyl group leads to organolithium species *syn*- and *anti*-**3-22** and the following trapping experiments have indicated a significant change in equilibration kinetics and stereochemical control, compared

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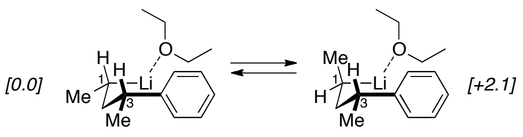
[57] See also Chapter 9 experimental section to obtain the detail information.

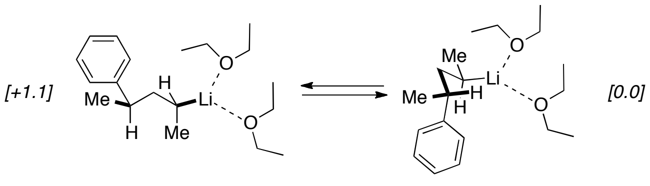
to **3-4a** (Figure 3-4). Calculations have again been performed for the monomeric organolithium compound complexed to one diethyl ether molecule. The more favorable stereoisomer is now *anti*-**3-22** (e,e) with respect to the two methyl substituents. This conformation implies that the phenyl substituent is again capable of interacting with the lithium atom as a complexation partner such as to form a 5-membered ring structure. The less favorable conformer of the *syn*-**3-22** (a,e) isomer is located only 2.1 kJ/mol higher in energy. The energy difference of 2.1 kJ/mol translates into a *anti*:*syn*-ratio of 4.3:1 at 173.15 K.



anti-**3-22** (e,e) *syn*-**3-22** (a,e)

Figure 3-4. Relative free energies at −100 °C [ΔG_{173}, in kJ/mol] for *syn*- and *anti*-**3-22** (complexed to one diethyl ether molecule)

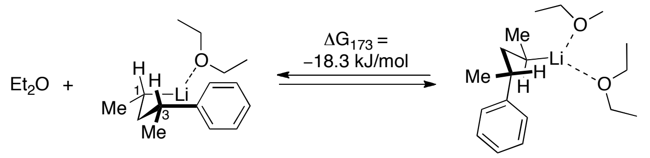
In contrast to the OTBS substituent in **3-4a**, the phenyl substituent in **3-22** interacts with the lithium atom much less efficiently, making the complexation of the lithium atom with a second diethyl ether solvent molecule as an energetically attractive alternative (Figure 3-5). Calculations for **3-22** have therefore been repeated with a second solvent molecule attached to the lithium atom. Conformational preferences in these *syn*- and *anti*-**3-22** isomers are distinctly different as complexation of the second solvent molecule leads to stabilization of acyclic conformers lacking direct contacts between the phenyl substituent and the lithium atom. The energy difference between the *syn*- and *anti*-isomers is now quite small and favors the *syn*-**3-22** isomer by 1.1 kJ/mol. This energy difference translates into a *anti*:*syn*-ratio of 1:2.1 at 173.15 K under equilibrating conditions.



anti-**3-22** (2Eth) *syn*-**3-22** (2Eth)

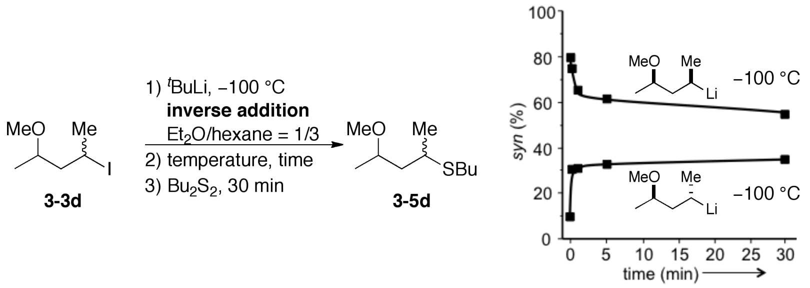
Figure 3-5. Relative free energies at –100 °C [ΔG_{173}, in kJ/mol] for *syn*- and *anti*-**3-22** (complexed to two diethyl ether molecules).

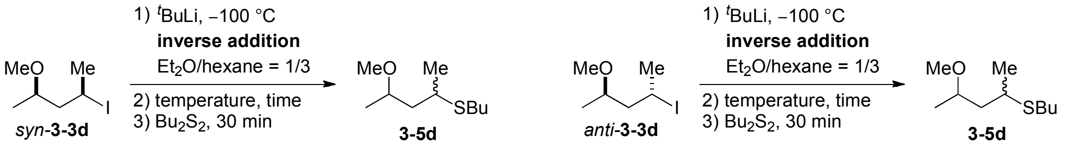
The free energies calculated for *anti*-**3-22** (Eth) and *syn*-**3-22** (e,e, 2Eth) as the most stable isomers of **3-22** coordinating one or two solvent molecules, respectively, allow a quantitative evaluation of the equilibrium between mono- and disolvated species (Figure 3-6). In the hexane solvent chosen here, the equilibrium is clearly on the side of the disolvated species *syn*-**3-22** (e,e, 2Eth) with a reaction free energy at 173.15 K of $\Delta G_{173} = -18.3$ kJ/mol. The loss of stereoselectivity observed under equilibrating conditions for **3-22** can thus most easily be rationalized by assuming the population of acyclic species with disolvated lithium, in which only minor energy differences exist between *syn*- and *anti*-stereoisomers.



anti-**3-22** (e,e) *syn*-**3-22** (e,e, 2Eth)

Figure 3-6. Equilibrium between the energetically most favorable mono- and disolvated isomers *anti*-**3-22** (e,e) and *syn*-**3-22** (e,e, 2Eth)





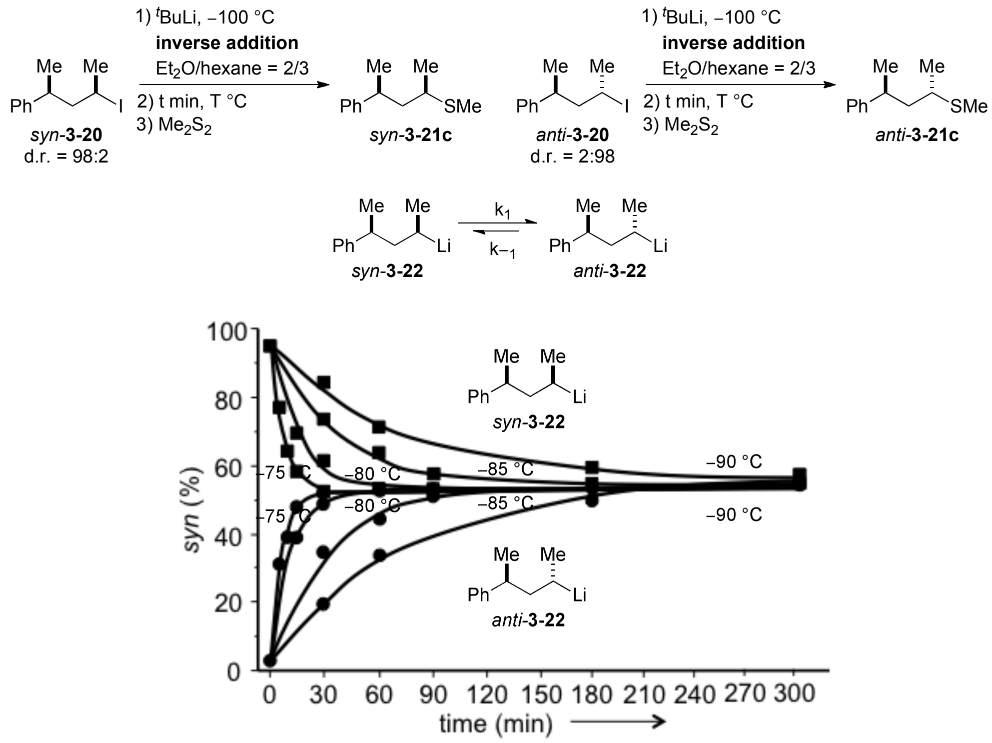
Time	Temperature	d.r. (*syn*:*anti*)
0 min	−100 °C	79.8:20.2
10 sec	−100 °C	75.2:24.8
1 min	−100 °C	65.5:34.5
5 min	−100 °C	61.5:38.5
30 min	−100 °C	56.3:43.7

Time	Temperature	d.r. (*syn*:*anti*)
0 min	−100 °C	9.7:90.3
10 sec	−100 °C	30.3:69.7
1 min	−100 °C	30.5:69.4
5 min	−100 °C	32.5:67.5
30 min	−100 °C	34.7:65.3

d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis

Figure 3-7. Kinetic studies of epimerization of alkyllithiums generated from *syn*- and *anti*-**3-3d**.

In addition, kinetic studies on 3-methoxy substituted alkyllithium reagent were also performed (Figure 3-7). Although the final thermodynamically stable ratio is around 1:1, the initial dramatic change of the diastereoselectivity was still observed and it may be caused by the coordination effect of oxygen atom to the lithium center.



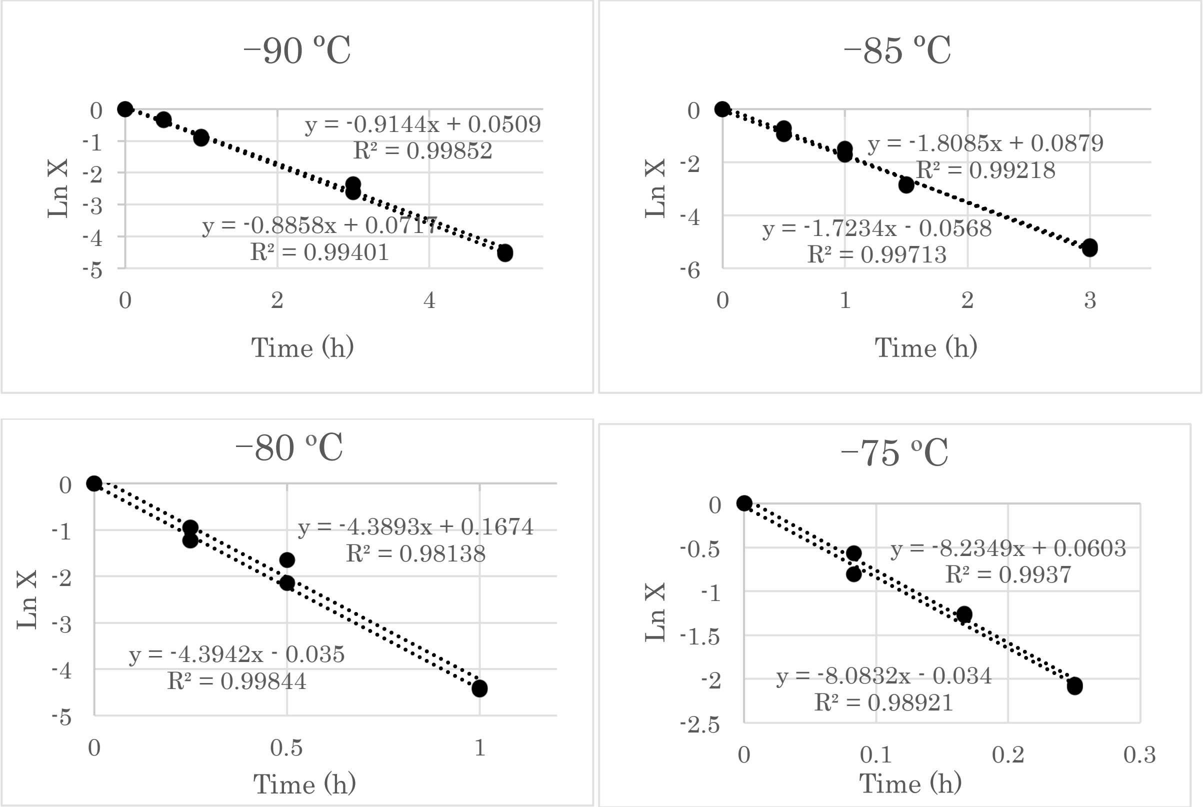
syn%	−90 °C		−85 °C		−80 °C		−75 °C	
min	from *syn*	from *anti*	from *syn*	from *anti*	from *syn*	from *anti*	from *syn*	from *anti*
0	94.9	3.1	94.9	3.1	94.9	3.1	94.9	3.1
5							76.9	31.0
10							65.2	39.3
15					69.8	39.2	58.6	47.1
30	84.3	18.9	74.5	34.7	61.9	48.2	53.4	53.2
60	71.7	34.1	64.0	45.8	54.6	53.5		
90			57.4	52.1	54.2	54.0		
180	59.4	51.5	55.4	54.9				
300	57.0	56.0	55.2	55.2				
420	56.7	56.5						

d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis

Figure 3-8. Kinetic studies of epimerization of alkyllithiums **3-22**, generated from **3-20**.

In order to discuss the general mechanism of epimerization of unstabilized secondary alkyllithium reagents, the kinetic study on alkyllithium reagents **3-22** was also examined in detail.

$$K_{eq} = \frac{[anti]^{eq}}{[syn]^{eq}} \qquad \frac{d[syn]}{dt} = k_{-1}[anti] - k_1[syn] \Longrightarrow \ln \underbrace{\frac{[syn] - [syn]^{eq}}{[syn]^{\circ} - [syn]^{eq}}}_{X} = -(k_1 + k_{-1})\,t$$



		–90 °C	–85 °C	–80 °C	–75 °C
k_1	s^{-1}	1.09×10^{-4}	2.20×10^{-4}	5.60×10^{-4}	1.07×10^{-3}
k_{-1}	s^{-1}	1.42×10^{-4}	2.71×10^{-4}	6.60×10^{-4}	1.22×10^{-3}
1/T	K^{-1}	5.46×10^{-3}	5.31×10^{-3}	5.18×10^{-3}	5.05×10^{-3}
syn^{eq}		56.6%	55.2%	54.1%	53.2%
K_{eq}		0.767	0.812	0.848	0.880
$\ln(k_1/T)$		–14.3	–13.7	–12.8	–12.1

Figure 3-9. Rate constants for the epimerization of alkyllithiums **3-22**, generated from **3-20**.

Alkyllithium reagents **3-22** were prepared from the corresponding alkyl iodides **3-20** with inverse addition at –100 °C in solvent mixture (Et_2O/hexane = 2/3) and the plot of the epimerization percentage for *syn*-**3-22** versus time at different temperatures was recorded (Figure 3-8). In the same way as Figure 3-2, the decay of diastereoselectivity was mono-exponential, showing that the epimerizations proceed via first-order mechanism. Therefore, the first-order kinetics rate constants (k_1 and k_{-1}) can be calculated with these following equations (Figure 3-9). Additionally, the thermodynamic parameters also can be determined by these two equations with the values obtained in this kinetic study (Figure 3-10).

Thus, kinetic parameters of the epimerization process ΔH°, ΔS° and ΔG° can be calculated with Van't Hoff equation (ΔH° = 2.8 kJ/mol, ΔS° = 0.012 kJ/mol·K, ΔG° = 0.40 kJ/mol at –90 °C). These values indicate that the two diastereomers *syn*- and *anti*-**3-22** has small energy difference caused by their conformation stability. Moreover, kinetic parameters of the epimerization activation $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta G^{\ddagger}$ also can be calculated with Eyring plot ($\Delta H^{\ddagger}$ = 45.5 kJ/mol, $\Delta S^{\ddagger}$ = –0.070 kJ/mol·K, $\Delta G^{\ddagger}$ = 58.4 kJ/mol at –90 °C). The negative activation entropy suggests that ether solvent molecules are bound in the epimerization step, or more possible that cleavage of the carbon-lithium bond is connected with the formation of a large dipole resulting in electrostriction of the solvent molecules. Some examples are cited here (Figure 3-11).[17a,58] In fact, the ion pair solvation hypothesis (dissociation process in Figure 1-6) was proposed for the epimerization of alkyllithium reagents with similar kinetic parameters to *syn*- and *anti*-**3-22**.

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[58] a) H. Ahlbrecht, J. Harbach, R. W. Hoffmann, T. Ruhland, *Liebigs. Ann.* **1995**, 211; b) N. J. Ashweek, P. Brandt, I. Coldham, S. Dufour, R. E. Gawley, F. Hæffner, R. Klein, G. Sanchez-Jimenez, *J. Am. Chem. Soc.* **2005**, *127*, 449.

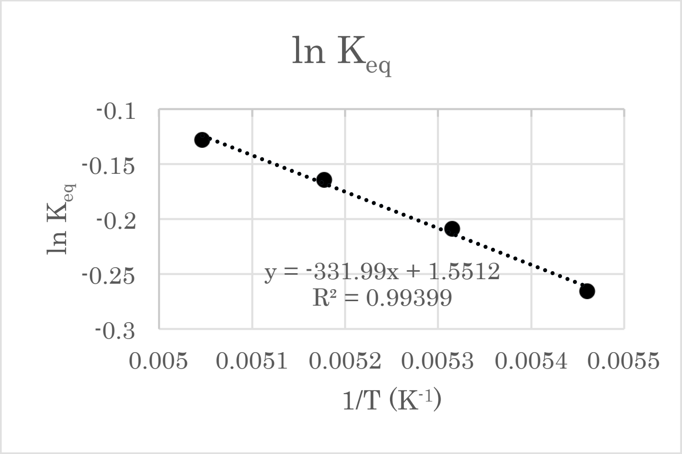
Van't Hoff equation

$$\ln K_{eq} = -\frac{\Delta H^{\circ}}{RT} + \frac{\Delta S^{\circ}}{R}$$

ΔH°: Free enthalpy change of the equilibrium
ΔS°: Free entropy change of the equilibrium

$\Delta H^{o} = 2.76$ kJ/mol (0.66 kcal/mol)

$\Delta S^{o} = 0.012$ kJ/mol·K
(0.0031 kcal/mol·K)



$$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$$

	–90 °C	–85 °C	–80 °C	–75 °C
ΔG° (kJ/mol)	0.40	0.33	0.27	0.20
(kcal/mol)	0.095	0.080	0.064	0.049

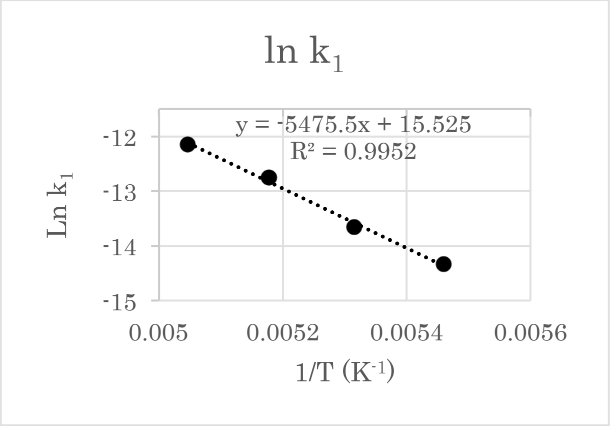
$$\Delta G^{\circ} = -RT\ln K_{eq}$$

	–90 °C	–85 °C	–80 °C	–75 °C
ΔG° (kJ/mol)	0.40	0.33	0.26	0.21
(kcal/mol)	0.096	0.078	0.063	0.050

Eyring plot

$$\ln \frac{k}{T} = -\frac{\Delta H^{\ddagger}}{RT} + \ln \frac{k_B}{h} + \frac{\Delta S^{\ddagger}}{R}$$

$\Delta H^{\ddagger}$: Enthalpy of activation, $\Delta S^{\ddagger}$: Entropy of activatior
k_B: Boltzmann constant, h: Planck's constant



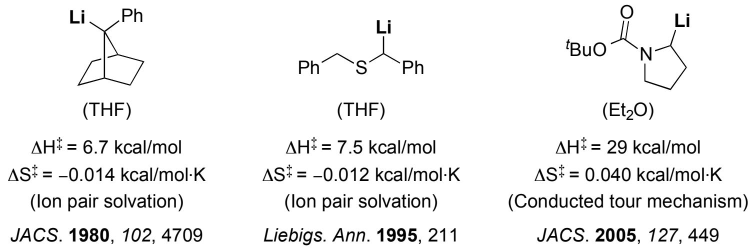
$\Delta H^{\ddagger} = 45.5$ kJ/mol (10.9 kcal/mol)

$\Delta S^{\ddagger} = -0.070$ kJ/mol·K
(–0.017 kcal/mol·K)

$$\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$$

	–90 °C	–85 °C	–80 °C	–75 °C
ΔG‡ (kJ/mol)	58.4	58.7	59.1	59.4
(kcal/mol)	13.9	14.0	14.1	14.2

Figure 3-10. Kinetic parameters of epimerization of alkyllithiums **3-22**, generated from **3-20**.

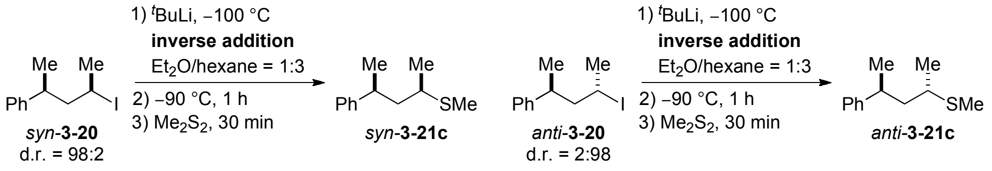


(THF)	(THF)	(Et_2O)
$\Delta H^{\ddagger}$ = 6.7 kcal/mol	$\Delta H^{\ddagger}$ = 7.5 kcal/mol	$\Delta H^{\ddagger}$ = 29 kcal/mol
$\Delta S^{\ddagger}$ = −0.014 kcal/mol·K	$\Delta S^{\ddagger}$ = −0.012 kcal/mol·K	$\Delta S^{\ddagger}$ = 0.040 kcal/mol·K
(Ion pair solvation)	(Ion pair solvation)	(Conducted tour mechanism)
JACS. **1980**, *102*, 4709	*Liebigs. Ann.* **1995**, 211	*JACS*. **2005**, *127*, 449

Figure 3-11. Kinetic parameters of epimerization of alkyllithium reagents in previous literature.

However, the state of aggregation of *syn*- and *anti*-**3-22** in solution has not been determined. Therefore, the effect of concentration on the epimerization rate was examined as a preliminary experiment to get insight about the aggregation state (Table 3-4). In the usual concentration (expected concentration of the desired alkyllithium reagents: 0.09–0.02 M), the epimerization rate was found to be constant but the epimerization speed became much slower in more diluted conditions (< 0.01 M) probably because the aggregation state of the key intermediate for this epimerization was affected in such highly dilute conditions.

Table 3-4. Concentration effect on the epimerization rate of 3-phenyl substituted secondary alkyllithium reagents.



Initial concentration of ^{t}BuLi	Expected concentration of the desired alkyllithiums[a]	d.r.[b]	Initial concentration of ^{t}BuLi	Expected concentration of the desired alkyllithiums[a]	d.r.[b]
0.38 M	0.086 M	72.1:27.9	0.38 M	0.078 M	33.5:66.5
0.19 M	0.052 M	71.7:28.3	0.19 M	0.045 M	34.1:65.8
0.096 M	0.024 M	72.3:27.7	0.096 M	0.024 M	30.6:69.4
0.038 M	0.0087 M	78.3:21.7	0.038 M	0.0087 M	26.4:73.6

[a] Determined by GC yield of the corresponding quenched product **3-21c**. [b] d.r. (*syn*:*anti*) was determined by capillary GC and NMR analysis

3.4 Summary

In summary, we have shown that 3-OTBS substituted alkyllithium reagents can be generated in a stereoconvergent way by an I/Li exchange and trapped by electrophiles with retention of the configuration. Such stereoconvergence was not observed for 3-phenyl substituted alkyllithiums, which were generated stereoselectively from diastereomeric alkyl iodide precursors, indicating that the OTBS group is essential for the stereoconvergence. Kinetic studies showed that epimerization is much faster for the 3-OTBS substituted alkyllithiums than for the corresponding 3-phenyl substituted analogues. This observation can be explained by the O-Li coordination, which increases the ionic character of the C-Li bond and thus facilitates the change of configuration at position 1. Furthermore, we investigate the general epimerization mechanism of unstabilized secondary alkyllithiums by the kinetic study with 3-phenyl substituted alkylithium reagents. Further computational investigations of this mechanistic consideration are still ongoing to obtain more insight.

4 Stereoretentive Preparation of Open-Chain Secondary Alkyllithiums Functionalized at the 2-Position

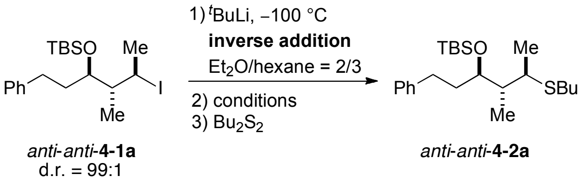
4.1 Introduction

We have established a stereoconvergent preparation of secondary alkyllithium reagents bearing a OTBS group at 3-position.[31] As challenging expansion of substrate scope we tried stereoselective generation of alkyllithium reagents with functional groups at both 2- and 3-positions. Usually proximity between substituents and lithium center was not recommended for halogen-lithium exchange and such stereoselective approach to alkyllithium reagents with substituents at 2-position have scarcely been investigated because elimination reaction may become more favored due to steric hindrance.

4.2 Results

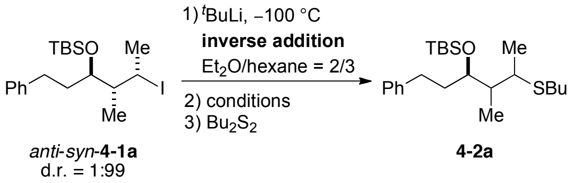
Stereodefined alkyl iodide *anti*-*anti*-**4-1a** was subjected to an I/Li exchange by inverse addition (Table 4-1). The resulting alkyllithium reagent was trapped with Bu_2S_2 under thermodynamic control (stirring for 30 min at −50°C before the addition of Bu_2S_2) to afford the *anti*-*anti*-**4-2a** in 50 % yield and d.r. (*anti*-*anti*:*anti*-*syn*) = 82:18. Similarly, the other diastereomer *anti*-*syn*-**4-1a** was also converted to the corresponding alkyllithium reagent and the thermodynamic controlled quenching with Bu_2S_2 formed the same mixture of *anti*-*anti*-**4-2a** (d.r. = 82:18). Thus, stereoconvergence to the more thermodynamically stable stereoisomer of alkyllithium reagent was still observed. On the other hand, the generation of the alkyllithium reagent from *anti*-*anti*-**4-1a** and subsequent trapping reaction with Bu_2S_2 under kinetic control (immediate quench after the generation of the alkyllithium species) led to *anti*-*anti*-**4-2a** in 50% yield and with excellent retention of the configuration. Moreover, the same procedure with *anti*-*syn*-**4-1a** provided *anti*-*syn*-**4-2a** in 53% yield and with retention of the configuration, which was quite different from the results obtained under thermodynamic control. Actually such a slower stereoconvergence in this case compared to alkyllithium reagent **3-4a** (stereoconvergence already proceeded in 10 sec; Figure 3-2) resulted from the presence of the methyl group at position 2 (Scheme 4-1). Since the steric repulsion between methyl groups at position 3 and on a silyl protecting group is important (Figure 3-3), *anti*-*anti* and *anti*-*syn*-**4-3a** can be assigned as *anti*-*anti*-**4-3a** (e,a,a) and *anti*-*syn*-**4-3a** (a,a,a) respectively. As shown in their possible structures both diastereomers have steric repulsion, leading to the smaller energy difference compared to that without a methyl group at position 2.

Table 4-1. I/Li exchange on alkyl liodides **4-1a** under thermodynamic and kinetic control.



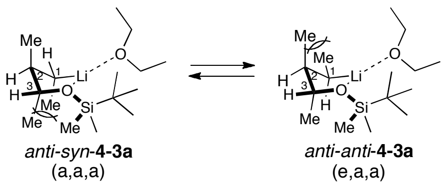
Conditions	Yield[a]	d.r.[b]
−50 °C, 30 min (thermodynamic control)	50%	82:18
−100 °C, 10 sec (kinetic control)	50%	98:2

[a] Isolated yield. [b] d.r. (*anti-anti*:*anti-syn*) was determined by capillary GC and NMR analysis.



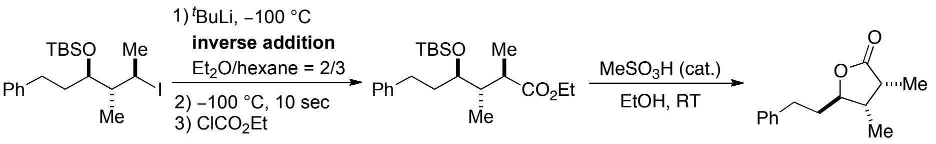
Conditions	Yield[a]	d.r.[b]
−50 °C, 30 min (thermodynamic control)	50%	82:18
−100 °C, 10 sec (kinetic control)	50%	3:97

[a] Isolated yield. [b] d.r. (*anti-anti*:*anti-syn*) was determined by capillary GC and NMR analysis.



Scheme 4-1. Possible structures of alkyllithium reagents **4-3a**.

We applied this method for the stereoselective synthesis of the trisubstituted butyrolactone *trans*-*cis*-**4-4**.[53] Thus, treatment of *anti*-*anti*-**4-2b** with MeSO$_3$H (10 mol%) produced the *trans*-*cis*-**4-4** in 90% yield and d.r. = 99:1 (Scheme 4-2).



anti-anti-**4-1a**
d.r. = 99:1

anti-anti-**4-2b**
57% yield, d.r. = 99:1

trans-cis-**4-4**
57% yield, d.r. = 99:1

Scheme 4-2. Stereoselective synthesis of trisubstitued lactone *trans-cis*-**4-4**.

More typical 1,2-fuctionalized alkyl iodides **4-1b** were also synthesized and subjected to an I/Li exchange (Table 4-3). Thus, alkyl iodide *anti*-**4-1b** (d.r. = 97:3) was treated with ^{t}BuLi with the inverse addition and the resulting alkyllithium reagent was trapped with Bu_2S_2 to provide the expected product *anti*-**4-5a** in 69% yield with retention of the configuration (d.r. = 97:3; entry 1). The other diastereomer *syn*-**4-1b** (d.r. = 2:98) also could be converted to the desired product *syn*-**4-5a** in 61% yield and d.r. = 4:96 (entry 3). However, this system may suffer more from steric hindrance. Thus, reaction with the Weinreb amide PhCON(OMe)Me led to a lower diastereoselectivity than **4-5a** especially in the case of the *syn*-diastereoisomer. (entries 2 and 4).

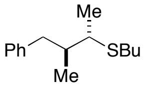
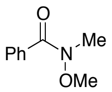
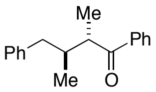
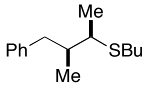
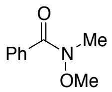
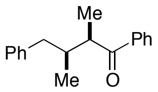
Table 4-3. Stereoselective preparations of *syn*- and *anti*-secondary alkyllithium from alkyl idodes **4-1b**.

anti-**4-1b**
d.r. = 97:3

anti-**4-5a–b**

syn-**4-1b**
d.r. = 97:3

syn-**4-5a–b**

Entry	Electrophile	Products	Yield[a]	d.r.[b]
1	Bu_2S_2	 *anti*-**4-5a**	69%	97:3
2		 *anti*-**4-5b**	57%	89:11
3	Bu_2S_2	 *syn*-**4-5a**	61%	4:96
4		 *syn*-**4-5b**	32%	31:69

[a] Isolated yield. [b] d.r. (*anti*:*syn*) was determined by ^{1}H and ^{13}C NMR spectroscopy.

Further extension of the reaction scope and mechanistic study are ongoing.[32]

5 Intramolecular Carbolithiation of Secondary Alkyllithiums Prepared by Stereoselective I/Li Exchange

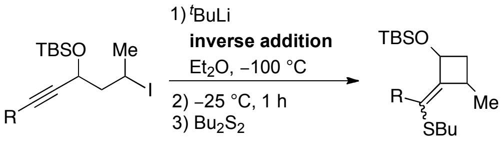
5.1 Introduction

Carbolithiation is a useful reaction of lithium reagents since it enables successive functionalizations of a double or a triple bond.[59] Especially intramolecular carbolithiation shows huge synthetic utility to access various carbocyclic and heterocyclic compounds, which can be found in bioactive compounds.[60]

5.2 Results

We have prepared different kinds of secondary alkyl iodides **5-1** with various alkynyl moieties in the molecules and tested the influence of the terminal groups at the alkynes on the reaction outcome (Table 5-1).

Table 5-1. Effect of terminal groups of alkynyl moieties on the reaction outcome.



5-1

Entry	Substrates			Yield[a]	d.r.[b]	Comment
1	**5-1a**:	R = ^{n}Bu	(d.r. = 50:50)	(58%)	(90:10)	uncyclized products
2	**5-1b**:	R = Ph	(d.r. = 99:1)	trace	-	mixture of 4-*endo* and 5-*exo* cyclization
3	**5-1c**:	R = Me$_3$Si	(d.r. = 70:30)	70%	16:84	stereoconvergence
4	**5-1d**:	R = Ph$_3$Si	(d.r. = 66:34)	60%	65:35	retention

[a] Isolated yield of products. [b] d.r. (*syn*:*anti*) was determined by ^{1}H and ^{13}C-NMR spectroscopy.

From alkyl iodide **5-1a** with a ^{n}Bu group as substituents at the alkynyl group, the uncyclized products were obtained selectively after the I/Li exchange and trapping reaction sequence (entry 1).[31] Replacement of the substituent of alkynyl group to a phenyl group afforded a

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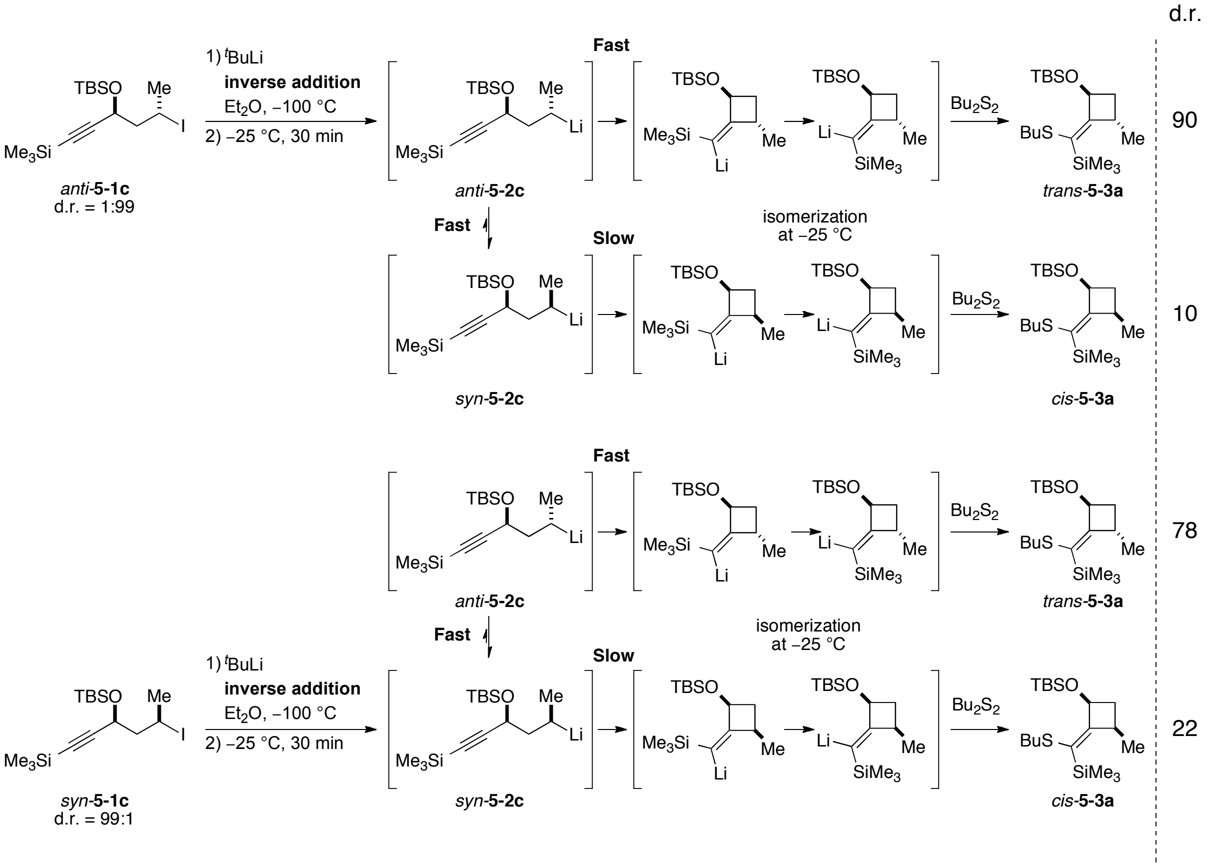
[59] a) A. L. Hogan, D. F. O'Shea, *Chem. Commun.* **2008**, 3839; b) M. J. Mealy, W. F. Bailey, *J. Organometallic. Chem.* **2002**, *646*, 59.

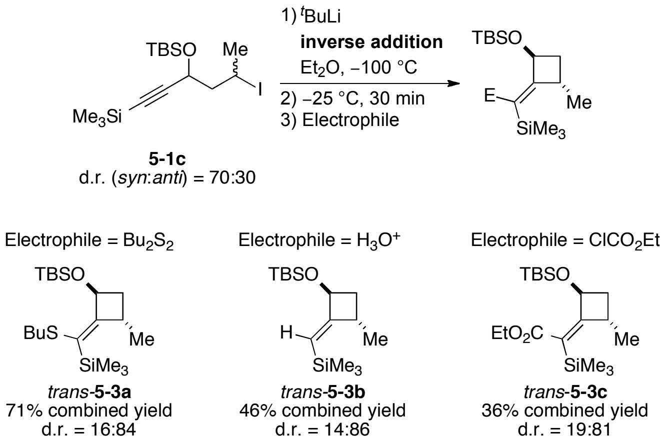
[60] a) C. Meyer, I. Marek, J. F. Normant, *Tetrahedron Lett.***1994**, *35*, 5645; b) K. Tomooka, N. Komine, T. Nakai, *Tetrahedron Lett.* **1997**, *38*, 8939; c) M. Oestreich, R. Fröhlich, D. Hoppe, *J. Org. Chem.* **1999**, *64,* 8616; d) D. Cheng, S. Zhu. Z. Yu, T. Cohen, *J. Am. Chem. Soc.* **2001**, *123*, 30; e) G. Gralla, B. Wibbeling, D. Hoppe, *Org. Lett.* **2002**, *4*, 2193; f) G. Gralla, B. Wibbeling, D. Hoppe, *Tetrahedron Lett.* **2003**, *44*, 8979.

complex mixture including both 4-*endo* and 5-*exo* cyclization products (entry 2). Thus, activation of alkyne moiety by Ph group is not stereoselective. However, activation by silyl group is stereoselective (entries 3 and 4). In the case of **5-1c** kinetic resolution occurred during cyclization and the thermodynamically unstable minor diastereomer of alkyllithium reagent mainly gave the corresponding cyclic compounds (entry 3, Scheme 5-1). In addition, activation of the alkyne moiety by the triphenylsilyl group is greater than by trimethylsilyl group and cyclization reaction proceeded faster than epimerization of alkylithium reagents prepared from **5-1d**. Finally the cyclic compound with the same diastereoselectivity as starting alkyl iodide **5-1d** was obtained (entry 4, Scheme 5-3).



Scheme 5-1. Kinetic resolution during the cyclization reaction of secondary alkyllithium reagent **5-2c**.

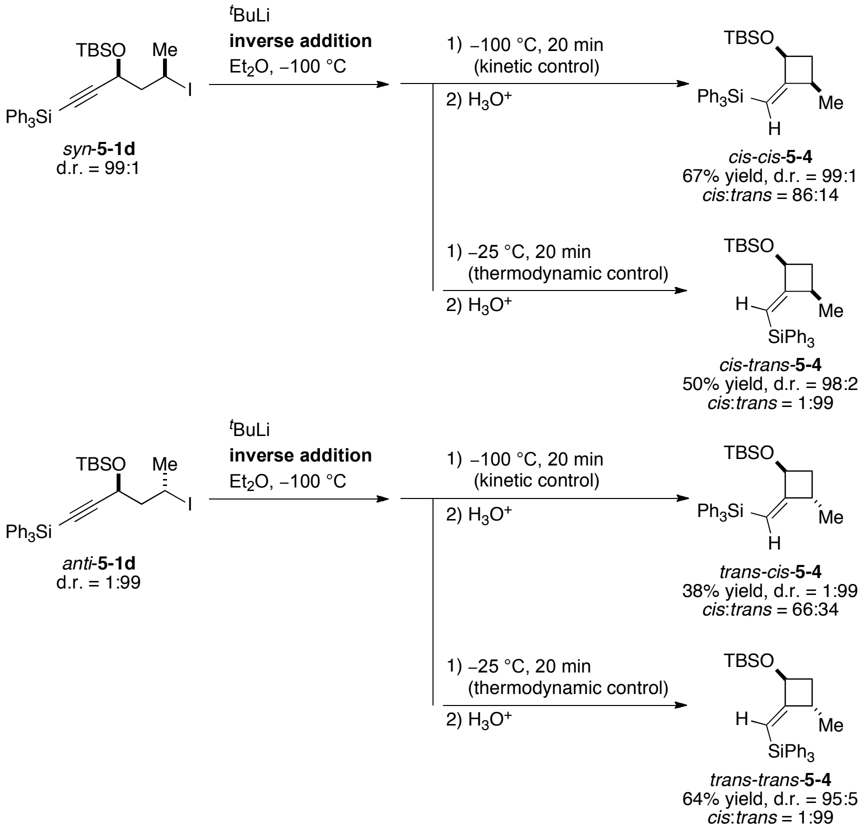
First cyclization reaction with **5-1c** was examined (Scheme 5-1). *Anti*-**5-1c** (d.r. = 1:99) was subjected to an I/Li exchange to form the corresponding lithium reagent *anti*-**5-2c**, which was transformed to the cyclic form at −25 °C. After isomerization of the double bond, which happened at −25 °C, its trapping reaction with Bu_2S_2 yielded selectively the product *trans*-**5-3a** (d.r. (*cis*:*trans*) = 10:90). On the other hand, *syn*-**5-1c** was converted to alkyllithium reagent *syn*-**5-2c**, which is more thermodynamically stable than *anti*-**5-2c**.[31] However, the cyclization of *syn*-**5-2c** was relatively slow at −25 °C and thermodynamically unstable alkyllithium reagent *anti*-**5-2c**, which was formed by epimerization of *syn*-**5-2c**, was mainly transformed to the cyclic alkyllithium intermediate at −25 °C and its trapping reaction with Bu_2S_2 provided *trans*-**5-3a** (d.r. = 22:78) after isomerization of the double bond. Thus, this cyclization proceeded through kinetic resolution. Starting from the diastereomeric mixture of **5-1c** (d.r. (*syn*:*anti*) = 70:30), the I/Li exchange and cyclization reaction sequence led to *trans*-**5-3a** in 61% yield (combined yield of both *trans*- and *cis*-**5-3a** was 71% yield with d.r. = 16:84) after trapping reaction with Bu_2S_2 (Scheme 5-2). Moreover, the trapping reaction of the corresponding alkyllithium reagents with protons and $ClCO_2Et$ also gave the expected products *trans*-**5-3b** (46% combined yield, d.r. = 14:86) and *trans*-**5-3c** (36% combined yield, d.r. = 81:19) respectively.



Scheme 5-2. Kinetic resolution during cyclization reaction of secondary alkyllithiums generated with **5-1c**.

As shown in Table 5-1, the triphenylsilyl group activates the alkyne moiety so much that cyclization reaction becomes much faster than epimerization of the alkyllithium reagents (Scheme 5-3). Thus, *syn*-**5-1d** (d.r. = 99:1) was reacted with ^{t}BuLi (**inverse addition**) to generate the corresponding alkyllithium reagent. It cyclized during stirring at −100 °C (under kinetic control) and its quenching reaction with protons provided *cis*-*cis*-**5-4** in 67% yield, d.r. (*cis*:*trans*) = 99:1 and *cis*:*trans* = 86:14. If the same alkyllithium reagent was stirred at −25 °C (under thermodynamic control), the isomerization of double bond happened leading to *cis*-*trans*-**5-4** (50% yield, d.r. = 98:2, *cis*:*trans* = 1:99) after quenching reaction with protons. Similarly, the other diastereomer *anti*-**5-1d** (d.r. = 1:99) was transformed via an I/Li exchange and cyclization under kinetic control or thermodynamic control to *trans*-*cis*-**5-4** (38% yield, d.r. = 99:1, *cis*:*trans* = 66:34) or *trans*-*trans*-**5-4** (64% yield, d.r. = 95:5, *cis*:*trans* = 1:99) respectively, after quenching reactions with proton. Thus, stereoselective synthesis of every isomer of **5-4** can be achieved by choosing proper substrates and adjusting reaction conditions.

Further extension of the reaction scope is ongoing.[33]

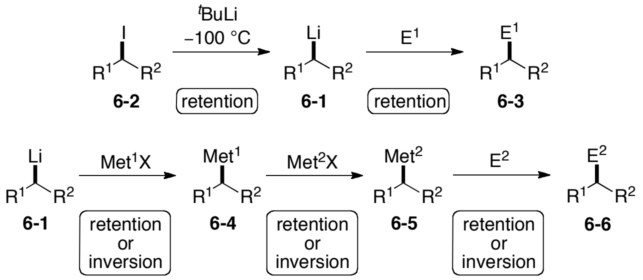


Scheme 5-3. Stereoselective synthesis of **5-4** from the corresponding alkyllthium reagents under kinetic or thermodynamic control.

6 Stereoselective Retentive Domino-Transmetalations of Secondary Alkyllithiums to Functionalized Secondary Alkylcopper Reagents

6.1 Introduction

Organolithiums are key intermediates for organic synthesis.[13] Stereoselective transformations involving chiral organolithiums, generally α-heteroatom substituted alkyllithium reagents,[15,16] have been used for the stereoselective synthesis of various organic molecules. As shown in Scheme 6-1, we recently developed experimental conditions allowing the stereoselective preparation of unstabilized functionalized secondary alkyllithium reagents of type **6-1** from the corresponding alkyl iodides of type **6-2** using a retentive I/Li exchange. After the addition of an electrophile (E^1) various products of type **6-3** were obtained with an overall retention of the configuration.[22,30,31] Unfortunately, only limited classes of electrophiles (E^1) could be used with these highly reactive lithium reagents. In order to expand the synthetic utility of this method, we have envisioned to perform successive stereoselective transmetalations[61,62] of the alkyllithium reagents **6-1** with metallic salts (Met^1-X, Met^2-X) leading to intermediate organometallics **6-4** and **6-5** and leading to products of type **6-6** after quenching with a new set of electrophiles (E^2; Scheme 6-1).[25,28,63,64]



Scheme 6-1. Stereoselective domino-transmetalations of unstabilized secondary alkyllithium reagents.

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[61] Selected examples for transmetalation to alkylcopper reagents: a) P. Knochel, T. S. Chou, H. G. Chen, M. C. P. Yeh, M. J. Rozema, *J. Org. Chem.* **1989**, *54*, 5202; b) T. N. Majid, P. Knochel, *Tetrahedron lett.* **1990**, *31*, 4413; c) W. Dohle, D. M. Lindsay, P. Knochel. *Org. Lett.* **2001**, *3*, 2871.

[62] Stereoselective transmetalation of alkyllithium reagents: a) K. Tomooka, H. Shimizu, T. Nakai, *J. Organomet. Chem*, **2001**, *624*, 364; b) J. P. N. Papillon, R. J. K. Taylor, *Org. Lett.* **2002**, *4,* 119; c) R. K. Dieter, G. Oba, K. R. Chandupatla, C. M. Topping, K. Lu, R. T. Watson, *J. Org. Chem.* **2004**, *69*, 3076; d) D. Stead, P. O'Brien, A. J. Sanderson, *Org. Lett*, **2005**, *7*, 4459; e) I. Coldham, D. Leonori, *J. Org. Chem.* **2010**, *75*, 4069.

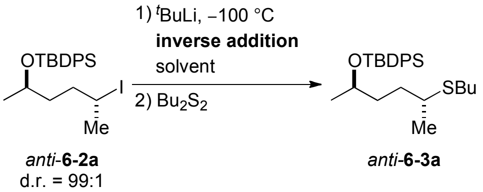
[63] Examples of chiral alkylmagnesium reagents: a) J. Beckmann, D. Darkternieks, M. Dräger, A. Duthie, *Angew. Chem. Int. Ed.* **2006**, *45*, 6509; b) A. A. Zuzek, S. C. Reynolds, D. S. Glueck, J. A. Golen, A. L. Rheingold, *Organometallics* **2011**, *30*, 1812.

[64] Examples of chiral alkylzincs: a) R. Duddu, M. Eckhardt, M. Furlong, H. P. Knoess, S. Berger, P. Knochel, *Tetrahedron* **1994**, *50*, 2415; b) A. Boudier, P. Knochel, *Tetrahedron Lett.* **1999**, *40*, 687.

6.2 Results

First, we tried to improve the I/Li exchange step by changing the way of addition (Table 6-1). Thus, a solution of *anti*-**6-2a** (d.r. (*anti*:*syn*) = 99:1) was added dropwise to a ^{t}BuLi solution over 10 min leading to the formation of *anti*-**6-3a** in 74% yield and d.r. = 96:4 after trapping reaction with Bu_2S_2 (entry 1). A faster dropwise addition over 1 min improved the diastereoselectivity (d.r. = 98:2) with a little loss of the yield (69% yield). Pure Et_2O accelerate the epimerization rate compared to the solvent mixture Et_2O/hexane = 2/3 (entry 3). In THF, a hydrolysis product was obtained dominantly (entry 4). Pure Et_2O was used for further optimization due to the solubility of metal salts although it decreased the diastereoselectivity (Table 6-2).

Table 6-1. The effect of solvents and addition speed on the I/Li exchange.



entry	solvent mixture	addition	yield[a]	d.r.[b]
1	Et_2O/hexane = 2/3	slow dropwise (10 min)	74%	96:4
2	Et_2O/hexane = 2/3	fast dropwise (1 min)	69%	98:2
3	Et_2O only	fast dropwise (1 min)	68%	93:7
4	THF	slow dropwise (10 min)	0%	n.d.

[a] Isolated yield. [b] d.r. (*anti*:*syn*) was determined by ^1H and ^{13}C NMR spectroscopy.

Although the performance of one stereoselective transmetalation is desirable, previous work in our laboratory as well as stereoselective transmetalations of stabilized alkyllithium reagents performed by Taylor[62b], Dieter[62c] and Coldham[62e] indicated that a first transmetalation from lithium to zinc, followed by a second transmetalation from zinc to copper may give the best results. Furthermore, transmetalations of unstabilized alkyllithium reagents may be difficult to realize stereoselectively since Hoffmann has reported that transmetalations from Grignard reagents to alkylcopper or alkylmanganese reagents are complicated by single electron transfer (SET) processes which depend on the nature of the metallic salts or of the electrophiles used.[65] Therefore, we have examined in detail the domino-transmetalation[66] of

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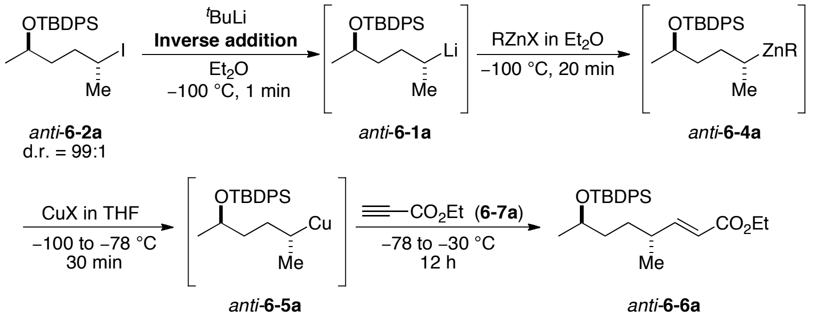
[65] R. W. Hoffmann, B. Hölzer, *J. Am. Chem. Soc.* **2002**, *124*, 4204.

the secondary alkyllithium reagent *anti*-**6-1a** generated by an I/Li exchange from the corresponding functionalized secondary alkyl iodide *anti*-**6-2a** (Table 6-2).

Table 6-2. Optimization of domino-transmetalations of a secondary alkyllithium reagent *anti*-**6-1a** to an alkylcopper reagent *anti*-**6-5a** via an alkylzinc reagent *anti*-**6-4a**.



Entry	RZnX	CuX	Yield[a]	d.r. [b]
1	-	-	0%	-
2	-	$CuBr{\cdot}2LiCl{\cdot}Me_2S$	(40%)	65:35
3	$TMSCH_2ZnI$	$CuCl{\cdot}2LiCl{\cdot}Me_2S$	(40%)	83:17
4	$TMSCH_2ZnI$	$CuBr{\cdot}2LiCl{\cdot}Me_2S$	44%	87:13
5	$TMSCH_2ZnI$	$CuI{\cdot}2LiCl{\cdot}Me_2S$	(46%)	83:17
6	$TMSCH_2ZnBr{\cdot}LiBr$	$CuBr{\cdot}2LiCl{\cdot}Me_2S$	46%	91:9
7	$TMSCH_2ZnCl{\cdot}LiCl$	$CuBr{\cdot}2LiCl{\cdot}Me_2S$	(51%)	87:13
8[c]	$TMSCH_2ZnBr{\cdot}LiBr$	$CuBr{\cdot}2LiCl{\cdot}Me_2S$	52%	94:6

[a] Isolated yield of diastereomers of **6-6a**. NMR yields in parentheses. [b] d.r. (*anti*:*syn*) was determined by ^1H and ^{13}C NMR spectroscopy. [c] Et_2O/hexane = 2/3 was used as solvent mixture.

A preliminary experiment showed that the carbolithiation of ethyl propiolate **6-7a** with *anti*-**6-1a** did not provide the expected product *anti*-**6-6a** (entry 1). However, the addition of the alkyl iodide *anti*-**6-2a** (d.r. = 99:1) to an ether solution of ^{t}BuLi (2.5 equiv, −100 °C, 1 min; **inverse addition**[14b,14c,22,30,31]) followed by the addition of $CuBr{\cdot}2LiCl{\cdot}Me_2S$ (2.5 equiv, −100 to −78 °C, 30 min) and ethyl propiolate (**6-7a**, 5.0 equiv, −78 °C to −30 °C, 12 h) provided the acrylate *anti*-**6-6a** in 40% yield but unfortunately with d.r. = 65:35 (entry 2) showing that the direct transmetalation from lithium to copper is not stereoselective under these conditions. This may be explained by an unselective transmetalation step or by an unselective addition reaction of *anti*-**6-5a** to ethyl propiolate **6-7a** due to the nature of the copper species or by SET-processes. Better results were obtained by using domino-transmetalations with the

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[66] *Domino Reactions: Concept for Efficient Organic Synthesis* (Eds. L. F. Tietze), Wiley-VCH, Weinheim, **2014**.

soluble stabilized zinc organometallic Me_3SiCH_2ZnI[67] (2.5 equiv, −100 °C, 20 min) followed by $CuCl{\cdot}2LiCl{\cdot}Me_2S$. In this case, the diastereoselectivity jumped to d.r. = 83:17 (entry 3) Interestingly, this diastereoselectivity was found to depend on the counter anion of the copper species and the corresponding bromide ($CuBr{\cdot}2LiCl{\cdot}Me_2S$) led to slightly increased d.r. = 87:13 (entry 4), but the copper iodide ($CuI{\cdot}2LiCl{\cdot}Me_2S$) afforded only d.r. = 73:27 (entry 5). These results led us to examine the influence of the halide of the organozinc reagents (Me_3SiCH_2ZnX) and we have found that $Me_3SiCH_2ZnBr{\cdot}LiBr$ gave enhanced d.r. = 91:9 (entry 6). We noticed that the corresponding chloride $Me_3SiCH_2ZnCl{\cdot}LiCl$ did not improve the diastereoselectivity (entry 7). Switching the solvents from pure Et_2O to Et_2O/hexane = 2/3 allowed further improvement of the diastereoselectivity to d.r. = 94:6 (entry 8). $Me_3SiCH_2ZnBr{\cdot}LiBr$ was found to be a much better zinc halide source for the Li/Zn transmetalation compared to $ZnCl_2$ or related zinc halides and lithium complexes.

These conditions proved to be broadly applicable. Thus, secondary alkyl iodide *syn*-**6-2a** (d.r. = 3:97) underwent the same reaction sequence providing the expected acrylate *syn*-**6-6a** in 48% yield and d.r. = 9:91 (Table 2, entry 1). The domino-transmetalations allowed to perform not only carbocuprations[68] but also a range of typical reactions of organocopper derivatives.[69] Thus, whereas secondary alkyllithium reagents required the use of Weinreb-amides[30], the acylation with benzoyl chloride **6-7b** provides the 5-hydroxy ketone derivatives *anti*- and *syn*-**6-6b** with excellent overall retention of the configuration (d.r. = 94:6 and 6:94; entry 2). An addition-elimination reaction on 3-iodocyclopentenone **6-7c**[70] provided both *anti*- and *syn*-cyclopentenones (*anti*-**6-6c**: d.r. = 94:6 and *syn*-**6-6c**: d.r. = 7:93; entry 3). The intermediate copper reagents of type **6-5** also opened ethylene oxide to provide the corresponding hydroxyl-ethylated compounds.[71] Thus, the alkyllithium reagents *syn*- and *anti*-**6-1a** were converted via a domino-transmetalation sequence using ethylene oxide **6-7d** to the selectively protected *syn*- and *anti*-1,6-diols (*syn*-**6-6d**: d.r. = 93:7 and *anti*-**6-6d**: d.r. = 9:91). BF_3-mediated acetal-opening of organocopper reagents, as pioneered by Alexakis and Normant,[72]

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[67] a) S. H. Bertz, M. Eriksson, G. Miao, J. P. Snyder, *J. Am. Chem. Soc.* **1996**, *118*, 10906; b) S. Berger, F. Langer, C. Lutz, P. Knochel, T. A. Mobley, C. K. Reddy, *Angew. Chem. Int. Ed.* **1997**, *36*, 1496; c) P. Jones, C. K. Reddy, P. Knochel, *Tetrahedron* **1998**, *54*, 1471.

[68] a) M. Gardette, A. Alexakis, J. F. Normant, *Tetrahedron Lett.* **1982**, *23*, 5155; b) M. Gardette, A. Alexakis, J. F. Normant, *Tetrahedron* **1985,** *41*, 5887.

[69] *Modern Organocopper Chemistry* (Eds., N. Krause), Wiely-VCH, Weinheim, **2002**.

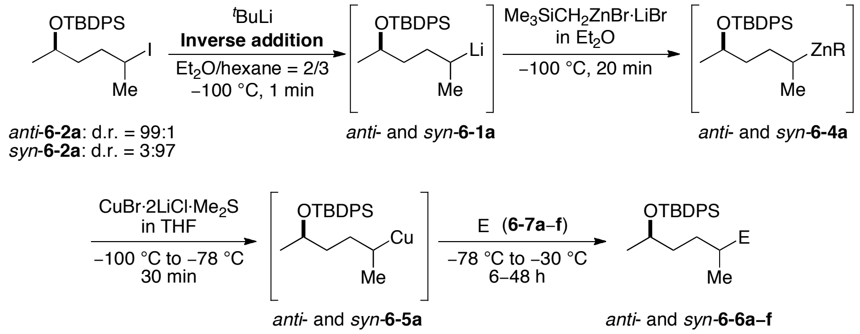
[70] In contrast, methyl vinyl ketone or ethyl acrylate gave the desired products in low yield.

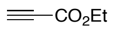
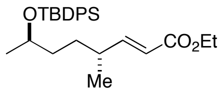
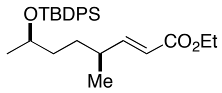
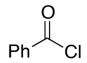
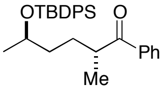
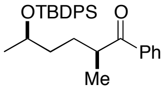
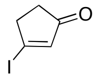
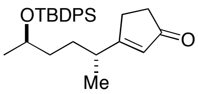
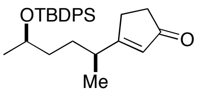
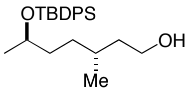
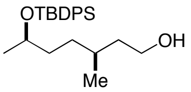
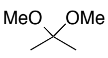
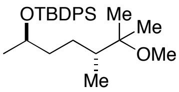
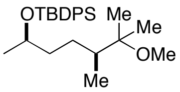
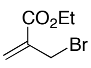
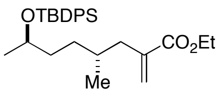
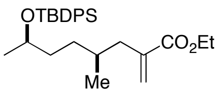
[71] a) A. Ghribi, A. Alexakis, J. F. Normant, *Tetrahedron Lett.* **1984**, *25*, 3075; b) A. Alexakis, D. Jachiet, N. F. Normant, *Tetrahedron* **1986**, *42*, 5607.

[72] J. F. Normant, A. Alexakis, A. Ghribi, P. Mangeney. *Tetrahedron* **1989**, *45*, 507.

proceeded with 2,2-dimethoxypropane **6-7e** leading to the 1,5-diol derivatives (*anti*-**6-6e**: d.r. = 91:9 and *syn*-**6-6e**: d.r. = 9:91; entry 5).

Table 6-3. Scope of electrophiles for the trapping reaction with alkylcopper reagents (*anti*- and *syn*-**6-5a**) prepared by domino-transmetalations of secondary alkylithium reagents (*anti*- and *syn*-**6-1a**).

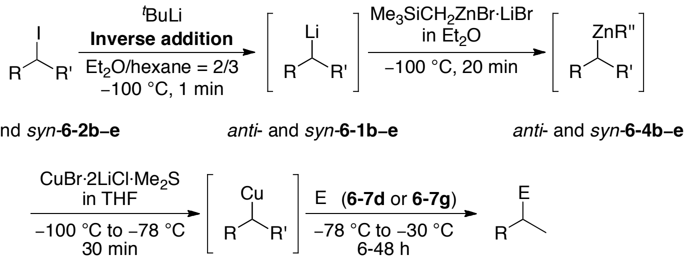


Entry	Electrophiles	From *anti*-**6-1a**[a],[b]	From *syn*-**6-1a**[a],[b]
1	 **6-7a**	 *anti*-**6-6a** 52%, d.r. = 94:6	 *syn*-**6-6a** 48%, d.r. = 9:91
2	 **6-7b**	 *anti*-**6-6b** 62%, d.r. = 94:6	 *syn*-**6-6b** 65%, d.r. = 6:94
3	 **6-7c**	 *anti*-**6-6c** 63%, d.r. = 94:6	 *syn*-**6-6c** 59%, d.r. = 7:93
4	 **6-7d**	 *anti*-**6-6d** 37%, d.r. = 93:7	 *syn*-**6-6d** 37%, d.r. = 9:91
5[c]	 **6-7e**	 *anti*-**6-6e** 43%, d.r. = 91:9	 *syn*-**6-6e** 44%, d.r. = 9:91
6	 **6-7f**	 *anti*-**6-6f** 62%, d.r. = 85:15	 *syn*-**6-6f** 63%, d.r. = 15:85

[a] Isolated yield of the diastereomers of **6-6**. [b] d.r. (*anti*:*syn*) was determined by ^1H and ^{13}C NMR spectroscopy. [c] In the presence of $BF_3{\cdot}Et_2O$.

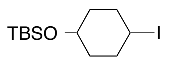
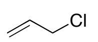
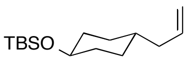
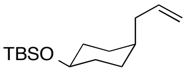
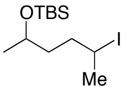
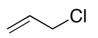
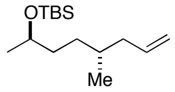
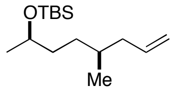
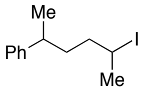
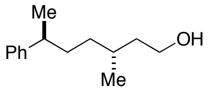
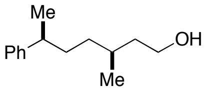
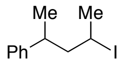
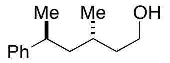
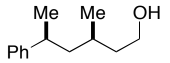
The highly reactive allylic reagent, ethyl (2-bromomethyl)acrylate **6-7f**[73] underwent a moderately selective allylation showing that in this case SET-pathways may compete with the non-radical substitution.[74]

Table 6-4. Scope of substrates for domino-transmetalations of secondary alkylithium reagents.



anti- and *syn*-**6-2b–e** *anti-* and *syn*-**6-1b–e** *anti-* and *syn*-**6-4b–e**

anti- and *syn*-**6-5b–e** *anti-* and *syn*-**6-6g–j**

Entry	Substrates	Electrophiles	From *anti* or *trans* [a],[b]	From *syn* or *cis*[a],[b]
1	 *trans*-**6-2b**: d.r. = 98:2 *cis*-**6-2b**: d.r. = 1:99	 **6-7g**	 *trans*-**6-6g** 84%, d.r. = 98:2	 *syn*-**6-6g** 75%, d.r. = 7:93
2	 *anti*-**6-2c**: d.r. = 98:2 *syn*-**6-2c**: d.r. = 1:99	 **6-7g**	 *anti*-**6-6h** 55%, d.r. = 92:8	 *syn*-**6-6h** 60%, d.r. = 8:92
3	 *anti*-**6-2d**: d.r. = 93:7 *syn*-**6-2d**: d.r. = 5:95	 **6-7d**	 *anti*-**6-6i** 37%, d.r. = 89:11	 *syn*-**6-6i** 40%, d.r. = 11:89
4	 *anti*-**6-2e**: d.r. = 98:2 *syn*-**6-2e**: d.r. = 3:97	 **6-7d**	 *anti*-**6-6j** 40%, d.r. = 94:6	 *syn*-**6-6j** 35%, d.r. = 5:95

[a] Isolated yield of the diastereomers of **6-6**. [b] d.r. (*anti*:*syn*) were determined by ^{1}H and ^{13}C NMR spectroscopy.

This analysis was confirmed in Table 6-4 where we have delineated the reaction scope by varying the secondary alkyl iodides of type **6-2**. Thus, using allyl chloride[75] as an electrophile, allylation reaction had much less tendency to undergo SET-reactions as shown by Hoffmann.[74] From either cyclic secondary alkyl iodides *trans-* and *cis*-**6-2b** (*trans*-**6-2b**: d.r. =

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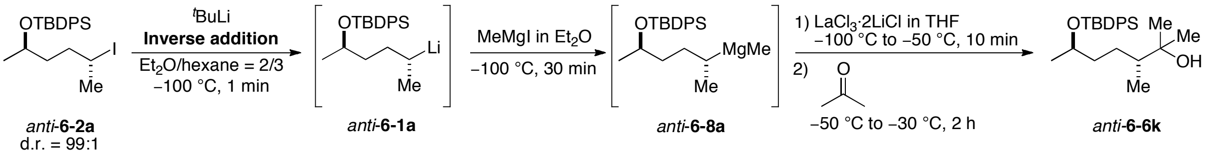
[73] J. Villieras, M. Rambaud, *Synthesis* **1982**, 924.

[74] R. W. Hoffmann, B. Hölzer, *Chem. Commun.* **2001**, 491.

[75] Preliminary experiments showed that the use of prenyl chloride provided a mixture of S_N2/S_N2' allylated products under these conditions.

98:2 and *cis*-**6-2b**: d.r. = 1:99) or acyclic iodides *anti*- and *syn*-**6-2c** (*anti*-**6-2c**: d.r. = 98:2 and *syn*-**6-2c**: d.r. = 1:99) we obtained high retention of the configuration in the allylation sequence leading to allylated products respectively (*trans*-**6-6g**: d.r. = 98:2 and *cis*-**6-6g**: d.r. = 7:93 as well as *anti*-**6-6h**: d.r. = 92:8 and *syn*-**6-6h**: d.r. = 8:92; entries 2 and 3). Unfunctionalized secondary alkyl iodides bearing a phenyl substituent either at position 4 or 3 (*anti*-**6-2d**: d.r. = 93:7 and *syn*-**6-2d**: d.r. = 5:95 as well as *anti*-**6-2e**: d.r. = 98:2 and *syn*-**6-2e**: d.r. = 3:97) behaved as expected and the diastereomerically enriched alcohols *anti*- and *syn*-**6-6i–j** were formed in 35–40% yield and good retentive diastereoselectivity.

Table 6-5. Scope of substrates for domino-transmetalations of secondary alkylithium reagents.



Entry	Conditions	Yield[a]	d.r.[b]
1	without MeMgI	54%	55:45
2	without $LaCl_3 \cdot 2LiCl$	15%	60:40
3	with $MeMgI/LaCl_3 \cdot 2LiCl$	30%	95:5

[a] Isolated yield of the diastereomers of **6-6k**. [b] d.r. (*anti*:*syn*) was determined by ^1H and ^{13}C NMR spectroscopy.

Domino-transmetalations proved to be efficient for undergoing additions to the carbonyl group of an enolizable ketone. Thus, we have briefly examined the diastereoselectivity obtained in the conversion of a diastereomerically pure secondary alkyl iodide into the corresponding lanthanum reagent (Table 6-5).[76] The secondary alkyllithium reagent *anti*-**6-1a** was generated from the corresponding alkyl iodide *anti*-**6-2a** (d.r. = 99:1) as shown before. A direct transmetalation to the corresponding alkyllanthanum by using $LaCl_3 \cdot 2LiCl$ followed by the addition of acetone provided the tertiary alcohol *anti*-**6-6k** in 54% yield, but low diastereoselectivity (d.r. = 55:45; entry 1). Repeating this reaction by transmetalating the intermediate alkyllithium reagent *anti*-**6-1a** to the magnesium derivative *anti*-**6-8a** and subsequent addition of acetone led to a decreasing yield and still low diastereoselectivity (d.r. = 60:40; entry 2). However, transmetalation of alkyllithium reagent *anti*-**6-1a** to the corresponding alkylmagnesium reagent *anti*-**6-8a** followed by the addition of $LaCl_3 \cdot 2LiCl$

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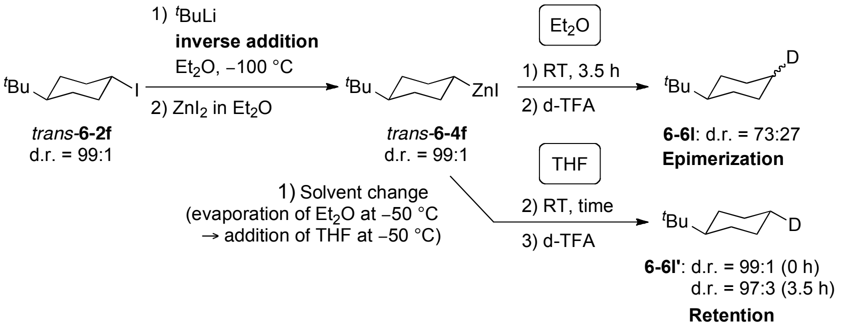
[76] A. Krasovskiy, F. Kopp, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 497.

and acetone led to the desired product *anti*-**6-6k** with an excellent diastereoselectivity (30% yield, d.r. = 95:5; entry 3).

These examples (Table 6-3, 6-4, 6-5) demonstrate that sequential highly retentive transmetalations of secondary alkyllithium reagents can be achieved with high diastereoselectivity under appropriate reaction conditions. The degree of retention in transmetalations depends on the nature of the metallic salt used (Table 6-2), but also the solvent polarity and therefore of the solvent mixture used.[15y,17m,22,26,36j,77,78] The influence of the nature of the solvent on the epimerization rate of a secondary alkylzinc reagent is demonstrated in the case of cyclohexylzinc iodide *trans*-**6-4f** obtained by an I/Li exchange and subsequent transmetalation with ZnI_2 (Scheme 6-2).



Scheme 6-2. Solvent effect on stereostability of cyclohexylzinc reagent *trans*-**6-4f**.

Under these conditions, the secondary alkylzinc reagent *trans*-**6-4f** was generated in ether with good diastereoselectivty (d.r. = 99:1), but we noticed that it has only a limited configurational stability in Et_2O at 25 °C and significant epimerization to a diastereomeric mixture (d.r. = 73:27) was observed after 3.5 h at 25 °C. The epimerization rate was monitored by deuterolysis of the reaction mixture with *d*-TFA. Interestingly, removal of Et_2O and dissolution in THF showed a high configurational stability for *trans*-**6-4a** (d.r. = 97:3 after 3.5 h).

6.3 Summary

In summary, we have developed sequential retentive domino-transmetalations of unstabilized functionalized secondary alkyllithiums prepared from the corresponding secondary alkyl

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[77] M. Gao, N. N. Patwardhan, P. R. Carlier, *J. Am. Chem. Soc.* **2013**, *135*, 14390.

[78] Experiments on the configurational stability of acyclic secondary alkylzinc reagents did not show the same behavior. In several cases, we observed a higher configurational stability in Et_2O compared to THF.

iodides via a stereoselective I/Li exchange. We found reaction conditions allowing performing two successive transmetalations from Li to Zn and from Zn to Cu leading to secondary alkylcopper reagents with high retention of the configuration. This domino-transmetalation sequence allows trappings with a new set of electrophiles leading to various polyfunctionalized products with predictive diastereoselectivity. A related domino-transmetalation sequence involving successively Li-, Mg- and La-organometallic intermediates provides an access to diastereomerically defined tertially alcohols.

7 Diastereoconvergent Negishi Cross-coupling Using Functionalized Cyclohexylzinc Reagents

7.1 Introduction

The performance of diastereoselective cross-coupling reactions on Csp^3 centers[79] is an important synthetic task for an efficient set-up of multiple stereocenters. Several diastereoselective Pd-catalyzed reactions on cyclic systems have been reported so far[80] and other transition metals such as Ni[81], Fe[82] and Co[83] have been used.[84] We have reported that cyclohexylzinc reagents with alkyl substituents at positions 2, 3 and 4 undergo Pd-catalyzed Csp^2 and Csp^3 coupling reactions in a diastereoconvergent way.[80a, 85] High diastereoselectivities were usually obtained in these systems; however, the presence of functional groups on the ring complicated such cross-couplings (lower yields and diastereoselectivities). Herein, we report an improved cross-coupling procedure allowing the use of various functionalized cyclohexylzinc reagents. Such Pd-catalyzed Negishi cross-

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[79] Recent reviews of Csp^3 cross-couplings: a) A. Rudolph, M. Lautens, *Angew. Chem. Int. Ed.* **2009**, *48*, 2656; b) R. Jana, T. P. Pathak, M. S. Sigman, *Chem. Rev.* **2011**, *111*, 1417; c) F. Bellina, R. Rossi, *Chem. Rev.* **2010**, *110* 1082; d) M. Wasa, K. M. Engle, J.-Q. Yu, *Isr. J. Chem.* **2010**, *50*, 605.

[80] a) T. Thaler, B. Haag, A. Gavryushin, K. Schober, E. Hartmann, R. M. Gschwind, H. Zipse, P. Mayer, P. Knochel, *Nature Chem.* **2010**, *2*, 125; b) S. Seel, T. Thaler, K. Takatsu, C. Zhang, H. Zipse, B. F. Straub, P. Mayer, P. Knochel, *J. Am. Chem. Soc.* **2011**, *133*, 4774; c) T. Thaler, L.-N. Guo, P. Mayer, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 2174; d) E. A. Bercot, S. Caille, T. M. Bostick, K. Ranganathan, R. Jensen, M. M. Faul, *Org. Lett.* **2008**, *10*, 5251; e) R. J. Mycka, S. Duez, S. Bernhardt, J. Heppekausen, P. Knochel, F. F. Fleming, *J. Org. Chem.* **2012**, *77*, 7671; f) A. Boudier, P. Knochel, *Tetrahedron Lett.* **1999**, *40*, 687; g) I. Coldham, D. Leonori, *Org. Lett.* **2008**, *10*, 3923; h) K. R. Campos, A. Klapars, J. H. Waldman, P. G. Dormer, C. Chen, *J. Am. Chem. Soc.* **2006**, *128*, 3538; i) B. M. Trost, S. M. Silverman, J. P. Stambuli, *J. Am. Chem. Soc.* **2011**, *133*, 19483.

[81] a) P. M. P. Garcia, T. D. Franco, A. Orsino, P. Ren, X. Hu, *Org. Lett.* **2012**, *14*, 4286; b) D. A. Powell, G. C. Fu, *J. Am. Chem. Soc.* **2004**, *126*, 7788; c) D. A. Powell, T. Maki, G. C. Fu, *J. Am. Chem. Soc.* **2005**, *127*, 510; d) H. Gong, M. R. Gagné, *J. Am. Chem. Soc.* **2008**, *130*, 12177; e) F. González-Bobes, G. C. Fu, *J. Am. Chem. Soc.* **2006**, *128*, 5360; f) H. Gong, R. S. Andrews, J. L. Zuccarello, S. J. Lee, M. R. Gagné, *Org. Lett.* **2009**, *11*, 879; g) L. Melzig, A. Gavryushin, P. Knochel, *Org. Lett.* **2007**, *9*, 5529.

[82] a) M. Nakamura, K. Matsuo, S. Ito, E. Nakamura, *J. Am. Chem. Soc.* **2004**, *126*, 3686; b) T. Hatakeyama, Y. Kondo, Y. Fujiwara, H. Takaya, S. Ito, E. Nakamura, M. Nakamura, *Chem. Commun.* **2009**, 1216; c) S. Kawamura, T. Kawabata, K. Ishizuka, M. Nakamura, *Chem. Commun.* **2012**, *48*, 9376; d) A. K. Steib, T. Thaler, K. Komeyama, P. Mayer, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 3303; e) C. Bensoussan, N. Rival, G. Hanquet, F. Colobert, S. Reymond, J. Cossy, *Tetrahedron* **2013**, *69*, 7759.

[83] a) H. Ohmiya, T. Tsuji, H. Yorimitsu, K. Oshima, *Chem. Eur. J.* **2004**, *10*, 5640; b) H. Ohmiya, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2006**, *128*, 1886; c) L. Nicolas, P. Angibaud, I. Stanfield, P. Bonnet, L. Meerpoel, S. Reymond, J. Cossy, *Angew. Chem. Int. Ed.* **2012**, *51*, 11101.

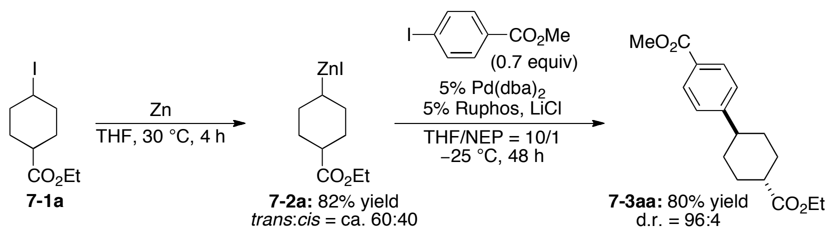
[84] Other metals catalyzed conditions: a) S. Yasuda, H. Yorimitsu, K. Oshima, *Bull. Chem. Soc. Jpn.* **2008**, *81*, 287; b) H. Someya, H. Yorimitsu, K. Oshima, *Tetrahedron* **2010**, *66*, 5993; c) S. J. Pastine, D. V. Gribkov, D. Sames, *J. Am. Chem. Soc.* **2006**, *128*, 14220.

[85] Enantioconvergent cross-couplings: a) C. J. Cordier, R. J. Lundgren, G. C. Fu, *J. Am. Chem. Soc.* **2013**, *135*, 10946; b) Z. Lu, A. Wilsily, G. C. Fu, *J. Am. Chem. Soc.* **2011**, *133*, 8154.

coupling reactions with various aryl, heteroaryl and alkenyl iodides proceed in very high stereoselectivities and good yields.

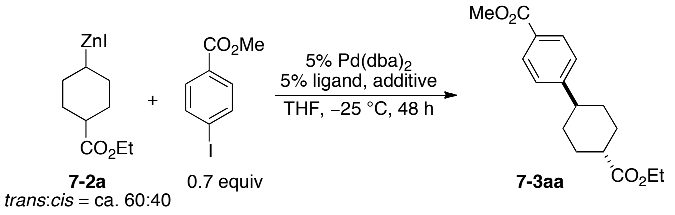
7.2 Results

First functionalized cyclohexylzinc reagents were prepared. Thus, ethyl 4-iodocyclohexylcarboxylate **7-1a** was treated with commercially available zinc dust (3 equiv) in THF to produce the corresponding cyclohexyzinc reagent **7-2a** (30 °C, 4 h; 82% yield).[86] The presence of an acidic proton at the α-position to the ester group did not hamper the zinc insertion and the resulting zinc reagent **7-2a** proved to be stable for several weeks without significant decomposition at 25 °C.[87] ^{1}H and ^{13}C NMR spectroscopy of this zinc reagent **7-1a** in THF-d_8 indicated that a *trans*:*cis* mixture of ca. 60:40 was produced (Scheme 7-1).



Scheme 7-1: Pd-catalyzed diastereoconvergent cross-coupling of functionalized cyclohexylzinc reagent **7-2a**.

Table 7-1. The effect of ligands and additives on the yield and stereoselectivity of the product.



Entry	Ligand	Additive[b]	Yield[a]	d.r.[b]
1	SPhos	-	41%	85:15
2	SPhos	NEP (10 vol%)	65%	92:8
3	SPhos	NEP (10 vol%), LiCl (1.5 equiv)	76%	92:8
4	RuPhos	NEP (10 vol%), LiCl (1.5 equiv)	80%	96:4

[a] Isolated yield of the *trans*-diastereomer. [b] d.r. (*trans*:*cis*) was determined by capillary GC and ^{1}H NMR analysis.

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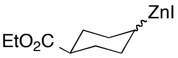
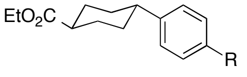
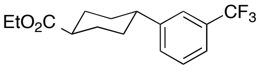
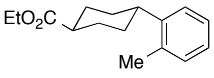
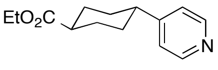
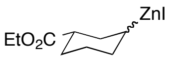
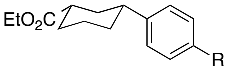
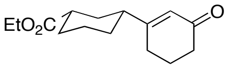
[86] a) P. Knochel, N. Millot, A. L. Rodriguez, C. E. Tucker, *Org. React.* **2001**, *58*, 417; b) P. Knochel, H. Leuser, L.-Z. Gong, S. Perrone, F. F. Kneisel, In *Handbook of Functionalized Organometallics* (Ed.: P. Knochel), Wiley-VCH, Weinheim, **2005**; pp 215-333.

[87] H. P. Knoess, M. T. Furlong, M. J. Rozema, P. Knochel, *J. Org. Chem.* **1991**, *56*, 5974.

Table 7-2. Scope of Pd-catalyzed diastereoconvergent cross-couplings of substituted cyclohexylzinc reagents with aryl iodides.

entry	zinc reagent	major product	yield[a]	d.r.[b]
1	 **7-2a**	 **7-3aa**: R = CO_2Me	80%	96:4
2		**7-3ab**: R = COMe	72%	94:6
3		**7-3ac**: R = CHO	73%	96:4
4		**7-3ad**: R = NO_2	74%	96:4
5		**7-3ae**: R = CN	70%	94:6
6		**7-3af**: R = OMe	74%	97:3
7		 **7-3ag**	68%	93:7
8[c]		 **7-3ah**	72%	97:3
9[d]		 **7-3ai**	69%	97:3
10	 **7-2b**	 **7-3ba:** R = CO_2Me	80%	95:5
11		**7-3bd:** R = NO_2	74%	97:3
12		**7-3bj:** R = Cl	79%	94:6
13[d]		 **7-3bk**	78%	96:4

[a] Isolated yield of the major diastereomer. [b] d.r. (major:minor) determined by capillary GC and ^1H NMR analysis. [c] This reaction was performed at –10 °C for 144 h. [d] This reaction was performed at –10 °C for 48 h.

The cross-couplings of this zinc reagent (1.0 equiv) with methyl 4-iodobenzoate[88] (0.7 equiv) in the presence of various Pd-catalysts were examined. Preliminary experiments showed that the ligands of Buchwald[89] were most promising. Thus, the use of SPhos[89b] led to moderate

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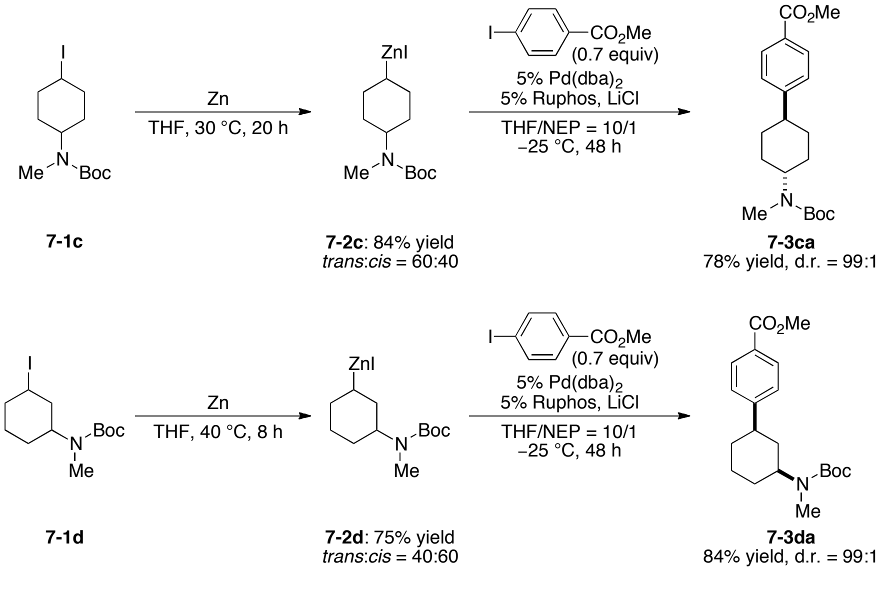
[88] These cross-couplings became much slower under our conditions if an aryl bromide is used (for example, 4-bromoanisole instead of 4-iodoanisole).

[89] a) D. S. Surry, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2008**, *47*, 6338; b) S. D. Walker, T. E. Barder, J. R. Martinelli, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2004**, *43*, 1871; c) J. E. Milne, S. L. Buchwald, *J. Am. Chem. Soc.* **2004**, *126*, 13028.

yield (41% yield) and diastereoselectivity (d.r. = 85:15) at –25 °C.[90] (Table 7-1, entry 1). The addition of *N*-ethylpyrrolidone (NEP, 10 vol %) improved the yield as well as the diastereoselectivity (65% yield, d.r. = 92:8; entry 2).[91] Further addition of LiCl (1.5 equiv) increased the yield to 76% (entry 3).[92] The best results were obtained by replacing SPhos with Ruphos[89c] and the thermodynamically favored *trans*-product **7-3aa** was obtained in 80% isolated yield[93] with a *trans*:*cis* ratio of 96:4 (entry 4).

This cross-coupling procedure using the cyclohexylzinc reagent **7-2a** was extended to various aryl iodides (Table 7-2, entry 1-8). Sensitive functional groups such as a ketone (entry 2), an aldehyde (entry 3), a nitro group (entry 4) and a cyano group (entry 5) were tolerated under the reaction conditions. In addition to electron-poor aryl iodides, an electron rich aryl iodide can also be used (entry 6). Moreover, *meta*- and *ortho*- substituted aryl and heterocyclic iodides gave equally high diastereoselectivities (entry 7–9). Furthermore, the 3-substituted cyclohexylzinc reagent **7-2b** produced the thermodynamically favored *cis*-cross-coupling products (entry 10–13). An aromatic chloride substituent (entry 12) and an enone group (entry 13) are both compatible with the cross-coupling conditions.



Scheme 7-2. Diastereoconvergent cross-couplings of cyclohexylzinc reagents with a nitrogen functional group.

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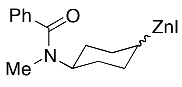
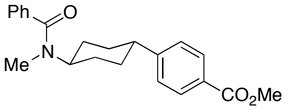
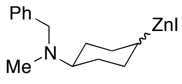
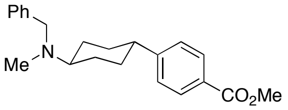
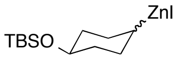
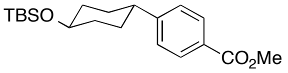
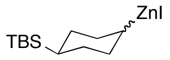
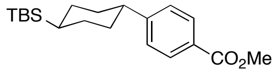
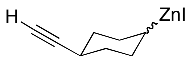
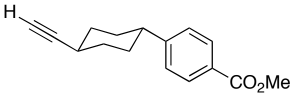
[90] Usually higher reaction temperatures led to a lower diastereoselectivity. However, in some cases (Table 2, entries 8, 9, 13) the performance of the coupling reactions at –10 °C improved the yields without significant loss of diastereoselectivity compared to –25 °C.

[91] A. Gavryushin, C. Kofink, G. Manolikakes, P. Knochel, *Org. Lett.* **2005**, *7*, 4871.

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

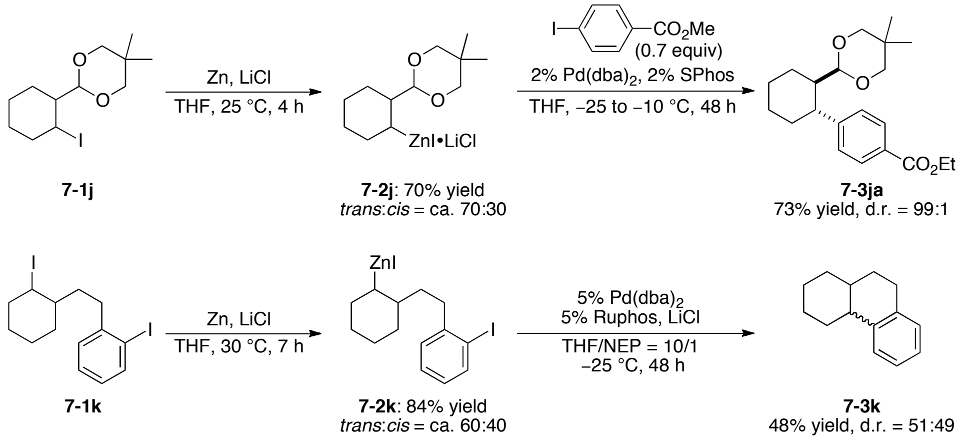
[93] Homo-coupling byproducts (biphenyls) were also formed in these cross-couplings in small amount (6–10% NMR yield).

Table 7-3. Scope of Pd-catalyzed diastereoconvergent cross-couplings of substituted cyclohexylzinc reagents with ethyl 4-iodobenzoate.

entry	zinc reagent	major product	yield[a]	d.r.[b]
1	 **7-2e**	 **7-3ea**:	76%	99:1
2	 **7-2f**	 **7-3fa**:	76%	99:1
3	 **7-2g**	 **7-3ga**:	75%	97:3
4	 **7-2h**	 **7-3ha**:	70%	98:2
5	 **7-2i**	 **7-3ia**:	59%	88:12

[a] Isolated yield of the *trans*-diastereomer. [b] d.r. (*trans*:*cis*) determined by capillary GC and ^{1}H NMR analysis.

Cyclohexylzinc reagents bearing other functional groups were subjected to the cross-coupling reaction (Scheme 7-2 and Table 7-3). Thus, the 4-amino substituted cyclohexylzinc reagent **7-2c** prepared from the corresponding cyclohexyl iodide **7-1c** (30 °C, 20 h; 84% yield) underwent a smooth cross-coupling with methyl 4-iodobenzoate affording the *trans*-1,4-disubstituted cyclohexane **7-3ca** in 78% yield and excellent diastereoselectivity (d.r. = 99:1). Similarly, in the case of the 3-amino substituted cyclohexylzinc reagent **7-2d** prepared from the corresponding cyclohexyl iodide **7-1d** (40 °C, 8 h; 75% yield) the *cis*-1,3-disubstituted cyclohexane **7-3da** was obtained in 84% yield and excellent diastereoselectivity (d.r. = 99:1). Also, cyclohexylzinc reagents with nitrogen-containing functional groups such as an amide (**7-2e**, entry 1, Table 7-3) or a benzylamine substituent (**7-2f**, entry 2) underwent the cross-couplings with excellent diastereoselectivity (d.r. = 99:1). In the case of cyclohexylzinc reagents bearing an OTBS group (**7-2g**, entry 3) or TBS group (**7-2h**, entry 4), the cross-coupling reaction proceeded well, leading to the expected products **7-3ga** and **7-3ha** in 70–75% yield and d.r. > 97:3. A cyclohexylzinc reagent bearing a terminal alkynyl group[87] was readily prepared and led to the cross-coupling product **7-3ia** in 59% yield and moderate diastereoselectivity (d.r. = 88:12). The reduced selectivity might be a consequence of the lower bulkiness of the alkynyl group.[94]



Scheme 7-3. Diastereoconvergent cross-coupling reactions of 1,2-substituted cyclohexylzinc reagents.

Furthermore, cross-coupling reactions using 2-substituted cyclohexylzinc reagents[95] were examined (Scheme 7-3). Thus, cyclohexylzinc reagent **7-2j** (*trans*:*cis* = ca. 70:30)[96] was treated with methyl 4-iodobenzoate under similar conditions to form cross-coupling product **7-3ja** in excellent diastereoselectivity. However, this behavior is not general and may be complicated, especially in ring closure reactions. We have prepared the diiodide **7-1k** by standard methods.[97] Its treatment with zinc dust in THF provided selectively the alkylzinc derivative **7-2k** (30 °C, 7 h; 84% yield) as a mixture of diastereomers. The addition of a Pd-catalyst led to a ring closure reaction, furnishing the tricyclic product **7-3k** in 48% yield as 1:1 mixture of diastereomers.

7.3 Mechanistic consideration

In order to obtain mechanistic explanations for this diastereoconvergence during Pd-catalyzed cross-couplings, the rate of epimerization of the cyclohexylzinc reagent **7-2l** was examined. The cyclohexylzinc iodide *trans*-**7-2l** was obtained by an I/Li exchange and subsequent transmetalation with ZnI_2 as shown in Chapter 6 (Scheme 7-4).

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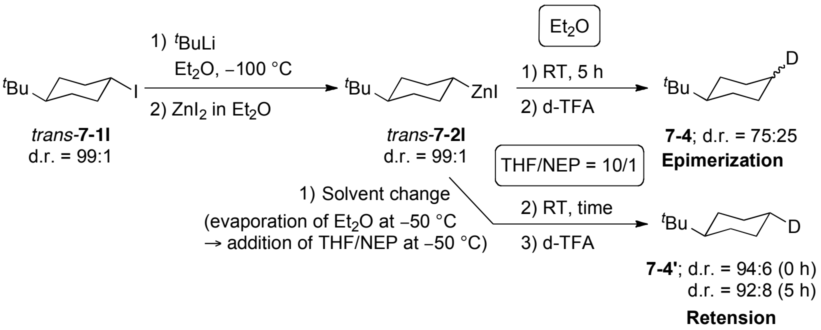
[94] *A* value of a terminal alkyne (*A* = 0.41) is smaller than other substituents such as CO_2Me (*A* = 1.31). F. R. Jensen, C. H. Bushweller, B. H. Beck, *J. Am. Chem. Soc.* **1969**, *91*, 344.

[95] a) T. N. Majid, M. C. P. Yeh, P. Knochel, *Tetrahedron Lett.* **1989**, *30*, 5069; b) A. Boudier, C. Darcel, F. Flachsmann, L. Micouin, M. Oestreich, P. Knochel, *Chem. Eur. J.* **2000**, *6*, 2748; c) E. Hupe, P. Knochel, *Org. Lett.* **2001**, *3*, 127.

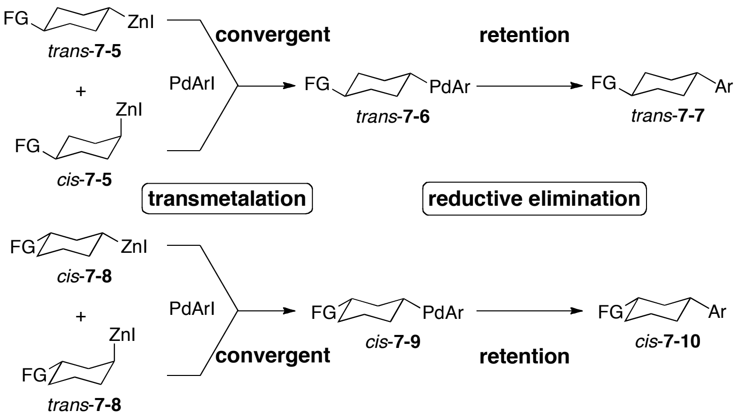
[96] Seel, S. Stereoselective Preparation and Stereochemical Behaviour of Organozinc and Organolithium Reagents. Ph.D. Thesis, Ludwig-Maximilian-Universität München, **2012**.

[97] See experimantal part.



Scheme 7-4. Solvent effects on stereostability of cyclohexylzinc reagent *trans*-**7-2I**.

The epimerization rate was monitored by deuterolysis of the reaction mixture with *d*-TFA. In the same way in Chapter 6, removal of Et_2O and dissolution in the solvent mixture (THF/NEP = 10/1) of the cross-coupling reactions showed a high configurational stability for *trans*-**7-2I** (d.r. = 92:8 after 5 h). Based on the fact that epimerization of cyclohexylzinc reagents is slow under cross-coupling reaction conditions, a tentative mechanism can be suggested for explaining the observed diastereoselectivity in this cross-coupling reaction (Scheme 7-5)



Scheme 7-5. Tentative mechanism for the diastereoconvergent cross-couplings.

In the case of 4-substituted cyclohexylzinc reagents, *trans*-**7-5** is converted to the thermodynamically favored *trans*-palladium intermediate *trans*-**7-6** via retentive transmetallation.[98] On the other hand, the *cis*-reagent *cis*-**7-5** is converted to the same palladium intermediate *trans*-**7-6** via inversive transmetallation.[99] The introduction of a

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[98] a) D. Imao, B. W. Glasspoole, V. S. Laberge, C. M. Crudden, *J. Am. Chem. Soc.* **2009**, *131*, 5024; b) J. C. H. Lee, R. McDonald, D. G. Hall, *Nature Chem.* **2011**, *3*, 894; c) J. R. Falck, P. K. Patel, A. Bandyopadhyay, *J. Am. Chem. Soc.* **2007**, *129*, 790; d) L. Li, C. -Y. Wang, R. Huang, M. R. Biscoe, *Nature Chem.* **2013**, *5*, 607. e) B. H. Ridgway, K. A. Woerpel, *J. Org. Chem.* **1998**, *63*, 458.

[99] S_E2 mechanism: a) K. W. Kells, J. M. Chong, *J. Am. Chem. Soc.* **2004**, *126*, 15666; b) T. Ohmura, T. Awano, M. Suginome, *J. Am. Chem. Soc.* **2010**, *132*, 13191; c) D. L. Sandrock, L. Jean-Gérard, C. Chen, S. D. Dreher,

palladium moiety in the axial position was highly disfavored[100] due to the repulsive interactions of the bulky phosphine ligands on the palladium center with the cyclohexyl ring, which was confirmed by DFT calculations.[80a] Thus, the thermodynamically favored *trans*-cross-coupling product *trans*-**7-7** would be obtained through the usual retentive reductive elimination.[80a,98,99,101] Again we propose that the mixture of *cis*- and *trans*-cyclohexylzinc reagents **7-8** are converted in a convergent way to the thermodynamically more stable *cis*-Pd-intermediate *cis*-**7-9** bearing the PdAr group in an equatorial position. The *cis*-cross-coupling product *cis*-**7-10** will be formed via retentive reductive elimination. [80a,98,99,101]

7.4 Summary

In summary, we have developed stereoconvergent cross-coupling reactions of various functionalized cyclohexylzinc reagents, which can be prepared by direct insertion of zinc dust to the corresponding cyclohexyl iodides. The stereoselectivity is excellent for 3- or 4-substituted cyclohexyl ring systems and the reaction is also applicable for some 2-substituted zinc reagents.

G. A. Molander, *J. Am. Chem. Soc.* **2010**, *132*, 17108; d) Y. Hatanaka, T. Hiyama, *J. Am. Chem. Soc.* **1990**, *112*, 7793.

[100] C. Munro-Leighton, L. L. Adduci, J. J. Becker, M. R. Gagné, *Organometallics* **2011**, *30*, 2646.

[101] a) J. K. Still, *Angew. Chem. Int. Ed.* **1986**, *25*, 508; b) J. W. Labadie, J. K. Still, *J. Am. Chem. Soc.* **1983**, *105*, 6129; c) D. Milstein, J. K. Still, *J. Am. Chem. Soc.* **1979**, *101*, 4981; d) P. M. Krizkova, F. Hammerschmidt, *Eur. J. Org. Chem.* **2013**, 5143.

8 Summary

We have established stereo-controlled preparation of organometallics containing lithium (Chapter 2–5) and other metals (Chapter 6), and we also have developed stereoselective applications of secondary organometallics to organic syntheses (Chapter 2–7). These methodologies realized stereoselective functionalization at a certain position in aliphatic compounds, which cannot be achieved easily with existing methods. The research on these topics is ongoing in Prof. Knochel group and I am looking forward to seeing further development in this field.

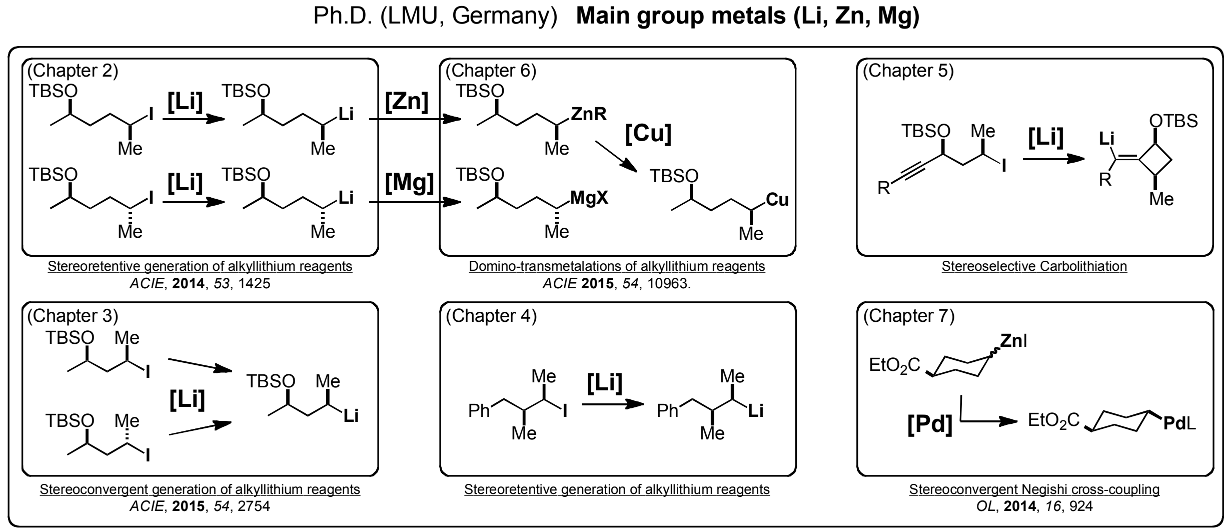

Figure 8-1. Outlook of this Ph.D. thesis.

9 Experimental Section

9.1 General considerations

All reactions were carried out with magnetic stirring and, if the reagents were air or moisture sensitive, in flame-dried glassware under Ar atomosphere. Syringes which were used to transfer reagents and solvents were purged with argon prior to use.

9.1.1 Solvents

Solvents were dried according to standard procedures by distillation over drying agents and stored under argon.

CH_2Cl_2 was predried over $CaCl_2$ and distilled from CaH_2.

DMF was heated to reflux for 14 h over CaH_2 and distilled from CaH_2.

Et_2O was predried over calcium hydride and dried with the solvent purification system SPS-400-2 from INNOVATIVE TECHNOLOGIES INC.

Hexane was refluxed and distilled from sodium benzophenone ketyl under Ar atomosphere.

NEP was heated to reflux for 14 h over CaH_2 and distilled from CaH_2.

PMDTA was dried over KOH and distilled.

Pyridine was dried over KOH and distilled.

THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under N_2 atomosphere.

THF-*d_8* was dried with activated molecular sieve 3A and stored in a glove box.

TMEDA was dried over KOH and distilled.

Toluene was predried over $CaCl_2$ and distilled from CaH_2.

Triethylamine was dried over KOH and distilled.

Solvents for column chromatography were simple-distilled prior to use.

9.1.2 Reagents

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

Purification of electorphiles

Dibutyl sulfide (**Bu_2S_2**) was passed through a pad of alumina, followed by vacuum distillation (100 °C, 1 mbar).

Cyclopropanecarbonyl chloride was distilled (75 ºC, 100 mbar) in the presence of small amount of PCl_5.

Benzoyl chloride was distilled (140 ºC, 50 mbar) in the presence of small amount of PCl_5.

Ethyl chloroformate (**$ClCO_2Et$**) was distilled (90 ºC, 5.0 mbar).

Phenyl isocyanate (**PhNCO**) was distilled (80 ºC, 5.0 mbar).

3-Pentenone was refluxed over CaH_2 and distilled (130 ºC, normal pressure).

2-Methoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**MeOBpin**) was distilled (50 ºC, 5.0 mbar).

Chloromethyl ethyl ether (**$EtOCH_2Cl$**) was distilled (45 ºC, 180 mbar).

2,2-dimethoxypropane was distilled (65 ºC, 180 mbar).

Allylchloride was distilled (60 ºC, normal pressure)

Acetone as an electrophile was purchased from Acros.

Organometallics and metal salts solution

^{n}BuLi solution in *n*-hexane was purchased from Rockwood Lithium (Chemetall).

^{t}BuLi solution in *n*-pentane was purchased from Rockwood Lithium (Chemetall).

Me_3SiCH_2Li in *n*-pentane was purchased from Aldrich.

$LaCl_3 \cdot LiCl$ solution in THF was purchased from Rockwood Lithium (Chemetall).

Content determination of organometallic reagents: The respective organometallic reagents were titrated using either the method reported by Paquette *et. al.*[102] or Knochel *et. al.*[103] prior to their use.

$ZnCl_2$ in THF

The solution (1.0 M) was prepared by drying $ZnCl_2$ (13.6 g, 10.0 mmol) in a *Schlenk*-flask under vacuum at 140 °C for overnight. After cooling to room temperature, 10 mL dry THF were added and stirring was continued until the salt was dissolved. The reagent was stirred under N_2 atmosphere.

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[102] H. S. Lin, L. A. A. Paquette, *Synth. Commun*. **1994**, *24*, 2503.

[103] A. Krasovskiy, P. Knochel, *Synthesis* **2006**, *5*, 890.

ZnI_2 in Et_2O

The dry and Ar flushed 50 mL *Schlenk* tube was charged with Zn dust (2.0 g, 30.0 mmol) and it was heated by a heat-gun for 5 min. After cooling it to room temperature, Et_2O (10 mL) was added. I_2 (2.5 g, 10.0 mmol) was added portionwise and slowly at 0 °C not to boil it and the mixture was stirred until the color of I_2 disappeared. The solution was transferred to other dry and Ar flushed Schelenk tube with a syringe and a smembrane filter to remove unreacted Zn dust to have the solution (1.0 M).

CuCN·2LiCl in THF

The solution (1.0 M) was prepared by drying LiCl (8.5 g, 200.0 mmol) and CuCN (9.0 g, 100.0 mmol) for 5 h at 140 ^{o}C under high vacuum. After cooling to room temperature, 100 mL dry THF were added and stirring was continued until the salt was dissolved. The *Schlenk*-tube was wrapped in an aluminium-foil to protect from light. The reagent appears as a slightly greenish solution and has to be stored under Ar atmosphere.

9.1.3 Chromatography

Flash column chromatography was performed using silica gel 60 (SiO_2, 0.040–0.063 mm, 230–400 mesh) from Merck or Florisil® ($MgSiO_3$, 0.150–0.250 mm, 60–100 mesh) from Alfa aeser.

Thin layer chromatography was performed using SiO_2 pre-coated aluminum plates (Merck 60, F-254) or SiO_2 pre-coated glass plate (Merck 60, F-254). The chromatograms were examined under UV light at 254 nm and/or by staining of the TLC plate with one of the solutions given below followed by heating with a heat-gun:

$KMnO_4$ (3.0 g), K_2CO_3 (20.0 g) and KOH (1.3 g) in water (180 mL)

Phosphomolybdic acid hydrate (4.3 g) in EtOH (100 mL).

9.1.4 Analytical data

NMR spectra were recorded on VARIAN Mercury 200, BRUKER AXR 300, VARIAN VXR 400 S, BRUKER AVANCE III 400, and BRUKER AMX 600 instruments. Chemical shifts are reported as δ-values in ppm relative to the residual solvent peak of chloroform d_8 ($CDCl_3$: δ_H: 7.26 ppm, δ_C: 77.16 ppm), benzene d_8 (C_6D_6: δ_H: 7.16 ppm and δ_C: 128.08 ppm) and tetrahydrofuran d_8 (δ_H: 3.85 and 1.72 ppm, δ_C: 67.21 and 25.31 ppm). For the characterization of the observed signal multiplicities the following appreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), h (sextet), m (multiplet) as well as br (broad).

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

For the combination of gas chromatography with mass spectroscopic detection, a GC/MS from Hewlett-Packard HP 6890 / MSD 5973 was used.

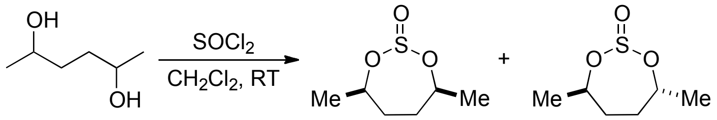
Infrared spectra (IR) were recorded from 3500 cm^{-1} to 650 cm^{-1} on a PERKIN ELMER Spectrum BX-59343 instrument. For detection a SMITHS DETECTION DuraSampl*IR* II Diamond ATR sensor was used. The absorption bands are reported in wavenumbers (cm^{-1}) and abbreviations for intensity are as follows: vs (very strong: maximum intensity), s (strong: above 75% of max. intensity), m (medium: from 50% to 75% of max. intensity), w (weak: below 50% of max. intensity) as well as br (broad).

Melting points (M.p.) were determined on a BÜCHI B-540 apparatus and are uncorrected.

Single-crystal X-ray diffraction data were measured with Agilent Technologies Xcalibur or with a Spellman generator (50 kV, 40 mA) and a Kappa CCD detector, operating with Mo-K_α radiation (λ = 0.71071 Å).

9.2 Diastereoretentive Preparation of Open-Chain Secondary Alkyllithiums Functionalized at the 4-Position

9.2.1 Preparation of starting materials



2-S1 *syn*-**2-S2** *anti*-**2-S2**

2-S2[104]

A dry and N_2-flushed *Schlenk*-flask was charged with **2-S1** (11.8 g, 100.0 mmol) in CH_2Cl_2 (100 mL). $SOCl_2$ (7.4 mL, 102.0 mmol) was added dropwise for 20 min and the resulting solution was stirred for 1 h at room temperature. Then reaction mixture was placed under vacuum to remove all volatile compounds. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/9 to afford *syn*-**2-S2** (5.8 g, 35% yield, d.r. = 99:1) as the first fraction and as colorless oil and *anti*-**2-S2** (5.0 g, 30% yield, d.r. = 99:1) as the second fraction and as colorless oil. The relative configurations were confirmed by NMR spectra.

syn-**2-S2** (CAS: 89772-99-6)

^{1}H-NMR (400 MHz, CDCl$_3$) δ: 5.08-4.96 (m, 2H), 2.07-1.93 (m, 2H), 1.90-1.76 (m, 2H), 1.34 (d, J = 6.5 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 72.0, 33.5, 21.6.

MS (70 eV, EI) *m/z* (%): 165 (1) $[M+H]^{+\bullet}$, 149 (2), 120 (4), 101 (19), 85 (53), 67 (13), 56 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2978 (w), 2935 (w), 1449 (w), 1380 (w), 1177 (s), 1130 (w), 1073 (w), 1040 (w), 1004 (w), 987 (w), 923 (m), 897 (s), 861 (m), 816 (vs), 706 (s).

HRMS (EI) *m/z*: calcd for $C_6H_{13}O_3S^{+\bullet}$ $[M+H]^{+\bullet}$: 165.0585, found: 165.0586.

anti-**2-S2** (CAS: 89772-98-5)

^{1}H-NMR (400 MHz, CDCl$_3$) δ: 5.17 (qt, J = 6.0 and 5.8 Hz, 1H), 4.34 (dqd, J = 9.5, 6.4 and 2.3 Hz, 1H), 1.90-1.57 (m, 4H), 1.34 (d, J = 6.4 Hz, 3H), 1.33 (d, J = 6.4 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 73.3, 70.2, 36.2, 34.2, 22.7, 22.4.

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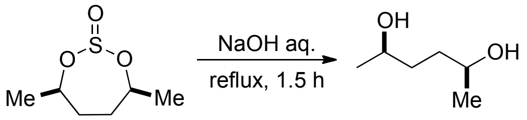
[104] G. Caron, R. J. Kazlauskas, *Tetrahedron Asymmetry* **1994**, *5*, 657.

MS (70 eV, EI) *m/z* (%): 165 (1) $[M+H]^{+\bullet}$, 149 (2), 120 (4), 101 (19), 85 (53), 67 (13), 56 (100)

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2978 (w), 2935 (w), 1449 (w), 1381 (w), 1200 (m), 1124 (w), 1095 (w), 1027 (m), 1004 (w), 925 (w), 903 (vs), 854 (s), 838 (s), 818 (m), 734 (s), 715 (s).

HRMS (EI) *m/z*: calcd for **$C_6H_{13}O_3S^{+\bullet}$** $[M+H]^{+\bullet}$: 165.0585, found: 165.0586.



syn-**2-S2** *syn*-**2-S1**

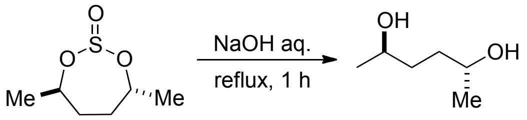
syn-**2-S1** (CAS: 38484-55-8)[104]

A 100 mL flask was charged with *syn*-**2-S2** (5.6 g, 34.1 mmol) in 2 M aqueous NaOH solution (50 mL) and the reaction mixture was stirred under reflux for 1.5 h. The reaction mixture was saturated with NaCl and it was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O to afford *anti*-**2-S1** (3.1 g, 76% yield, d.r. = 99:1) as colorless oil.

^{1}H-NMR (400 MHz, CDCl$_3$) δ: 3.90-3.78 (m, 2H), 2.83-2.65 (br s, 2H), 1.63-1.48 (m, 4H), 1.19 (d, J = 6.2 Hz, 6H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 67.9, 35.0, 23.5.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3330 (br w), 2967 (w), 2930 (w), 1460 (w), 1374 (w), 1330 (w), 1306 (w), 1200 (w), 1123 (w), 1056 (m), 1013 (w), 940 (m), 923 (w), 909 (w), 839 (w), 730 (vs).



anti-**2-S2** *anti*-**2-S1**

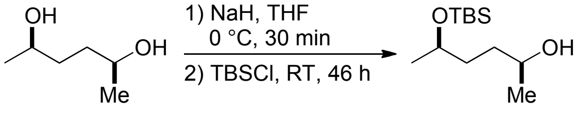
anti-**2-S1** (CAS: 38484-56-9)[104]

A 100 mL flask was charged with *anti*-**2-S2** (5.0 g, 30.4 mmol) in 2 M aqueous NaOH solution (50 mL) and the reaction mixture was stirred under reflux for 1 h. The reaction mixture was saturated with NaCl and it was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O to afford *anti*-**2-S1** (2.5 g, 69% yield, d.r. = 99:1) as colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.88-3.77 (m, 2H), 2.97-2.76 (br s, 2H), 1.65-1.48 (m, 4H), 1.20 (d, J = 6.2 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 68.6, 36.2, 23.9.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3316 (br m), 2966 (m), 2930 (m), 1460 (w), 1416 (w), 1373 (m), 1333 (w), 1252 (w), 1198 (w), 1116 (m), 1056 (vs), 1017 (s), 940 (s), 923 (m), 901 (w), 879 (w), 856 (w), 822 (w).



syn-**2-S1** *syn*-**2-S3**

syn-**2-S3** (CAS: 111524-01-7)

A dry and Ar-flushed *Schlenk*-flask was charged with NaH (1.07 g, 60wt%, 26.7 mmol) in THF (150 mL) and it was cooled down to 0 °C. *syn*-**2-S1** (3.0 g, 25.4 mmol) dissolved in THF (20 mL) was added dropwise for 5 min. The mixture was stirred at 0 °C to room temperature for 30 min. Then TBSCl (3.8 g, 25.4 mmol) was added and the mixture was stirred at room temperature for 46 h. The reaction was quenched with saturated NH_4Cl aqueous solution and the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/5 to afford *syn*-**2-S3** (4.3 g, 74% yield, d.r. = 99:1) as colorless oil.

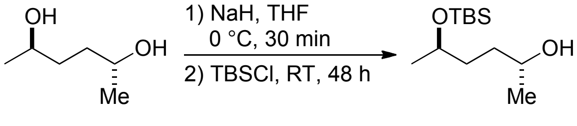
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.84-3.91 (m, 1H), 3.70-3.77 (m, 1H), 2.43 (s, 1H), 1.44-1.55 (m, 4H), 1.17 (d, J = 6.2 Hz, 3H), 1.14 (d, J = 6.2 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 68.6, 68.2, 35.9, 35.0, 25.8, 23.5, 23.2, 18.1, –4.5, –4.8.

MS (EI, 70 eV) m/z (%): 231 (2) [M–H]$^+$, 159 (23), 119 (71), 93 (10), 83 (49), 75 (100), 55 (31).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3349, 2959, 2929, 1462, 1374, 1253, 1066, 833, 772.

HRMS (EI): ***m/z*:** calcd for **$C_{12}H_{27}O_2Si^{+\bullet}$** [M–H]$^{+\bullet}$: 231.1780, found: 231.1776.

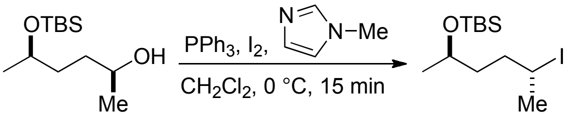


anti-**2-S1** *anti*-**2-S3**

anti-**2-S3** (CAS: 111490-76-7)

A dry and Ar-flushed *Schlenk*-flask was charged with NaH (0.88 g, 60wt%, 21.9 mmol) in THF (100 mL) and it was cooled down to 0 °C. *anti*-**2-S1** (2.5 g, 20.9 mmol) dissolved in THF (20 mL) was added dropwise for 5 min. The mixture was stirred at 0 °C to room temperature for 30 min. Then TBSCl (3.2 g, 20.9 mmol) was added and the mixture was stirred at room temperature for 48 h. The reaction was quenched with saturated NH_4Cl aqueous solution and the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/5 to afford *anti*-**2-S3** (4.2 g, 86% yield, d.r. = 99:1) as colorless oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.74-3.85 (m, 2H), 2.04 (s, 1H), 1.45-1.52 (m, 4H), 1.16 (d, *J* = 6.2 Hz, 3H), 1.12 (d, *J* = 6.1 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 6H).
^{13}C NMR ($CDCl_3$, 75 MHz) δ: 68.5, 67.8, 35.2, 34.9, 25.9, 23.5, 23.4, 18.1, –4.5, –4.8.
MS (EI, 70 eV) m/z (%): 231 (1) $[M–H]^+$, 159 (14), 83 (49), 75 (100), 73 (25), 55 (28).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3347, 2959, 2930, 1432, 1374, 1253, 1065, 833, 772.
HRMS (EI): ***m/z*:** calcd for $C_{12}H_{27}O_2Si^{+\bullet}$ $[M–H]^{+\bullet}$: 231.1780, found: 231.1758.



syn-**2-S3** *anti*-**2-1a**

***anti*-2-1a** (CAS: 1598405-79-2)[105]

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (24 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *syn*-**2-S3** (1.2 g, 5.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 15 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was

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[105] G. L. Lange, C. Gottardo, *Synth. Commun.* **1990**, *20*, 1473.

[106] Quenching with water or unsaturated ($NaHSO_4$+$Na_2S_2O_5$) aqueous solution sometimes cause epimerization of the product.

[107] Evaporation of higher temperature (>30 °C) sometimes causes epimerization of the product.

purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *anti*-**2-1a** (1.3 g, 77% yield, d.r. = 98:2) as colorless oil.

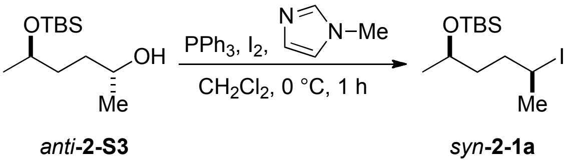
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 4.17-4.24 (m, 1H), 3.78-3.86 (m, 1H), 1.92 (d, *J* = 6.8 Hz, 3H), 1.49-1.71 (m, 4H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.05 (d, *J* = 2.6 Hz, 6H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 67.5, 39.2, 38.8, 30.6, 28.9, 25.9, 23.8, 18.1, −4.3, −4.8.

MS (EI, 70 eV) m/z (%): 341 (1) $[M-H]^+$, 285 (18), 159 (21), 83 (100), 75 (27), 55 (16).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956, 2928, 1375, 1253, 1074, 834, 772.

HRMS (EI): ***m/z*:** calcd for $\mathbf{C_{12}H_{26}O_2ISi^{+\bullet}}$ $[M-H]^{+\bullet}$: 341.0798, found: 341.0785.



***syn*-2-1a** (CAS: 1597405-80-5)[105]

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (24 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *anti*-**2-S3** (1.2 g, 5.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 15 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *syn*-**2-1a** (1.2 g, 71% yield, d.r. = 98:2) as colorless oil.

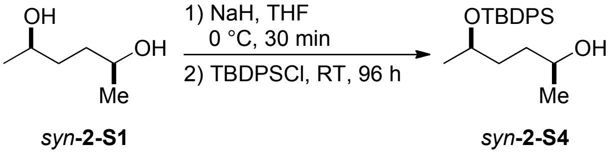
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 4.12-4.23 (m, 1H), 3.77-3.87 (m, 1H), 1.93 (d, *J* = 6.8 Hz, 3H), 1.75-1.81 (m, 2H), 1.47-1.62 (m, 2H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 67.9, 39.6, 39.3, 30.7, 29.2, 25.9, 23.8, 18.1, −4.4, −4.7.

MS (EI, 70 eV) m/z (%): 341 (1) $[M-H]^+$, 285 (25), 185 (72), 159 (35), 83 (62), 75 (100), 55 (33), 41 (15).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957, 2928, 1377, 1253, 1227, 1126, 1069, 834, 773.

HRMS (EI): ***m/z*:** calcd for $\mathbf{C_{12}H_{26}O_2ISi^{+\bullet}}$ $[M-H]^{+\bullet}$: 341.0798, found: 341.0756.



syn-**2-S4**

A dry and Ar-flushed *Schlenk*-flask was charged with NaH (0.34 g, 60wt%, 8.4 mmol) in THF (10 mL) and it was cooled down to 0 °C. *syn*-**2-S1** (0.95 g, 8.0 mmol) dissolved in THF (5 mL) was added dropwise for 5 min. The mixture was stirred at 0 °C to room temperature for 30 min. Then TBDPSCl (2.1 mL, 8.0 mmol) was added and the mixture was stirred at room temperature for 96 h. The reaction was quenched with saturated NH_4Cl aqueous solution and the reaction mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/1 to afford *syn*-**2-S4** (2.1 g, 74% yield, d.r. = 99:1) as colorless oil.

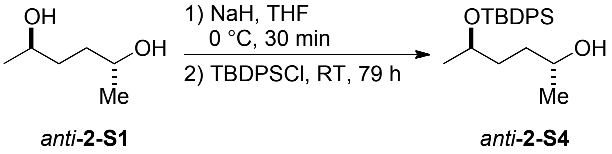
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.73-7.64 (m, 4H), 7.47-7.33 (m, 6H), 3.90 (h, J = 6.2 Hz, 1H), 3.77-3.62 (m, 1H), 1.63-1.38 (m, 4H), 1.13 (d, J = 6.2 Hz, 3H), 1.08 (d, J = 6.2 Hz, 3H), 1.06 (s, 9H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 136.04, 136.03, 134.7, 134.5, 129.73, 129.65, 127.7, 127.6, 69.7, 68.4, 35.7, 34.9, 27.2, 23.6, 23.0, 19.4.

MS (70 eV, EI) *m/z* (%): 299 (4) $[M-{}^t\mathrm{Bu}]^{+\bullet}$, 281 (4), 243 (4), 199 (100), 181 (10), 139 (31), 135 (9), 83 (50), 55 (27).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3348 (br w), 2964 (w), 2930 (w), 2858 (w), 1472 (w), 1462 (w), 1428 (w), 1376 (w), 1362 (w), 1104 (m), 1064 (m), 1023 (w), 997 (w), 976 (w), 937 (w), 880 (w), 843 (w), 821 (w), 778 (w), 739 (w), 700 (vs), 687 (m).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{18}H_{23}O_2Si^{+\bullet}}$ $[M-{}^t\mathrm{Bu}]^{+\bullet}$: 299.1476, found: 299.1471.



anti-**2-S4**

A dry and Ar-flushed *Schlenk*-flask was charged with NaH (0.34 g, 60wt%, 8.4 mmol) in THF (10 mL) and it was cooled down to 0 °C. *anti*-**2-S1** (0.95 g, 8.0 mmol) dissolved in THF (5 mL) was added dropwise for 5 min. The mixture was stirred at 0 °C to room temperature for 30 min. Then TBDPSCl (2.1 mL, 8.0 mmol) was added and the mixture was stirred at room temperature for 79 h. The reaction was quenched with saturated NH_4Cl aqueous solution and the reaction mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/1 to afford *anti*-**2-S4** (2.1 g, 74% yield, d.r. = 99:1) as colorless oil.

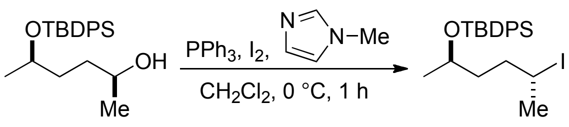
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.73-7.65 (m, 4H), 7.46-7.34 (m, 6H), 3.90 (qt, J = 5.7 and 5.4 Hz, 1H), 3.70 (qt, J = 5.8 and 5.6 Hz, 1H), 1.75-1.40 (m, 4H), 1.13 (d, J = 6.2 Hz, 3H), 1.08 (d, J = 6.2 Hz, 3H), 1.07 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 136.01, 135.98, 134.8, 134.5, 129.7, 129.6, 127.7, 127.6, 69.5, 68.1, 35.2, 34.6, 27.2, 23.5, 23.2, 19.4.

MS (70 eV, EI) *m/z* (%): 299 (2) $[M-{}^tBu]^{+\bullet}$, 281 (5), 243 (5), 199 (100), 181 (13), 139 (26), 135 (9), 83 (48), 55 (26).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3342 (br w), 2964 (w), 2931 (w), 2858 (w), 1472 (w), 1462 (w), 1428 (w), 1376 (w), 1362 (w), 1149 (w), 1131 (w), 1104 (m), 1063 (m), 1043 (w), 998 (w), 977 (w), 939 (w), 880 (w), 844 (w), 821 (w), 779 (w), 738 (w).

HRMS (EI) *m/z*: calcd for $C_{18}H_{23}O_2Si^{+\bullet}$ $[M-{}^tBu]^{+\bullet}$: 299.1476, found: 299.1458.

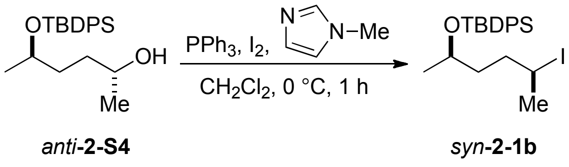


syn-**2-S4** *anti*-**2-1b**

anti-**2-1b**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.9 g, 7.4 mmol) in CH_2Cl_2 (60 mL) and cooled to 0 °C. PPh_3 (2.0 g, 7.4 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.59 mL, 7.4 mmol) was added. After 10 min of further stirring, *syn*-**2-S4** (2.2 g, 6.2 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/3. The precipitate was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *anti*-**2-1b** (2.5 g, 85% yield, d.r. = 99:1) as colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.77-7.65 (m, 4H), 7.50-7.35 (m, 6H), 4.08 (qt, *J* = 7.0 and 6.9 Hz, 1H), 3.91 (qt, *J* = 6.5 and 5.4 Hz, 1H), 1.87 (d, *J* = 6.9 Hz, 3H), 1.95-1.78 (m, 1H), 1.74-1.60 (m, 2H), 1.60-1.45 (m, 1H), 1.11 (d, *J* = 6.2 Hz, 3H), 1.09 (s, 9H).
^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 135.99, 135.96, 134.7, 134.3, 129.7, 129.6, 127.7, 127.6, 68.6, 39.3, 38.3, 30.8, 29.1, 27.2, 23.5, 19.4.
MS (70 eV, EI) *m/z* (%): 409 (4) $[M-{}^tBu]^{+\bullet}$, 353 (4), 309 (34), 281 (6), 249 (13), 199 (33), 181 (12), 135 (10), 83 (100), 55 (17).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2963 (w), 2930 (w), 2857 (w), 1472 (w), 1461 (w), 1444 (w), 1427 (w), 1377 (w), 1362 (w), 1223 (w), 1110 (m), 1072 (w), 1052 (w), 997 (w), 937 (w), 877 (w), 822 (w), 739 (w), 700 (w), 686 (w).
HRMS (EI) *m/z*: calcd for $\mathbf{C_{18}H_{22}OISi^{+\bullet}}$ $[M-{}^tBu]^{+\bullet}$: 409.0485, found: 409.0488.



syn-**2-1b**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.8 g, 7.1 mmol) in CH_2Cl_2 (60 mL) and cooled to 0 °C. PPh_3 (1.9 g, 7.1 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.56 mL, 7.1 mmol) was added. After 10 min of further stirring, *anti*-**2-S4** (2.1 g, 5.9 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/3. The precipitate was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was

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[108] Removal of triphenyl phosphine oxide before column chromatography is recommended to get higher yield of the product by washing and filtering the crude product with Et_2O/hexane mixture. Please look at the other procedures described below.

purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *syn*-**2-1b** (2.1 g, 77% yield, d.r. = 97:3) as colorless oil.

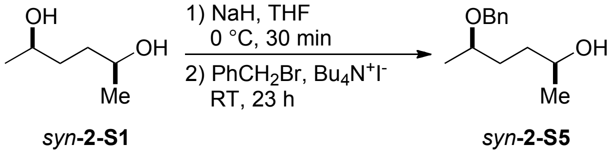
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.73-7.66 (m, 4H), 7.46-7.35 (m, 6H), 4.11 (qt, *J* = 6.9 and 6.5 Hz, 1H), 3.88 (qt, *J* = 6.7 and 5.6 Hz, 1H), 1.86 (d, *J* = 6.8 Hz, 3H), 1.83-1.46 (m, 4H), 1.08 (d, *J* = 6.5 Hz, 3H), 1.07 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 136.01, 136.00, 134.8, 134.4, 129.7, 129.6, 127.7, 127.6, 69.0, 39.4, 38.8, 30.8, 29.0, 27.2, 23.5, 19.4.

MS (70 eV, EI) *m/z* (%): 409 (8) $[M-{}^tBu]^{+\bullet}$, 353 (5), 309 (37), 281 (7), 249 (16), 199 (36), 181 (14), 135 (10), 83 (100), 55 (30).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2962 (w), 2930 (w), 2857 (w), 1472 (w), 1461 (w), 1444 (w), 1427 (w), 1377 (w), 1361 (w), 1223 (w), 1171 (w), 1127 (w), 1104 (m), 1066 (m), 996 (m), 938 (w), 899 (w), 877 (w), 822 (w), 739 (m), 700 (w), 686 (w), 612 (m).

HRMS (EI) *m/z*: calcd for $C_{18}H_{22}OISi^{+\bullet}$ $[M-{}^tBu]^{+\bullet}$: 409.0485, found: 409.0477.



syn-**2-S5** (CAS: 114142-15-3)

A dry and Ar-flushed *Schlenk*-flask was charged with NaH (0.28 g, 60wt%, 7.1 mmol) in THF (10 mL) and it was cooled down to 0 °C. *syn*-**2-S1** (0.80 g, 6.8 mmol) dissolved in THF (5 mL) was added dropwise for 5 min. The mixture was stirred at 0 °C to room temperature for 30 min. After cooling the reaction mixture to 0 °C, benzyl bromide (0.80 mL, 6.8 mmol) and $Bu_4N^+I^-$ (2.5 g, 6.8 mmol) were added successively and the mixture was stirred at room temperature for 48 h. The reaction was quenched with saturated NH_4Cl aqueous solution and the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/3 to afford *syn*-**2-S5** (1.4 g, 96% yield, d.r. = 99:1) as colorless oil.

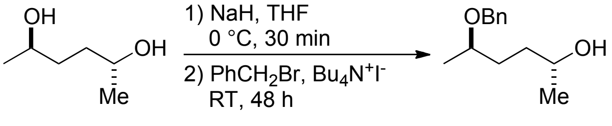
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.36-7.23 (m, 5H), 4.59 (d, *J* = 11.7 Hz, 1H), 4.45 (d, *J* = 11.7 Hz, 1H), 3.84-3.70 (m, 1H), 3.62-3.50 (m, 1H), 2.00 (br s, 1H), 1.74-1.49 (m, 4H), 1.22 (d, *J* = 6.1 Hz, 3H), 1.18 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 138.9, 128.5, 127.9, 127.7, 75.0, 70.5, 68.2, 35.4, 33.1, 23.7, 19.6.

MS (70 eV, EI) *m/z* (%): 190 (1) $[M–H_2O]^{+\bullet}$, 135 (3), 107 (12), 91 (100), 65 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3391 (br s), 2967 (w), 2930 (w), 2865 (w), 1496 (w), 1454 (w), 1373 (w), 1341 (w), 1249 (w), 1206 (w), 1150 (w), 1228 (w), 1089 (m), 1066 (s), 1028 (m), 932 (w), 847 (w), 733 (s), 696 (vs).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{13}H_{18}O^{+\bullet}}$ $[M–H_2O]^{+\bullet}$: 190.1358, found: 190.1348.



anti-**2-S1** *anti*-**2-S5**

anti-**2-S5** (CAS: 114142-14-2)

A dry and Ar-flushed *Schlenk*-flask was charged with NaH (0.29 g, 60wt%, 7.3 mmol) in THF (15 mL) and it was cooled down to 0 °C. *anti*-**2-S1** (0.82 g, 6.9 mmol) dissolved in THF (10 mL) was added dropwise for 5 min. The mixture was stirred at 0 °C to room temperature for 30 min. After cooling the reaction mixture to 0 °C, benzyl bromide (0.82 mL, 6.9 mmol) and $Bu_4N^+I^-$ (2.6 g, 6.9 mmol) were added successively and the mixture was stirred at room temperature for 23 h. The reaction was quenched with saturated NH_4Cl aqueous solution and the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/3 to afford *anti*-**2-S5** (1.2 g, 86% yield, d.r. = 99:1) as colorless oil.

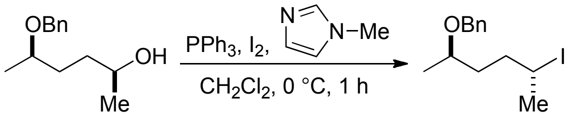
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.41-7.26 (m, 5H), 4.61 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H), 3.86-3.73 (m, 1H), 3.59 (qt, *J* = 6.1 and 5.8 Hz, 1H), 2.32 (br s, 1H), 1.70-1.47 (m, 4H), 1.24 (d, *J* = 6.1 Hz, 3H), 1.20 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 138.8, 128.5, 127.8, 127.6, 75.0, 70.5, 68.0, 35.2, 33.0, 23.6, 19.6.

MS (70 eV, EI) *m/z* (%): 190 (1) $[M–H_2O]^{+\bullet}$, 135 (3), 107 (12), 91 (100), 65 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3391 (br s), 2967 (w), 2930 (w), 2865 (w), 1496 (w), 1454 (w), 1373 (w), 1341 (w), 1252 (w), 1206 (w), 1126 (m), 1089 (m), 1066 (s), 1028 (m), 937 (w), 844 (w), 733 (s), 696 (vs).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{13}H_{18}O^{+\bullet}}$ $[M–H_2O]^{+\bullet}$: 190.1358, found: 190.1348.



syn-**2-S5** *anti*-**2-1c**

anti-**2-1c**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.9 g, 7.2 mmol) in CH_2Cl_2 (60 mL) and cooled to 0 °C. PPh_3 (1.8 g, 7.2 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.57 mL, 7.2 mmol) was added. After 10 min of further stirring, *syn*-**2-S5** (1.3 g, 6.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/3. The precipitation was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/20 to afford *anti*-**2-1c** (0.62 g, 32% yield, d.r. = 97:3) as colorless oil.

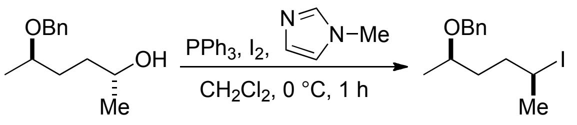
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.40-7.26 (m, 5H), 4.58 (d, J = 11.7 Hz, 1H), 4.46 (d, J = 11.7 Hz, 1H), 4.16 (qt, J = 6.8 and 6.6 Hz, 1H), 3.54 (qt, J = 6.1 and 5.9 Hz, 1H), 1.93 (d, J = 6.8 Hz, 3H), 1.86-1.56 (m, 4H), 1.20 (d, J = 6.1 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 138.9, 128.5, 127.8, 127.6, 74.2, 70.5, 39.1, 37.0, 31.1, 29.2, 19.8

MS (70 eV, EI) *m/z* (%): 182 (1), 173 (1), 128 (2), 92 (8), 91 (100), 55 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2967 (w), 2915 (w), 2862 (w), 1496 (w), 1453 (w), 1375 (w), 1340 (w), 1259 (w), 1224 (w), 1173 (w), 1128 (m), 1087 (m), 1068 (s), 1028 (m), 982 (w), 918 (w), 733 (s), 696 (vs).

LRMS (EI) *m/z*: calcd for **$C_4H_9I^{+\bullet}$** [M–BnEt]$^{+\bullet}$: 182.96, found: 182.19.



anti-**2-S5** *syn*-**2-1c**

syn-**2-1c**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.7 g, 6.6 mmol) in CH_2Cl_2 (60 mL) and cooled to 0 °C. PPh_3 (1.7 g, 6.6 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.52 mL, 6.6 mmol) was added. After 10 min of further stirring, *anti*-**2-S5** (1.2 g, 5.9 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/3. The precipitation was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/20 to afford *syn*-**2-1c** (1.1 g, 62% yield, d.r. = 97:3) as colorless oil.

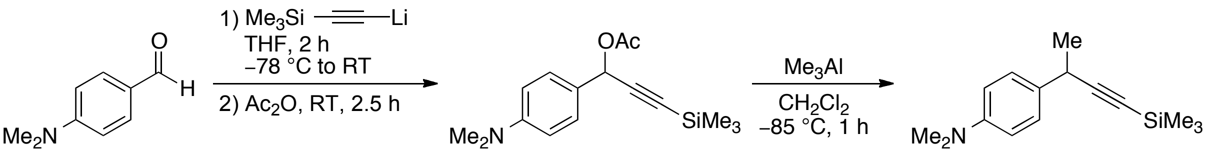
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.42-7.27 (m, 5H), 4.61 (d, *J* = 11.8 Hz, 1H), 4.46 (d, *J* = 11.8 Hz, 1H), 4.17 (qt, *J* = 7.0 and 6.4 Hz, 1H), 3.58 (qt, *J* = 6.1 and 6.0 Hz, 1H), 2.03-1.92 (m, 1H), 1.93 (d, *J* = 6.9 Hz, 3H), 1.86-1.57 (m, 4H), 1.25 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 138.9, 128.5, 127.8, 127.6, 73.6, 70.4, 38.5, 36.5, 30.8, 29.1, 19.7

MS (70 eV, EI) *m/z* (%): 197 (4), 182 (1), 105 (20), 91 (100), 77 (21), 51 (8).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2967 (w), 2930 (w), 2862 (w), 1496 (w), 1452 (w), 1375 (w), 1340 (w), 1258 (w), 1224 (w), 1175 (w), 1124 (m), 1087 (m), 1068 (s), 1028 (m), 984 (w), 921 (w), 897 (w), 733 (s), 696 (vs).

LRMS (EI) *m/z*: calcd for **$C_4H_9I^{+\bullet}$** [M–BnEt]$^{+\bullet}$: 182.96, found: 182.19.



2-S6 2-S7 2-S8

2-S8 (CAS: 1597406-15-9)[109]

^{n}BuLi (31 mL, 2.3 M in *n*-hexane, 70.0 mmol) was added dropwise to a solution of TMS-acetylene (9.9 mL, 70.0 mmol) in THF (80 mL) at –78 °C under Ar atmosphere and the mixture was stirred at this temperature for 1 h. A solution of **2-S6** (10.4 g, 70.0 mmol) in THF

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[109] G. A. Kraus, I. Jeon, *Org. Lett.* **2006**, *8*, 5315.

(35 mL) was added. It was stirred at –78 °C for 30 min and it was warmed up to room temperature gradually for 1.5 h. After it was cooled down to 0 °C, acetic anhydride (7.0 mL, 73.5 mmol) was added and it was stirred and warmed up to room temperature for 2.5 h. The reaction was quenched with H_2O and the mixture was extracted with EtOAc. The combined organic phase was dried over $MgSO_4$. After filtration, the solvent was removed under vacuum. The obtained crude product containing **2-S7** was dissolved in CH_2Cl_2 (220 mL) under Ar atmosphere and it was cooled to –85 °C. Me_3Al (26.1 mL, 136.0 mmol) was added dropwise over 15 min and it was stirred at this temperature for 1 h. The reaction was poured into ice-cold water (300 mL) very slowry. The resulting foam was filttered off with Celite. The solution was extraced with CH_2Cl_2 and the foam was also washed with CH_2Cl_2 many times. The combined organic phase was dried over $MgSO_4$. After filtration, the solvent was removed under vacuum. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/6 to afford **2-S8** (10.4 g, 61% yield over 2 steps) as yellow oil.

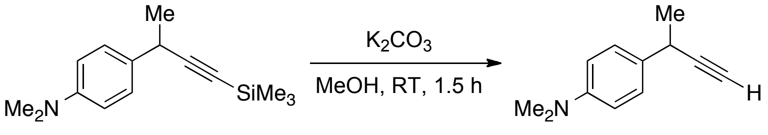
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.29 (d, J = 7.9 Hz, 2H), 6.77 (d, J = 8.1 Hz, 2H), 3.76 (q, J = 7.0 Hz, 1H), 2.97 (s, 6H), 1.50 (d, J = 7.1 Hz, 3H), 0.23 (s, 9H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 149.4, 131.1, 127.4, 112.8, 110.4, 85.4, 40.8, 31.8, 24.6, 0.2.

MS (EI, 70 eV) m/z (%): 245 (35) $[M]^{+\bullet}$, 230 (100), 215 (3), 202 (16), 186 (4), 172 (12), 156 (4), 148 (16), 128 (5), 115 (11), 107 (31), 99 (7), 91 (5), 73 (9), 59 (3).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2797 (w), 2163 (w), 1615 (w), 1519 (s), 1480 (w), 1444 (w), 1344 (w), 1248 (s), 1163 (w), 1095 (w), 947 (w), 916 (w), 837 (vs), 814 (s), 757 (m), 696 (w), 654 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{23}NSi^{+\bullet}$** $[M]^{+\bullet}$: 245.1600, found: 245.1600.



2-S8

2-S9

2-S9 (CAS: 159706-16-0)

K_2CO_3 (8.4 g, 61.1 mmol) was added to a solution of **2-S8** (10.0 g, 40.7 mmol) in MeOH (150 mL) and it was stirred at room temperature for 1.5 h. Unsolved solid was filtered off and MeOH was reduced by evaporation. Then H_2O and EtOAc were added. The reaction mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$.

After filtration, the solvent was removed under vacuum. The analytically pure product was obtained (90% yield) as orange oil.

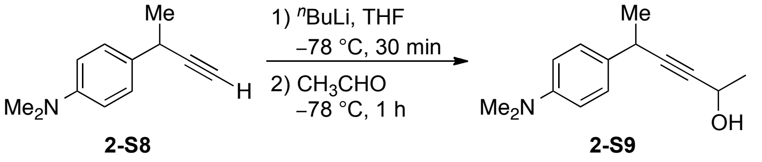
^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 7.28 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 8.5 Hz, 2H), 3.72 (qd, *J* = 7.0 and 2.1 Hz, 1H), 2.95 (s, 6H), 2.25 (d, *J* = 1.9 Hz, 1H) 1.51 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 149.5, 130.7, 127.4, 112.9, 87.9, 69.5, 40.8, 40.8, 30.6, 24.4.

MS (EI, 70 eV) m/z (%): 173 (32) $[M]^{+\bullet}$, 158 (100), 142 (15), 128 (7), 115 (11), 102 (3), 89 (3), 78 (5), 63 (3), 51 (3).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3290 (w), 2973 (w), 2871 (w), 2799 (w), 1614 (m), 1518 (vs), 1479 (w), 1444 (w), 1344 (w), 1223 (w), 1205 (w), 1187 (w), 1163 (w), 1129 (w), 1057 (w), 946 (m), 815 (s), 731 (w).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{15}N^{+\bullet}$** $[M]^{+\bullet}$: 173.1204, found: 173.1190.



2-S9[110]

To a solution of **2-S8** (6.3 g, 36.5 mmol) in THF (100 mL) was slowly added ^{n}BuLi (16.2 mL, 2.5 M in *n*-hexane, 40.1 mmol) at –78 °C. The reaction mixture was stirred for 30 min. Acetaldehyde (2.7 mL, 47.5 mmol) was added and the mixture was stirred for 1 h at –78 °C. After completion of the reaction, saturated NH_4Cl aqueous solution was added and the mixture was extracted with Et_2O three times. The combined organic phase was washed with water and brine, and dried over $MgSO_4$. After filtration, the solvent was evaporated and the crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 3:17 to afford **2-S9** (6.4 g, 81% yield) as colorless oil and as a 1:1 mixture of diastereomers.

^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 7.24 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 8.7 Hz, 2H), 4.57 (q, *J* = 6.4 Hz, 1H), 3.71 (q, *J* = 6.7 Hz, 1H), 2.93 (s, 6H), 1.46 (d, *J* = 6.3 Hz, 3H) 1.45 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 149.4, 131.4, 127.4, 113.0, 87.8, 83.6, 58.6, 40.9, 30.7, 24.7, 24.3.

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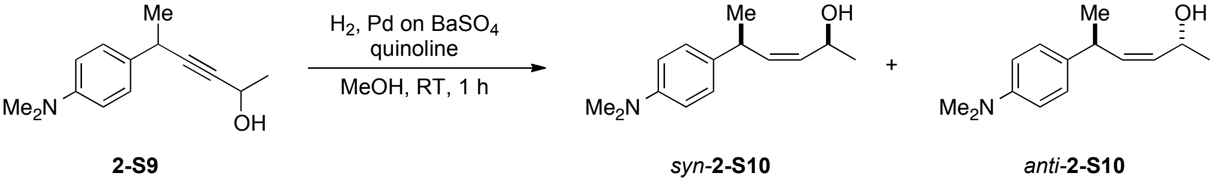
[110] T. Schwier, M. Rubin, V. Gevorgyan, *Org. Lett.* **2004**, *6*, 1999.

MS (EI, 70 eV) m/z (%): 217 (67) $[M]^{+\bullet}$, 202 (71), 187 (14), 173 (16), 158 (100), 144 (23), 134 (6), 128 (16), 121 (9), 115 (25), 102 (5), 91 (8), 85 (4), 77 (10), 63 (6), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3342, 2973, 2928, 2868, 2798, 1613, 1518, 1477, 1444, 1333, 1223, 1205, 1188, 1165, 1089, 1043, 999, 944, 878, 816, 725.

HRMS (EI) *m/z*: calcd for **$C_{14}H_{19}NO^{+\bullet}$** $[M]^{+\bullet}$: 217.1467, found: 217.1459.



2-S10[111]

To a solution of **2-S9** (4.3 g, 19.8 mmol) in MeOH (60 mL) was added quinoline (2.3 mL, 19.8 mmol) and Pd on $BaSO_4$ (0.22 g, Alfa Aesar) at room temperature. H_2 was bubbled into the reaction for 10 min, and the reaction was stirred at room temperature for 1 h under H_2 atmosphere. The reaction mixture was concentrated and the crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 3/17 to afford *syn*-**2-S10** (1.8 g, 40% yield, d.r. = 97:3) as the first eluent and *anti*-**2-S10** (1.3 g, 29% yield, d.r. = 97:3) as the second eluent and their mixture (combined yield: 95%).

syn-**2-S10** (CAS: 1597406-24-0)

^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.10 (d, J = 8.7 Hz, 2H), 6.73 (d, J = 8.7 Hz, 2H), 5.56 (t, J = 10.5 Hz, 1H), 5.40 (dd, J = 8.8 Hz, J = 10.6 Hz, 1H), 4.73-4.82 (m, 1H), 3.72-3.82 (m, 1H), 2.93 (s, 6H), 1.77 (s, 1H), 1.36 (d, J = 6.9 Hz, 3H), 1.22 (d, J = 6.3 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 149.2, 136.5, 134.0, 131.8, 127.3, 113.1, 64.1, 40.8, 36.6, 23.7, 22.6.

MS (EI, 70 eV) m/z (%): 219 (17) $[M]^{+\bullet}$, 204 (11), 186 (22), 171 (16), 162 (14), 148 (60), 134 (10), 128 (6), 121 (100), 115 (11), 104 (5), 91 (9), 77 (12), 65 (5), 51 (4).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3358, 2965, 2872, 2800, 1613, 1518, 1446, 1346, 1059, 909, 817, 728.

HRMS (EI) *m/z*: calcd for **$C_{14}H_{21}NO^{+\bullet}$** $[M]^{+\bullet}$: 219.1623, found 219.1615.

anti-**2-S10** (CAS: 1597406-25-1)

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[111] a) K. A. Tallman, B. Roschek, N. A. Porter, *J. Am. Chem. Soc.* **2004**, *126*, 9240; b) R. L. Augustine, *Heterogeneous Catalysis for the Synthetic Chemist,* Marcel Dekker, New York, **1995**.

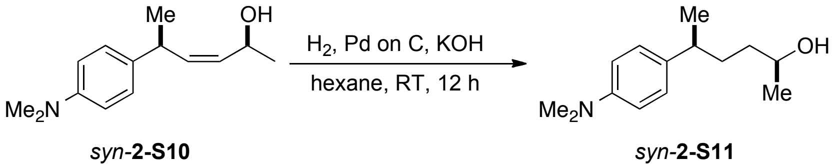
^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 7.14 (d, *J* = 8.7 Hz, 2H), 6.72 (d, *J* = 8.6 Hz, 2H), 5.57 (t, *J* = 10.3 Hz, 1H), 5.40 (dd, *J* = 8.7 Hz, *J* = 10.7 Hz, 1H), 4.73-4.79 (m, 1H), 3.71-3.80 (m, 1H), 2.92 (s, 6H), 1.51 (s, 1H), 1.31 (d, *J* = 7.0 Hz, 3H), 1.28 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 149.2, 136.7, 134.1, 132.0, 127.3, 113.1, 63.9, 40.8, 36.6, 23.6, 22.5.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3359, 2964, 2872, 2800, 1613, 1519, 1446, 1345, 1058, 909, 817, 729.

MS (EI, 70 eV) m/z (%): 219 (37) [M]$^{+\bullet}$, 204 (21), 186 (37), 171 (24), 162 (19), 148 (39), 134 (10), 121 (100), 115 (8), 104 (5), 91 (6), 77 (7), 65 (3), 51 (3).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{21}NO^{+\bullet}$** [M]$^{+\bullet}$: 219.1623, found: 219.1611.



syn-**2-S11** (CAS: 1597406-31-9)[112]

To a solution of *syn*-**2-S10** (2.0 g, 9.1 mmol) in *n*-hexane (50 mL) was added KOH (0.13 g, 2.3 mmol) and Pd on activated charcoal (0.40 g, Acros) at room temperature. Then H_2 was bubbled into the reaction for 10 min and the reaction mixture was stirred at room temperature for 12 h. After filtration of the catalyst through silica gel, the solvent was evaporated. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 3/7 to afford *syn*-**2-S11** (1.6 g, 80% yield, d.r. = 97:3) as colorless oil.

^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 7.08 (d, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 8.6 Hz, 2H), 3.69-3.78 (m, 1H), 2.93 (s, 1H), 2.58-2.66 (m, 1H), 1.52-1.69 (m, 3H), 1.34-1.41 (m, 2H), 1.24 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 149.1, 135.6, 127.5, 113.0, 68.2, 40.9, 38.9, 37.5, 34.5, 23.4, 22.6.

MS (EI, 70 eV) m/z (%): 221 (12) [M]$^{+\bullet}$, 206 (3), 188 (2), 148 (100), 132 (5), 120 (4), 104 (3), 91 (3), 77 (3).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3364, 2961, 2928, 2858, 1615, 1520, 1343, 1138, 946, 816, 732.

HRMS (EI) *m/z*: calcd for **$C_{14}H_{23}NO^{+\bullet}$** [M]$^{+\bullet}$: 221.1780, found: 221.1799.

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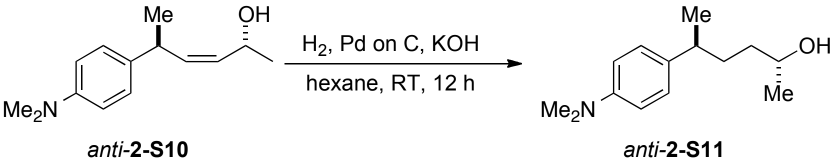
[112] a) R. J. Tedeschi, *J. Org. Chem.* **1962**, *27*, 2398; b) R. J. Tedeschi, G. Clark, *J. Org. Chem.* **1962**, *27*, 4323.



anti-**2-S11** (CAS: 1597406-30-8)[112]

To a solution of *anti*-**2-S10** (2.2 g, 10.1 mmol) in *n*-hexane (50 mL) was added KOH (0.13 g, 2.3 mmol) and Pd on activated charcoal (0.40 g, Acros) at room temperature. Then H_2 was bubbled into the reaction for 10 min and the reaction mixture was stirred at room temperature for 12 h. After filtration of the catalyst through silica gel, the solvent was evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 3/7 to afford *anti*-**2-S11** (2.1 g, 92% yield, d.r. = 93:7) as colorless oil.

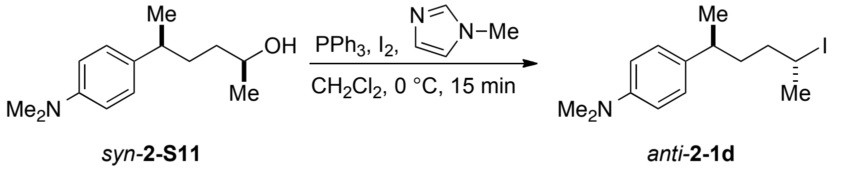
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.08 (d, J = 8.6 Hz, 2H), 6.72 (d, J = 8.7 Hz, 2H), 3.70-3.78 (m, 1H), 2.93 (s, 1H), 2.56-2.64 (m, 1H), 1.61-1.71 (m, 1H), 1.49-1.58 (m, 2H), 1.31-1.45 (m, 2H), 1.24 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 6.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 149.1, 135.7, 127.5, 113.0, 68.3, 40.9, 39.0, 37.6, 34.7, 23.4, 22.6.

MS (EI, 70 eV) m/z (%): 221 (20) $[M]^{+\bullet}$, 206 (3), 188 (3), 160 (2), 148 (100), 132 (5), 120 (3).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3362, 2966, 2928, 2856, 1615, 1520, 1435, 1372, 1253, 1143, 1053, 971, 826, 733, 690.

HRMS (EI) *m/z*: calcd for **$C_{14}H_{23}NO^{+\bullet}$** $[M]^{+\bullet}$: 221.1780, found: 221.1777.



anti-**2-1d** (CAS: 1597406-18-2)

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (24 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *syn*-**2-S11** (0.90 g, 5.0 mmol, d.r. = 97:3) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 15 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 3/97 to afford *anti*-**2-1d** (1.1 g, 82% yield, d.r. = 96:4) as colorless oil.

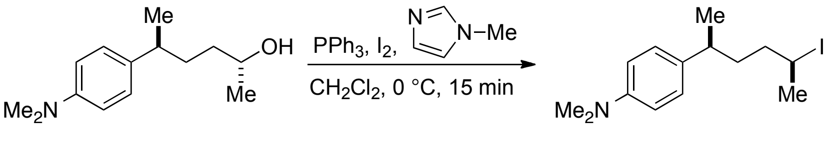
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.07 (d, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 8.7 Hz, 2H), 4.10-4.16 (m, 1H), 2.94 (s, 6H), 2.58-2.68 (m, 1H), 1.88 (d, *J* = 6.8 Hz, 3H), 1.72-1.82 (m, 2H), 1.60-1.69 (m, 1H), 1.48-1.56 (m, 1H), 1.24 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 149.1, 135.3, 127.4, 113.0, 41.2, 40.9, 38.7, 38.5, 31.1, 29.0, 22.5.

MS (EI, 70 eV) m/z (%): 331 (14) $[M]^{+\bullet}$, 216 (1), 148 (100), 147 (13), 128 (10), 71 (12), 57 (24), 44 (21).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955, 2865, 1614, 1519, 1443, 1344, 1130, 947, 815.

HRMS (EI) *m/z*: calcd for $C_{14}H_{22}IN^{+\bullet}$ $[M]^{+\bullet}$: 331.0797, found: 331.0783.



anti-**2-S11** *syn*-**2-1d**

syn-**2-1d** (CAS: 1597406-19-3)

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (24 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *anti*-**2-S11** (0.90 g, 5.0 mmol, d.r. = 93:7) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 15 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 3/97 to afford *syn*-**2-1d** (1.2 g, 87% yield, d.r. = 92:8) as colorless oil.

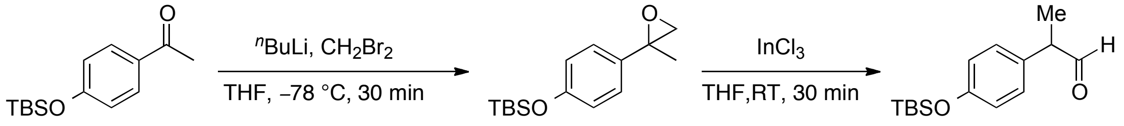
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.07 (d, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 8.7 Hz, 2H), 4.12-4.21 (m, 1H), 2.94 (s, 6H), 2.59-2.68 (m, 1H), 1.87 (d, *J* = 6.8 Hz, 3H), 1.64-1.80 (m, 3H), 1.50-1.58 (m, 1H), 1.24 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 149.1, 134.9, 127.5, 112.9, 40.9, 40.9, 38.2, 38.2, 31.0, 28.9, 23.0.

MS (EI, 70 eV) m/z (%): 331 (24) $[M]^{+\bullet}$, 148 (100), 147 (14), 134 (12), 84 (14), 71 (20), 57 (40), 55 (21), 43 (18).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955, 2920, 2866, 1614, 1519, 1443, 1344, 1132, 947, 815.

HRMS (EI) *m/z*: calcd for $\mathbf{C_{14}H_{22}IN^{+\bullet}}$ $[M]^{+\bullet}$: 331.0797, found: 331.0784.



2-S12 **2-S13** **2-S14**

2-S14 (CAS: 1424343-28-1)[113],[114]

^{n}BuLi (1.6 mL, 2.3 M in *n*-hexane, 3.6 mmol) was added dropwise for 15 min to a mixture of **2-S12** (0.75 g, 3.0 mmol, CAS: 149683-53-4) and CH_2Br_2 (0.27 mL, 3.9 mmol) in THF (15 mL) at –78 °C. The reaction mixture was warmed up to room temperature gradually and it was stirred for 30 min. Then the reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$. After filtration, the solvent was evaporated. The obtained crude product containing **2-S13** was dissolved in THF (3 mL) and this was added to a solution of $InCl_3$ (0.40 g, 1.8 mmol) in THF (4.5 mL) under Ar atmosphere. The reaction was stirred at room temperature for 30 min. Then saturated NH_4Cl aqueous solution was added to the reaction mixture and it was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$. After filtration, the solvent was evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/5 to afford **2-S14** (0.51 g, 64 % yield over 2 steps) as colorless oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 9.65 (s, 1H), 7.07 (d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 2H), 3.57 (q, *J* = 7.1 Hz, 1H), 1.41 (d, *J* = 7.1 Hz, 3H), 0.99 (s, 9H), 0.21 (s, 6H).

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[113] G. Cainell, N. Tangari, A. Umani Ronchi, *Tetrahedron* **1972**, *28*, 3009.

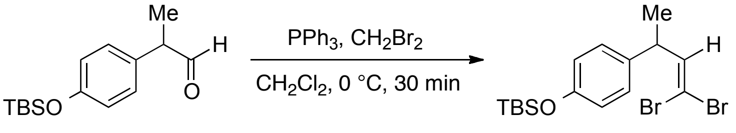
[114] B. C. Ranu, U. Jana, *J. Org. Chem.* **1998**, *63*, 8216.

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 201.2, 155.1, 130.1, 129.3, 120.6, 52.2, 25.7, 18.2, 14.6, –4.4.

MS (EI, 70 eV) m/z (%): 264 (11) $[M]^{+\bullet}$, 235 (100), 207 (68), 179 (9), 163 (9), 163 (9), 151 (4), 135 (4), 121 (5), 103 (3), 89 (3), 73 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955, 2929, 2857, 1721, 1606, 1509, 1472, 1463, 1252, 1173, 910, 833, 824, 807, 779, 691.

HRMS (EI) *m/z*: calcd for $C_{15}H_{24}O_2Si^{+\bullet}$ $[M]^{+\bullet}$: 264.1538, found: 264.1546.



2-S14 **2-S15**

2-S15 (CAS: 1597496-17-1)

2-S14 (9.2 g, 35.0 mmol) and PPh$_3$ (22.0 g, 84.0 mmol) was dissolved in CH$_2$Cl$_2$ (150 mL) and the solution was cooled to 0 °C. To this mixture a solution of CBr$_4$ (13.9 g, 42.0 mmol) in CH$_2$Cl$_2$ (75 mL) was added dropwise for 5 min. The yellow solution was warmed up to room temperature and stirred for 30 min. The reaction mixture was diluted with Et$_2$O and the resulting suspension was washed with H$_2$O and brine before the organic phase was dried over MgSO$_4$. Removal of volatile materials under reduced pressure and the crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/10→1/5 to afford **2-S15** (12.1 g, 82% yield) as colorless oil.

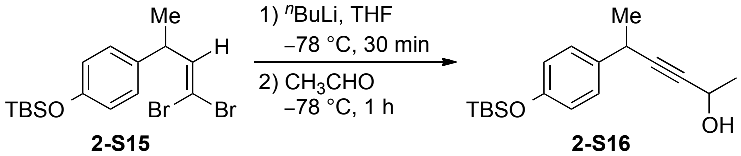
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.09 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 8.5 Hz, 2H), 6.47 (d, J = 9.5 Hz, 1H), 3.70 (qd, J = 9.4 and 7.1 Hz, 1H), 1.36 (d, J = 7.0 Hz, 3H), 0.99 (s, 9H), 0.20 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 154.4, 143.2, 135.5, 127.8, 120.1, 88.0, 42.6, 25.7, 20.1, 18.2, –4.4.

MS (EI, 70 eV) m/z (%): 418 (16) $[M]^{+\bullet}$, 405 (3), 363 (100), 349 (7), 283 (5), 259 (27), 235 (16), 213 (91), 201 (19), 193 (7), 177 (11), 151 (45), 133 (20), 115 (10), 101 (8), 73 (34), 57 (7).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955, 2928, 2857, 1606, 1508, 1471, 1462, 1252, 1171, 911, 831, 803, 778, 758, 688.

HRMS (EI) *m/z*: calcd for $C_{16}H_{24}Br_2OSi^{+\bullet}$ $[M]^{+\bullet}$: 417.9963, found: 417.9957.



2-S16[110]

To a solution of **2-S15** (11.6 g, 28.7 mmol) in THF (1.6 mL) was added ^{n}BuLi (26.7 mL, 2.3 M in *n*-hexane, 60.3 mmol) dropwise at –78 °C. After stirring for 30 min at –78 °C, acetaldehyde (3.2 mL, 57.4 mmol) was added to it. The reaction mixture was stirred at –78 °C for 1 h. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was subsequently extracted with EtOAc three times. The combined organic layers were dried over $MgSO_4$. After filtration, the solvent was evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/5 to afford **2-S16** (6.7 g, 77% yield) as colorless oil and 1:1 mixture of diastereomers.

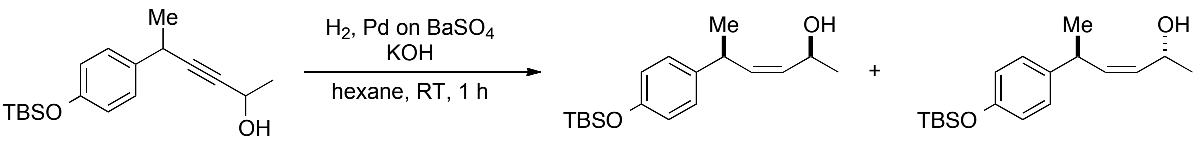
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.20 (d, J = 8.5 Hz, 2H), 6.77 (d, J = 8.5 Hz, 2H), 4.52-4.62 (m, 1H), 3.66-3.76 (m, 1H), 1.53 (s, 1H), 1.46 (d, J = 4.4 Hz, 3H), 1.43 (d, J = 4.9 Hz, 3H), 0.98 (s, 9H), 0.19 (s, 6H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 154.3, 135.7, 127.7, 120.0, 87.5, 83.9, 58.6, 31.0, 25.7, 24.7, 24.4, 18.2, –4.4.

MS (EI, 70 eV) m/z (%): 304 (51) $[M]^{+\bullet}$, 275 (84), 235 (36), 229 (100), 214 (30), 193 (38), 151 (23), 73 (87), 43 (46).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3353, 2957, 2931, 1679, 1597, 1508, 1252, 1168, 910, 835, 779.

HRMS (EI) *m/z*: calcd for $C_{18}H_{28}O_2Si^{+\bullet}$ $[M]^{+\bullet}$: 304.1859, found: 304.1849.



2-S16 *syn*-**2-S17** *anti*-**2-S17**

2-S17[111]

To a solution of **2-S16** (5.4 g, 17.6 mmol) in *n*-hexane (50 mL) was added KOH (0.10 g, 1.8 mmol) and Pd on $BaSO_4$ (0.13 g, Alfa Aesar) at room temperature. H_2 was bubbled into the reaction for 10 min, and the reaction was stirred at room temperature for 1 h under H_2 atmospheres. The reaction mixture was concentrated and the crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 2/23 to afford *anti*-**2-S17** (2.4 g, 44%

yield, d.r. = 99:1) as the first eluent and *syn*-**2-S17** (1.5 g, 28% yield, d.r. = 99:1) as the second eluent and their mixture (combined yield: 93%).

syn-**2-S17** (CAS: 1597406-26-2)

^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.10 (d, J = 8.5 Hz, 2H), 6.77 (d, J = 8.5 Hz, 2H), 5.55 (dd, J = 10.3 Hz, J = 10.7 Hz, 1H), 5.40 (dd, J = 9.1 Hz, J = 10.7 Hz, 1H), 4.70-4.79 (m, 1H), 3.72-3.79 (m, 1H), 1.48 (s, 1H), 1.30 (d, J = 6.1 Hz, 3H), 1.28 (d, J = 6.1 Hz, 3H), 0.98 (s, 9H), 0.19 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 153.9, 138.6, 136.5, 132.2, 127.6, 120.0, 63.9, 36.8, 25.7, 23.6, 22.5, 18.2, –4.4.

MS (EI, 70 eV) m/z (%): 306 (4) [M]$^{+\bullet}$, 288 (72), 273 (76), 231 (79), 151 (20), 115 (19), 98 (49), 75 (100), 43 (46).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3342, 2960, 2929, 1606, 1508, 1251, 1172, 913, 835, 778.

HRMS (EI) *m/z*: calcd for $C_{18}H_{30}O_2Si^{+\bullet}$ [M]$^{+\bullet}$: 306.2015, found: 306.2000.

anti-**2-S17** (CAS: 1597406-27-3)

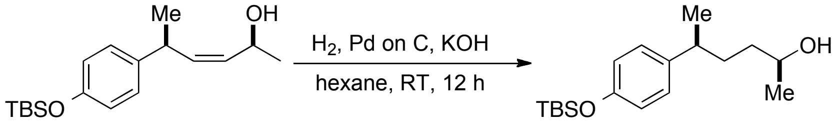
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.05 (d, J = 8.5 Hz, 2H), 6.76 (d, J = 8.5 Hz, 2H), 5.55 (dd, J = 10.3 Hz, J = 10.6 Hz, 1H), 5.40 (dd, J = 8.8 Hz, J = 10.6 Hz, 1H), 4.69-4.78 (m, 1H), 3.71-3.81 (m, 1H), 1.56 (s, 1H), 1.34 (d, J = 6.9 Hz, 3H), 1.18 (d, J = 6.3 Hz, 3H), 0.98 (s, 9H), 0.19 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 153.8, 138.6, 136.3, 132.2, 127.6, 119.9, 64.2, 36.9, 25.7, 23.5, 22.7, 18.2, –4.4.

MS (EI, 70 eV) m/z (%): 306 (3) [M]$^{+\bullet}$, 288 (100), 231 (89), 151 (22), 98 (42), 81 (20), 75 (97), 57 (39), 43 (52).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3349, 2960, 2929, 1607, 1508, 1252, 1172, 913, 835, 778.

HRMS (EI) *m/z*: calcd for $C_{18}H_{30}O_2Si^{+\bullet}$ [M]$^{+\bullet}$: 306.2015, found: 306.2014.



syn-**2-S17** *syn*-**2-S18**

syn-**2-S18** (CAS: 1597406-33-1)

To a solution of *syn*-**2-S17** (1.0 g, 3.2 mmol) in *n*-hexane (20 mL) was added KOH (0.04 g, 0.74 mmol) and Pd on activated charcoal (0.20 g, Acros) at room temperature. Then H$_2$ was bubbled into the reaction for 10 min and the reaction mixture was stirred at room temperature for 12 h. After filtration of the catalyst through silica gel, the solvent was evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 3/7 to afford *syn*-**2-S18** (0.83 g, 85% yield, d.r. = 99:1) as colorless oil.

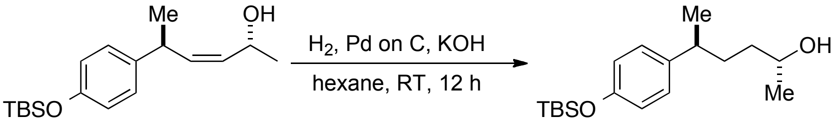
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.02 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.4 Hz, 2H), 3.69-3.78 (m, 1H), 2.60-2.69 (m, 1H), 1.51-1.68 (m, 2H), 1.31-1.42 (m, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 6.2 Hz, 3H), 0.99 (s, 9H), 0.20 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 153.6, 140.0, 127.7, 119.7, 68.2, 39.1, 37.4, 34.5, 25.7, 23.5, 22.5, 18.2, –4.4.

MS (EI, 70 eV) m/z (%): 308 (26) $[M]^{+\bullet}$, 235 (79), 195 (100), 181 (23), 177 (22), 163 (17), 75 (32), 73 (41), 55 (31), 41 (15).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3356, 2958, 2930, 2859, 1608, 1510, 1251, 911, 834, 778.

HRMS (EI) *m/z*: calcd for **$C_{18}H_{32}O_2Si^{+\bullet}$** $[M]^{+\bullet}$: 308.2172, found: 308.2159.



anti-**2-S17** *anti*-**2-S18**

anti-**2-S18** (CAS: 1597406-32-0)

To a solution of *anti*-**2-S17** (2.4 g, 7.7 mmol) in *n*-hexane (35 mL) was added KOH (0.11 g, 1.9 mmol) and Pd on activated charcoal (0.20 g, Acros) at room temperature. Then H_2 was bubbled into the reaction for 10 min and the reaction mixture was stirred at room temperature for 12 h. After filtration of the catalyst through silica gel, the solvent was evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 3/7 to afford *anti*-**2-S18** (2.0 g, 80% yield, d.r. = 97:3) as colorless oil.

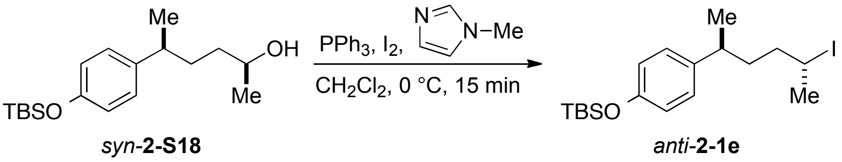
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.02 (d, *J* = 8.5 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 3.67-3.78 (m, 1H), 2.56-2.65 (m, 1H), 1.52-1.69 (m, 2H), 1.27-1.47 (m, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 6.2 Hz, 3H), 0.99 (s, 9H), 0.20 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 153.6, 140.0, 127.7, 119.7, 68.3, 39.3, 37.5, 34.7, 25.7, 23.5, 22.5, 18.2, –4.4.

MS (EI, 70 eV) m/z (%): 308 (28) $[M]^{+\bullet}$, 235 (92), 195 (100), 177 (23), 163 (17), 83 (13), 75 (26), 73 (33), 55 (28), 41 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3353, 2958, 2929, 2858, 1608, 1510, 1251, 914, 834, 778.

HRMS (EI) *m/z*: calcd for **$C_{18}H_{32}O_2Si^{+•}$** $[M]^{+•}$: 308.2172, found: 308.2166.



anti-**2-1e** (CAS: 1597406-20-6)

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (0.30 g, 1.2 mmol) in CH_2Cl_2 (5 mL) and cooled to 0 °C. PPh_3 (0.32 g, 1.2 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.10 mL, 1.2 mmol) was added. After 10 min of further stirring, *syn*-**2-S18** (0.31 g, 1.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (2 mL) was added and the reaction mixture was stirred for 15 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/99 to afford *anti*-**2-1e** (0.39 g, 94% yield, d.r. = 98:2) as colorless oil.

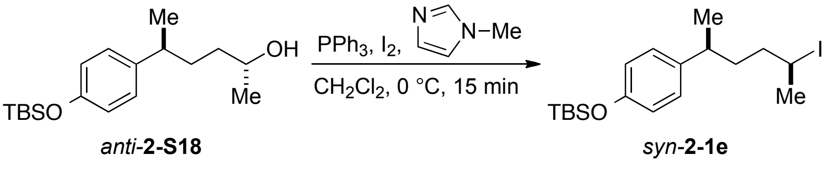
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.03 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 4.07-4.13 (m, 1H), 2.60-2.69 (m, 1H), 1.87 (d, J = 6.8 Hz, 3H), 1.71-1.80 (m, 2H), 1.58-1.65 (m, 1H), 1.44-1.49 (m, 1H), 1.23 (d, J = 6.9 Hz, 3H), 0.99 (s, 9H), 0.20 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 153.7, 139.7, 127.6, 119.8, 41.1, 38.7, 38.6, 30.8, 29.0, 25.7, 22.4, 18.2, –4.4.

MS (EI, 70 eV) m/z (%): 418 (46) $[M]^{+•}$, 291 (13), 235 (100), 177 (20), 73 (22), 55 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957, 2928, 2858, 1608, 1510, 1251, 913, 834, 778, 682.

HRMS (EI) *m/z*: calcd for **$C_{18}H_{31}OISi^{+•}$** $[M]^{+•}$: 418.1189, found: 418.1186.



syn-**2-1e** (CAS: 1597406-21-7)

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (0.30 g, 1.2 mmol) in CH_2Cl_2 (5 mL) and cooled to 0 °C. PPh_3 (0.32 g, 1.2 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.10 mL, 1.2 mmol) was added. After 10 min of further stirring, *anti*-**2-S18** (0.31 g, 1.0 mmol, d.r. = 97:3) dissolved in CH_2Cl_2 (2 mL) was added and the reaction mixture was stirred for 15 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/99 to afford *syn*-**2-1e** (0.41 g, 97% yield, d.r. = 98:2) as colorless oil.

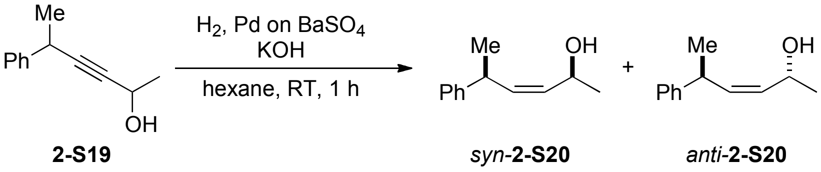
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.02 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 2H), 4.12-4.18 (m, 1H), 2.60-2.69 (m, 1H), 1.86 (d, *J* = 6.8 Hz, 3H), 1.62-1.77 (m, 3H), 1.50-1.56 (m, 1H), 1.24 (d, *J* = 6.9 Hz, 3H), 0.99 (s, 9H), 0.21 (s, 6H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 153.7, 139.4, 127.7, 119.8, 40.8, 38.4, 38.2, 30.7, 28.9, 25.7, 22.8, 18.2, –4.4.

MS (EI, 70 eV) m/z (%): 418 (41) [M$^+$], 291 (18), 235 (100), 177 (27), 83 (20), 73 (32), 55 (25), 41 (13).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958, 2928, 2858, 1608, 1510, 1251, 912, 834, 778, 682.

HRMS (EI) *m/z*: calcd for $C_{18}H_{31}OISi^{+\bullet}$ [M]$^{+\bullet}$: 418.1189, found: 418.1182.



2-S20[111]

To a solution of **2-S19**[115] (35.3 g, 202.7 mmol, CAS:1262322-89-3) in *n*-hexane (900 mL) was added KOH (1.1 g, 20.3 mmol) and Pd on $BaSO_4$ (1.5 g, Alfa Aesar) at room temperature. H_2 was bubbled into the reaction for 10 min, and the reaction was stirred at room temperature for 1 h under H_2 atmospheres. The reaction mixture was concentrated and the crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 2/23 to afford *anti*-**2-S20**

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[115] B. M. Trost, A. Breder, *Org. Lett.* **2011**, *13*, 398.

(10.0 g, 28% yield, d.r. = 99:1) as the first eluent and *syn*-**2-S20** (11.5 g, 32% yield, d.r. = 99:1) as the second eluent and their mixture (combined yield: 91%).

syn-**2-S20** (CAS: 1597406-28-4)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.15-7.35 (m, 5H), 5.60 (ddd, *J* = 10.8 Hz, *J* = 9.8 Hz, *J* = 1.0 Hz, 1H), 5.43 (ddd, *J* = 10.8 Hz, *J* = 8.6 Hz, *J* = 0.8 Hz, 1H), 4.76 (dq, *J* = 8.6 Hz, *J* = 6.4 Hz, 1H), 3.84 (dq, *J* = 9.8 Hz, *J* = 6.8 Hz, 1H), 1.65 (s, 1H), 1.39 (d, *J* = 6.8 Hz, 3H), 1.19 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 146.1, 135.9, 132.7, 128.6, 126.9, 126.2, 64.3, 37.8, 23.7, 22.7.

MS (EI, 70 eV) m/z (%): 176 (1) $[M]^{+\bullet}$, 158 (36), 143 (100), 128 (24), 117 (20), 105 (16), 91 (21), 77 (10), 65 (4), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3323, 3025, 2966, 2925, 2870, 1656, 1600, 1493, 1451, 1411, 1368, 1286, 1140, 1105, 1054, 1043, 1028, 1007, 997, 934, 892, 845, 794, 739, 697.

HRMS (ESI) *m/z*: calcd for $C_{12}H_{16}ONa^+$ $[M+Na]^+$: 199.1093, found: 199.1093.

anti-**2-S20** (CAS: 1597406-29-5)

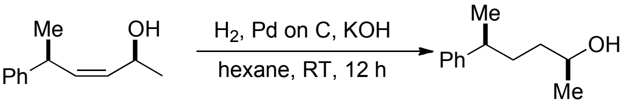
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.16-7.35 (m, 5H), 5.59 (ddd, *J* = 10.9 Hz, *J* = 9.7 Hz, *J* = 1.1 Hz, 1H), 5.43 (ddd, *J* = 10.9 Hz, *J* = 8.5 Hz, *J* = 0.7 Hz, 1H), 4.71-4.77 (m, 1H), 3.83 (dq, *J* = 9.7 Hz, *J* = 6.9 Hz, 1H), 1.42 (br. d, *J* = 2.2 Hz, 1H), 1.35 (d, *J* = 6.9 Hz, 3H), 1.29 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 146.1, 136.2, 132.7, 128.8, 126.9, 126.4, 64.0, 37.7, 23.8, 22.6.

MS (EI, 70 eV) m/z (%): 176 (1) $[M]^{+\bullet}$, 158 (37), 143 (100), 128 (25), 117 (21), 105 (16), 91 (20), 77 (11), 65 (4), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3342, 3026, 3006, 2965, 2926, 2871, 1656, 1601, 1493, 1451, 1370, 1266, 1181, 1140, 1105, 1050, 1029, 1009, 997, 933, 907, 890, 844, 796, 747, 740, 697.

HRMS (ESI) *m/z*: calcd for $C_{12}H_{16}ONa^+$ $[M+Na]^+$: 199.1093, found: 199.1097.



syn-**2-S20** *syn*-**2-S21**

syn-**2-S21** (CAS: 1597406-35-3)[112]

To a solution of *syn*-**2-S20** (8.0 g, 45.2 mmol) in *n*-hexane (200 mL) was added KOH (0.65 g, 11.1 mmol) and Pd on activated charcoal (1.53 g, Acros) at room temperature. Then H_2 was bubbled into the reaction for 10 min and the reaction mixture was stirred at room temperature for 12 h. After filtration of the catalyst through silica gel, the solvent was evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/9→1/1 to afford *syn*-**2-S21** (7.2 g, 89% yield, d.r. = 99:1) as colorless oil.

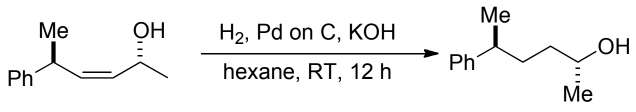
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.18-7.35 (m, 5H), 3.73 (qt, J = 6.3 Hz, J = 6.1 Hz, 1H), 2.70 (h, J = 6.8 Hz, 1H), 1.83 (br s, 1H), 1.24-1.78 (m, 4H), 1.29 (d, J = 6.8 Hz, 3H), 1.15 (d, J = 6.3 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 147.5, 128.4, 127.0, 125.9, 68.2, 40.1, 37.5, 34.5, 23.5, 22.5.

MS (EI, 70 eV) m/z (%): 178 (1) $[M]^{+\bullet}$, 160 (8), 143 (9), 131 (10), 181 (100), 105 (73), 91 (25), 77 (15), 71 (10), 65 (5), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3350, 3271, 3025, 2961, 2928, 2869, 1602, 1493, 1451, 1374, 1308, 1190, 1135, 1063, 1025, 1009, 999, 992, 946, 930, 906, 885, 844, 781, 760, 736, 698.

HRMS (ESI) *m/z*: calcd for **$C_{12}H_{18}O^+$** $[M]^+$: 178.1358, found: 178.1354.



anti-**2-S20** *anti*-**2-S21**

anti-**2-S21** (CAS: 1597406-34-2)[112]

To a solution of *anti*-**2-S20** (7.1 g, 40.5 mmol) in *n*-hexane (180 mL) was added KOH (0.58 g, 9.9 mmol) and Pd on activated charcoal (0.80 g, Acros) at room temperature. Then H_2 was bubbled into the reaction for 10 min and the reaction mixture was stirred at room temperature for 12 h. After filtration of the catalyst through silica gel, the solvent was evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/9→1/1 to afford *anti*-**2-S21** (6.8 g, 80% yield, d.r. = 99:1) as colorless oil.

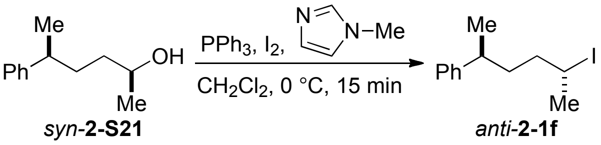
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.17-7.36 (m, 5H), 3.74 (qt, J = 6.4 Hz, J = 5.9 Hz, 1H), 2.71 (h, J = 6.9 Hz, 1H), 1.22-1.81 (m, 5H), 1.29 (d, J = 6.9 Hz, 3H), 1.16 (d, J = 6.4 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 147.5, 128.4 (2C), 127.0 (2C), 125.9, 68.2, 40.1, 37.5, 34.5, 23.5, 22.5.

MS (EI, 70 eV) m/z (%): 178 (2) $[M]^{+•}$, 160 (15), 145 (11), 131 (9), 181 (100), 105 (82), 91 (23), 77 (16), 65 (3), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3343, 3025, 2963, 2927, 2869, 1602, 1493, 1451, 1371, 1287, 1135, 1107, 1052, 1030, 1009, 996, 933, 907, 891, 844, 795, 759, 697.

HRMS (ESI) *m/z*: calcd for $C_{12}H_{18}O^+$ $[M]^+$: 178.1358, found: 178.1353.



anti-**2-1f** (CAS: 1597406-22-8)

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (0.30 g, 1.2 mmol) in CH_2Cl_2 (5 mL) and cooled to 0 °C. PPh_3 (0.32 g, 1.2 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.10 mL, 1.2 mmol) was added. After 10 min of further stirring, *syn*-**2-S21** (0.17 g, 1.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (2 mL) was added and the reaction mixture was stirred for 15 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with *i*-hexane to afford *anti*-**2-1f** (0.23 g, 84% yield, d.r. = 98:2) as colorless oil.

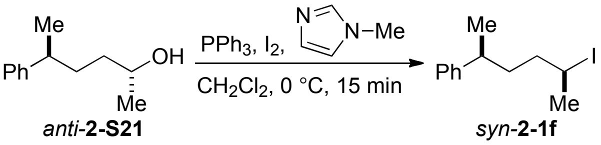
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.19-7.38 (m, 5H), 4.08-4.19 (m, 1H), 2.72 (h., *J* = 7.0 Hz, 1H), 1.89 (d, *J* = 6.6 Hz, 3H), 1.44-1.91 (m, 4H), 1.29 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 147.2, 128.5, 127.0, 126.2, 41.2, 39.6, 38.5, 30.8, 29.0, 22.4.

MS (EI, 70 eV) m/z (%): 288 (1) $[M]^{+•}$, 161 (20), 119 (7), 105 (100), 91 (30), 77 (9), 55 (3).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3060, 3024, 2958, 2923, 2868, 1602, 1582, 1493, 1451, 1376, 1299, 1278, 1215, 1196, 1149, 1128, 1087, 1050, 1028, 1013, 985, 907, 892, 869, 805, 760, 736, 698.

HRMS (ESI) *m/z*: calcd for $C_{12}H_{17}I^+$ $[M]^+$: 288.0375, found: 288.0362.



syn-**2-1f** (CAS: 1597406-23-9)

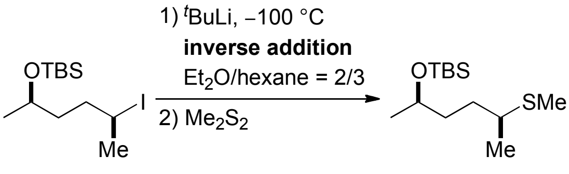
A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (0.30 g, 1.2 mmol) in CH_2Cl_2 (5 mL) and cooled to 0 °C. PPh_3 (0.32 g, 1.2 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.10 mL, 1.2 mmol) was added. After 10 min of further stirring, *anti*-**2-S21** (0.17 g, 1.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (2 mL) was added and the reaction mixture was stirred for 15 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with *i*-hexane to afford *syn*-**2-1f** (0.22 g, 79% yield, d.r. = 92:8) as colorless oil.

^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.17-7.38 (m, 5H), 4.13-4.24 (m, 1H), 2.75 (h, *J* = 7.0 Hz, 1H), 1.89 (d, *J* = 6.6 Hz, 3H), 1.49-1.91 (m, 4H), 1.30 (d, *J* = 6.9 Hz, 3H).
^{13}C NMR (CDCl$_3$, 75 MHz) δ: 146.9, 128.6, 127.0, 126.2, 40.9, 39.4, 38.1, 30.7, 29.0, 22.9.
MS (EI, 70 eV) m/z (%): 288 (1) $[M]^{+\bullet}$, 161 (21), 145 (3), 119 (7), 105 (100), 91 (29), 77 (8), 55 (3).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3081, 3060, 3024, 2958, 2923, 2868, 1602, 1493, 1451, 1376, 1299, 1278, 1215, 1196, 1149, 1128, 1087, 1028, 1013, 985, 907, 760, 736, 698, 666.
HRMS (ESI) *m/z*: calcd for $\mathbf{C_{12}H_{17}I^+}$ $[M]^+$: 288.0375, found: 288.0460.

9.2.2 I/Li exchange and subsequent trapping reaction

[General procedure]

A solution of *n*-hexane/Et_2O = 3/2 (5.5 mL) was placed into a flame-dried and Ar-flushed *Schlenk*-tube equipped with a stirring bar and cooled to –100 °C using frozen methanol. A ^{t}BuLi solution (2.2 equiv, 1.7 M in *n*-hexane, 0.65 mL, 1.1 mmol) was added via syringe. Then, a 0.50 M solution of the respective alkyl iodide (1.0 equiv, 0.50 mmol) in Et_2O was added dropwise in 10 min. The reaction mixture was then immediately quenched with the corresponding electrophile (2.5 equiv, 1.25 mmol; solid electrophiles were added as a 1.0 M solution in Et_2O). The reaction mixture was stirred for 5 min at –100 °C before saturated NH_4Cl aqueous solution (2.0 mL) was added. After warming to room temperature, the organic phases were separated and the aqueous phase was extracted with Et_2O three times. The combined organic phases were dried over $MgSO_4$ and the solvents were evaporated. Purification by flash chromatography of the crude material provided the respective products.



syn-**2-1a** *syn*-**2-3a**

syn-**2-3a**

According to general procedure *syn*-**2-1a** (171 mg, 0.50 mmol) as a starting material and Me_2S_2 (111 µL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/99 to afford *syn*-**2-3a** (99 mg, 75% yield, d.r. = 94:6) as colorless oil. The relative configuration was determined by the following S_N2 reaction.

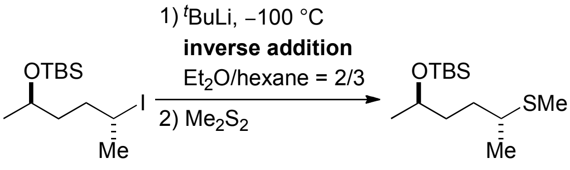
^{1}H NMR (CDCl$_3$, 400 MHz) δ: 3.74-3.78 (m, 1H), 2.57-2.64 (m, 1H), 2.03 (s, 3H), 1.48-1.56 (m, 4H), 1.24 (d, J = 6.7 Hz, 3H), 1.10 (d, J = 6.1 Hz, 3H), 0.86 (s, 9H), 0.02 (s, 6H).

^{13}C NMR (CDCl$_3$, 100 MHz) δ: 68.5, 41.3, 36.9, 32.4, 25.9, 23.8, 20.8, 18.1, 12.9, –4.4, –4.8.

MS (EI, 70 eV) m/z (%): 247 (1) $[M–CH_3]^{+\bullet}$, 205 (53), 157 (33), 149 (21), 105 (46), 75 (100), 55 (49), 41 (25).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956, 2928, 2857, 1462, 1374, 1253, 1131, 1051, 833, 772.

HRMS (ESI) *m/z*: calcd for $C_{12}H_{27}OSSi^+$ $[M–CH_3]^+$: 247.1552, found: 247.1527.



anti-**2-1a** *anti*-**2-3a**

anti-**2-3a**

According to typical procedure *anti*-2-**1a** (171 mg, 0.50 mmol, d.r. = 97:3) as a starting material and Me_2S_2 (111 µL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/99 to afford *anti*-**2-3a** (97 mg, 74% yield) as colorless oil. The relative configuration was determined by the following S_N2 reaction.

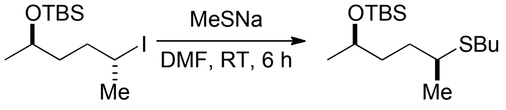
^{1}H NMR (CDCl$_3$, 400 MHz) δ: 3.74-3.80 (m, 1H), 2.59-2.64 (m, 1H), 2.03 (s, 3H), 1.60-1.67 (m, 1H), 1.41-1.52 (m, 3H), 1.24 (d, J = 6.7 Hz, 3H), 1.10 (d, J = 6.1 Hz, 3H), 0.86 (s, 9H), 0.02 (s, 6H).

^{13}C NMR (CDCl$_3$, 100 MHz) δ: 68.3, 41.2, 36.8, 32.2, 25.8, 23.8, 20.7, 18.1, 12.9, –4.4, –4.8.

MS (EI, 70 eV) m/z (%): 247 (1) [M–CH$_3$]$^{+\bullet}$, 205 (66), 157 (31), 149 (19), 115 (13), 105 (47), 83 (41), 75 (100), 55 (38), 41 (21).

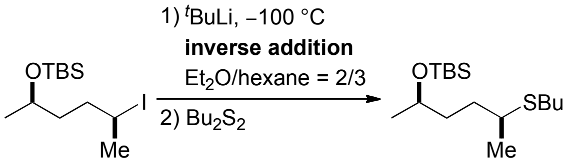
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956, 2928, 2856, 1462, 1374, 1253, 1130, 1050, 833, 772.

HRMS (ESI) *m/z*: calcd for **C$_{12}$H$_{27}$OSSi$^+$**[M–CH$_3$]$^+$: 247.1552, found: 247.1547.



anti-**2-1a** *syn*-**2-3a**

S$_N$2 reaction: A solution of *anti*-**2-1a** (171 mg, 0.50 mmol, d.r. = 98:2) in DMF (2.5 mL) was placed into a flame-dried and Ar-flushed *Schlenk*-tube equipped with a stirring bar. MeSNa (53 mg, 0.75 mmol) was added at room temperature and the reaction mixture was stirred for 6 h. A saturated NH$_4$Cl aqueous solution (2.0 mL) was added to the reaction mixuture and it was extracted with Et$_2$O three times. The combined organic phases were dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/99 to afford *syn*-**2-3a** (103 mg, 78% yield) as colorless oil.



syn-**2-1a** *syn*-**2-4a**

syn-**2-4a**

According to general procedure, *syn*-**2-1a** (103 mg, 0.30 mmol, d.r. = 99:1) as a starting material and Bu$_2$S$_2$ (142 µL, 0.75 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/100 to afford *anti*-**2-4a** (67 mg, 74% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

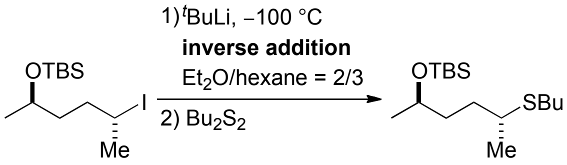
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 3.78 (qt, J = 6.1 and 6.0 Hz, 1H), 2.70 (qt, J = 6.6 and 6.5 Hz, 1H), 2.50 (t, J = 7.4 Hz, 2H), 1.73-1.60 (m, 1H), 1.57-1.46 (m, 4H), 1.47-1.34 (m, 3H), 1.25 (d, J = 6.7 Hz, 3H), 1.12 (d, J = 6.0 Hz, 3H), 0.91 (t, J = 7.5 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 68.6, 40.0, 37.0, 33.1, 32.1, 30.0, 26.0, 24.0, 22.3, 21.5, 18.3, 13.9, –4.2, –4.6.

MS (70 eV, EI) *m/z* (%): 289 (1) [M–Me]$^{+\bullet}$, 247 (55), 191 (5), 157 (27), 147 (32), 115 (14), 97 (7), 83 (32), 75 (100), 55 (9).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2928 (w), 2857 (w), 1462 (w), 1374 (w), 1253 (w), 1130 (w), 1048 (w), 1003 (w), 938 (w), 880 (w), 833 (s), 808 (m), 772 (vs), 718 (w), 661 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{33}OSSi^{+\bullet}$** [M–Me]$^{+\bullet}$: 289.2021, found: 289.2015.



anti-**2-1a** *anti*-**2-4a**

anti-**2-4a**

According to general procedure, *anti*-**2-1a** (103 mg, 0.30 mmol, d.r. = 98:2) as a starting material and Bu$_2$S$_2$ (142 µL, 0.75 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/100 to afford *anti*-**2-4a** (67 mg, 74% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

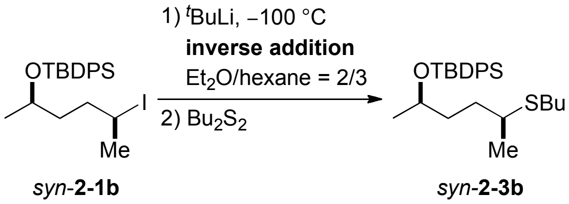
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 3.78 (qt, J = 6.1 and 6.0 Hz, 1H), 2.70 (qt, J = 6.6 and 6.5 Hz, 1H), 2.50 (t, J = 7.4 Hz, 2H), 1.73-1.60 (m, 1H), 1.57-1.46 (m, 4H), 1.47-1.34 (m, 3H), 1.25 (d, J = 6.7 Hz, 3H), 1.12 (d, J = 6.0 Hz, 3H), 0.91 (t, J = 7.5 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 68.6, 40.0, 37.0, 33.1, 32.1, 30.0, 26.0, 24.0, 22.3, 21.5, 18.3, 13.9, –4.2, –4.6.

MS (70 eV, EI) *m/z* (%): 289 (1) [M–Me]$^{+\bullet}$, 247 (55), 191 (5), 157 (27), 147 (32), 115 (14), 97 (7), 83 (32), 75 (100), 55 (9).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2928 (w), 2857 (w), 1462 (w), 1374 (w), 1253 (w), 1130 (w), 1048 (w), 1003 (w), 938 (w), 880 (w), 833 (s), 808 (m), 772 (vs), 718 (w), 661 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{33}OSSi^{+\bullet}$** [M–Me]$^{+\bullet}$: 289.2021, found: 289.2015.



syn-**2-3b**

According to general procedure, *syn*-**2-1b** (140 mg, 0.30 mmol, d.r. = 97:3) as a starting material and Bu_2S_2 (142 μL, 0.75 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/100 to afford *syn*-**2-3b** (90 mg, 70% yield, d.r. = 98:2) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

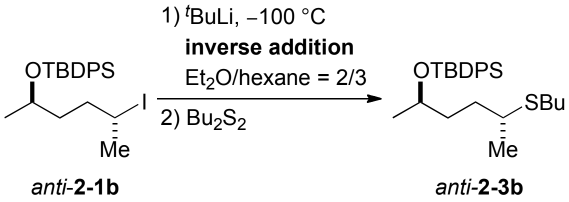
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.73-7.63 (m, 4H), 7.46-7.32 (m, 6H), 3.85 (h, J = 5.5 Hz, 1H), 2.62 (qt, J = 6.6 and 6.5 Hz, 1H), 2.48 (t, J = 7.4 Hz, 2H), 1.63-1.45 (m, 6H), 1.45-1.32 (m, 2H), 1.19 (d, J = 6.7 Hz, 3H), 1.07 (d, J = 5.6 Hz, 3H), 1.06 (s, 9H), 0.91 (t, J = 7.3 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 136.02, 136.01, 134.9, 134.6, 129.6, 129.5, 127.6, 127.5, 69.7, 40.2, 36.8, 32.5, 32.1, 30.1, 27.2, 23.4, 22.3, 21.4, 19.4, 13.9.

MS (70 eV, EI) *m/z* (%): 371 (59) [M–^{t}Bu]$^{+\bullet}$, 281 (13), 271 (30), 237 (6), 215 (11), 199 (100), 135 (17), 97 (10), 83 (30), 55 (23).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2959 (w), 2930 (w), 2859 (w), 1472 (w), 1462 (w), 1428 (w), 1377 (w), 1362 (w), 1130 (w), 1110 (m), 1071 (w), 1047 (w), 1006 (w), 998 (w), 907 (m), 822 (w), 731 (s), 700 (vs), 687 (m).

HRMS (EI) *m/z*: calcd for **$C_{22}H_{31}OSSi^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 371.1865, found: 371.1874.



anti-**2-3b**

According to general procedure, *anti*-**2-1b** (140 mg, 0.30 mmol, d.r. = 98:2) as a starting material and Bu_2S_2 (142 µL, 0.75 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *anti*-**2-3b** (91 mg, 71% yield, d.r. = 98:2) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

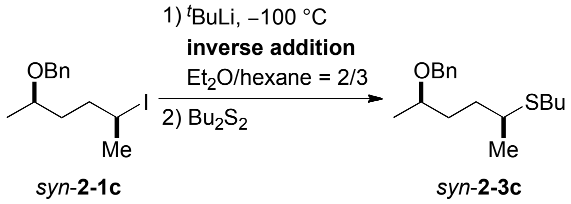
^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.73-7.67 (m, 4H), 7.46-7.33 (m, 6H), 3.86 (h, *J* = 5.7 Hz, 1H), 2.60 (qt, *J* = 6.6 and 6.5 Hz, 1H), 2.46 (t, *J* = 7.4 Hz, 2H), 1.66-1.33 (m, 8H), 1.19 (d, *J* = 6.7 Hz, 3H), 1.09 (d, *J* = 6.0 Hz, 3H), 1.08 (s, 9H), 0.91 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 136.02, 136.00, 134.9, 134.5, 129.6, 129.5, 127.6, 127.5, 69.4, 40.0, 36.7, 32.5, 32.1, 30.0, 27.2, 23.4, 22.3, 21.4, 19.4, 13.9.

MS (70 eV, EI) *m/z* (%): 371 (95) $[M{-}t\mathrm{Bu}]^{+\bullet}$, 281 (13), 271 (42), 237 (8), 215 (15), 199 (100), 183 (14), 155 (7), 135 (15), 105 (6), 83 (31).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2929 (w), 2857 (w), 1472 (w), 1462 (w), 1428 (w), 1376 (w), 1130 (w), 1105 (m), 1078 (w), 1047 (w), 998 (w), 822 (w), 739 (w), 700 (vs), 687 (m).

HRMS (EI) *m/z*: calcd for $C_{22}H_{31}OSSi^{+\bullet}$ $[M{-}{}^t\mathrm{Bu}]^{+\bullet}$: 371.1865, found: 371.1857.



syn-**2-3c**

According to general procedure, *syn*-**2-1c** (96 mg, 0.30 mmol, d.r. = 97:3) as a starting material and Bu_2S_2 (142 µL, 0.75 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/30 to afford *syn*-**2-3c** (62 mg, 74% yield, d.r. = 89:11) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.40-7.26 (m, 5H), 4.60 (d, *J* = 11.8 Hz, 1H), 4.48 (d, *J* = 11.8 Hz, 1H), 3.55 (qt, *J* = 6.0 and 5.9 Hz, 1H), 2.74 (qt, *J* = 6.7 and 6.6 Hz, 1H), 2.53 (t, *J* =

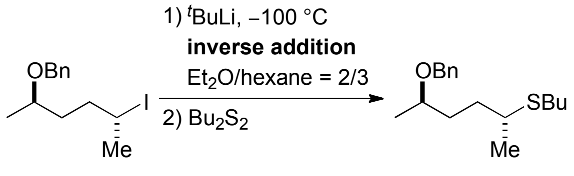
7.4 Hz, 2H), 1.80-1.47 (m, 6H), 1.43 (tq, *J* = 7.3 and 7.2 Hz, 2H), 1.29 (d, *J* = 6.7 Hz, 3H), 1.23 (d, *J* = 6.1 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 139.1, 128.4, 127.8, 127.5, 74.7, 70.4, 40.0, 33.9, 32.7, 32.1, 30.1, 22.3, 21.6, 19.8, 13.9.

MS (70 eV, EI) *m/z* (%): 280 (2) $[M]^{+\bullet}$, 189 (8), 174 (19), 117 (36), 107 (14), 99 (41), 91 (100), 83 (11), 75 (12), 55 (15).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2928 (w), 2862 (w), 1453 (w), 1374 (w), 1339 (w), 1130 (w), 1090 (m), 1066 (m), 1028 (w), 916 (w), 733 (s), 696 (vs), 610 (w).

HRMS (EI) *m/z*: calcd for $C_{17}H_{28}OS^{+\bullet}$ $[M]^{+\bullet}$: 280.1861, found: 280.1856.



anti-**2-1c** *anti*-**2-3c**

anti-**2-3c**

According to general procedure, *anti*-**2-1c** (96 mg, 0.30 mmol, d.r. = 97:3) as a starting material and Bu_2S_2 (142 μL, 0.75 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/30 to afford *syn*-**2-3c** (65 mg, 77% yield, d.r. = 90:10) as colorless oil. The relative configuration was determined by assuming the reaction proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

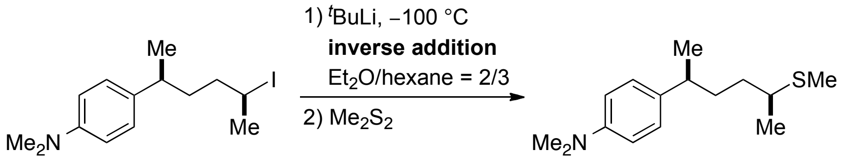
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.41-7.26 (m, 5H), 4.60 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H), 3.54 (qt, *J* = 5.9 and 5.8 Hz, 1H), 2.75 (qt, *J* = 6.4 and 6.3 Hz, 1H), 2.54 (t, *J* = 7.4 Hz, 2H), 1.80-1.50 (m, 6H), 1.43 (tq, *J* = 7.4 and 7.3 Hz, 2H), 1.30 (d, *J* = 6.7 Hz, 3H), 1.24 (d, *J* = 6.1 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 139.1, 128.4, 127.7, 127.5, 74.9, 70.4, 40.2, 34.2, 32.9, 32.1, 30.1, 22.3, 21.7, 19.8, 13.9.

MS (70 eV, EI) *m/z* (%): 280 (1) $[M]^{+\bullet}$, 189 (6), 174 (16), 117 (30), 107 (13), 99 (38), 91 (100), 83 (13), 75 (12), 55 (25).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2928 (w), 2861 (w), 1453 (w), 1374 (w), 1340 (w), 1267 (w), 1204 (w), 1137 (w), 1090 (m), 1066 (m), 1028 (w), 916 (w), 733 (s), 696 (vs).

HRMS (EI) *m/z*: calcd for $C_{17}H_{28}OS^{+\bullet}$ $[M]^{+\bullet}$: 280.1861, found: 280.1859.



syn-**2-1d** *syn*-**2-3d**

syn-**2-3d**

According to typical procedure *syn*-**2-1d** (166 mg, 0.50 mmol, d.r. = 92:8) as a starting material and Me$_2$S$_2$ (111 µL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/19 to afford *syn*-**2-3d** (88 mg, 70% yield, d.r. = 91:9) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

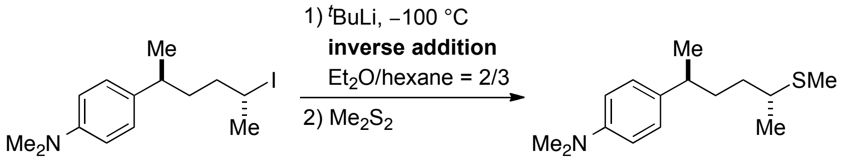
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.09 (d, J = 8.6 Hz, 2H), 6.73 (d, J = 8.6 Hz, 2H), 2.94 (s, 6H), 2.59-2.67 (m, 2H), 2.03 (s, 3H), 1.65-1.74 (m, 2H), 1.44-1.49 (m, 2H), 1.25 (d, J = 6.8 Hz, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 149.1, 135.6, 127.5, 113.0, 41.4, 40.9, 38.9, 35.7, 34.4, 22.7, 20.9, 12.9.

MS (EI, 70 eV) m/z (%): 251 (21) [M]$^{+\bullet}$, 149 (8), 148 (100), 134 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956, 2919, 1615, 1519, 1145, 1343, 1163, 947, 816, 730.

HRMS (EI) *m/z*: calcd for **$C_{15}H_{25}NS^{+\bullet}$** [M]$^{+\bullet}$: 251.1708, found: 251.1705.



anti-**2-1d** *anti*-**2-3d**

anti-**2-3d**

According to typical procedure using *anti*-**2-1b** (166 mg, 0.50 mmol, d.r. = 96:4) and Me$_2$S$_2$ (111 µL, 1.25 mmol) were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/19 to afford *anti*-**2-3d** (82 mg, 65% yield, d.r. = 94:6) as colorless oil. The relative configuration was determined by assuming the reaction with disulfide proceeds with retention of the configuration from *syn*- and *anti*-**2-3a**.

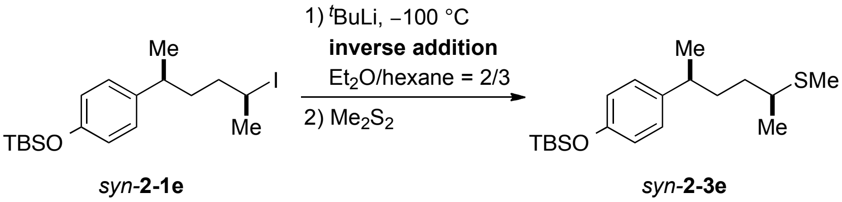
^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 7.09 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 8.6 Hz, 2H), 2.94 (s, 6H), 2.58-2.67 (m, 2H), 2.03 (s, 3H), 1.66-1.73 (m, 2H), 1.52-1.59 (m, 1H), 1.34-1.43 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 149.1, 135.6, 127.5, 113.0, 41.5, 40.9, 39.0, 35.8, 34.5, 22.8, 20.8, 13.1.

MS (EI, 70 eV) m/z (%): 251 (24) $[M]^{+\bullet}$, 149 (11), 148 (100), 71 (8), 57 (14), 42 (8).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956, 2918, 2798, 1615, 1520, 1445, 1343, 1163, 947, 815.

HRMS (EI) *m/z*: calcd for **$C_{15}H_{25}NS^{+\bullet}$** $[M]^{+\bullet}$: 251.1708, found: 251.1708.



syn-**2-3e**

According to typical procedure *syn*-**2-1e** (209 mg, 0.50 mmol, d.r. = 98:2) as a starting material and Me$_2$S$_2$ (111 µL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/99 to afford *syn*-**2-3e** (123 mg, 73% yield, d.r. = 94:6) as colorless oil. The relative configuration was determined by assuming the reaction proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

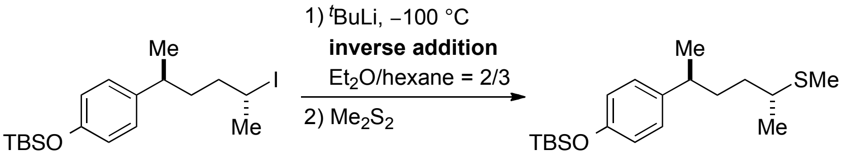
^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 7.03 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 2H), 2.57-2.66 (m, 2H), 1.99 (s, 3H), 1.63-1.71 (m, 2H), 1.38-1.45 (m, 2H), 1.23 (d, *J* = 6.7 Hz, 6H), 1.00 (s, 9H), 0.20 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 153.6, 140.0, 127.7, 119.8, 41.2, 39.1, 35.7, 34.2, 25.7, 22.6, 20.8, 18.2, 12.8, –4.4.

MS (EI, 70 eV) m/z (%): 338 (55) $[M]^{+\bullet}$, 248 (36), 235 (100), 225 (50), 191 (39), 177 (24), 73 (40), 55 (23).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956, 2928, 2858, 1607, 1510, 1250, 1170, 912, 834, 778.

HRMS (EI) *m/z*: calcd for **$C_{19}H_{34}OSSi^{+\bullet}$** $[M]^{+\bullet}$: 338.2100, found: 338.2088.



anti-**2-1e** *anti*-**2-3e**

anti-**2-3e**

According to typical procedure *anti*-**2-1e** (209 mg, 0.50 mmol, d.r. = 98:2) as a starting material and Me$_2$S$_2$ (111 μL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/99 to afford *anti*-**2-3e** (127 mg, 75% yield, d.r. = 95:5) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

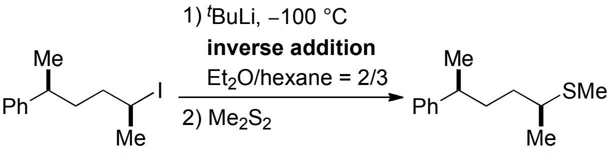
^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 7.04 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 2H), 2.57-2.64 (m, 2H), 1.99 (s, 3H), 1.62-1.70 (m, 2H), 1.48-1.55 (m, 1H), 1.30-1.38 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.7 Hz, 3H), 1.00 (s, 9H), 0.20 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 153.6, 140.0, 127.7, 119.8, 41.3, 39.2, 35.7, 34.3, 25.7, 22.6, 20.7, 18.2, 13.1, –4.4.

MS (EI, 70 eV) m/z (%): 338 (48) $[M]^{+\bullet}$, 248 (40), 233 (100), 225 (62), 191 (40), 177 (25), 105 (20), 73 (48), 55 (24).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957, 2929, 2858, 1608, 1510, 1251, 1171, 913, 834, 778.

HRMS (EI) *m/z*: calcd for **$C_{19}H_{34}OSSi^{+\bullet}$** $[M]^{+\bullet}$: 338.2100, found: 338.2098.



syn-**2-1f** *syn*-**2-3f**

syn-**2-3f**

According to typical procedure in 0.35 mmol scale *syn*-**2-1f** (101 mg, 0.35 mmol, d.r. = 92:8) as a starting material and Me$_2$S$_2$ (78 μL, 0.88 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/99 to afford *syn*-**2-3f** (53 mg, 73% yield, d.r. = 91:9) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

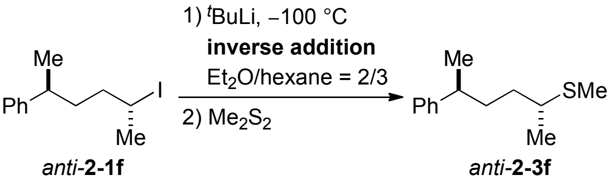
^{1}H NMR (CDCl$_3$, 600 MHz) *δ*: 7.27-7.32 (m, 2H), 7.18-7.20 (m, 3H), 2.58-2.71 (m, 2H), 1.99 (s, 3H), 1.64-1.76 (m, 2H), 1.39-1.46 (m, 2H), 1.26 (d, *J* = 7.0 Hz, 3H), 1.23 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (CDCl$_3$, 150 MHz) *δ*: 147.3, 128.3, 126.9, 125.9, 41.3, 39.9, 35.5, 34.2, 22.5, 20.8, 12.8.

MS (EI, 70 eV) m/z (%): 208 (25) $[M]^{+\bullet}$, 118 (93), 105 (92), 97 (31), 91 (39), 85 (51), 71 (64), 57 (100), 43 (48).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3027, 2959, 2920, 2869, 1576, 1494, 1452, 1375, 1283, 761, 699.

HRMS (EI) *m/z*: calcd for $C_{13}H_{20}S^{+\bullet}$ $[M]^{+\bullet}$: 208.1286, found: 208.1274.



anti-**2-1f** *anti*-**2-3f**

anti-**2-3f**

According to typical procedure in 0.35 mmol scale *anti*-**2-1f** (101 mg, 0.35 mmol, d.r. = 98:2) as a starting material and Me$_2$S$_2$ (78 μL, 0.88 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/99 to afford *anti*-**2-3f** (52 mg, 73% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by assuming the reaction proceeds with retention of the configuration from *syn*- and *anti*-**2-3a** and other reactions with disulfide.

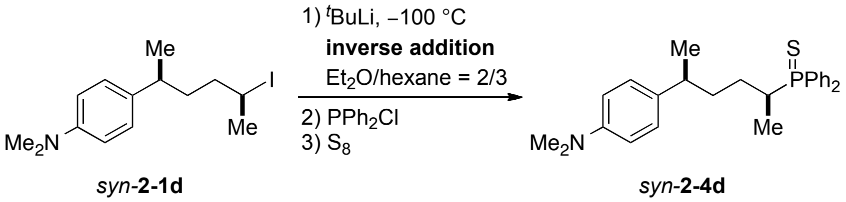
^{1}H NMR (CDCl$_3$, 600 MHz) *δ*: 7.28-7.31 (m, 2H), 7.18-7.20 (m, 3H), 2.65-2.69 (m, 1H), 2.58-2.64 (m, 1H), 2.00 (s, 3H), 1.69-1.74 (m, 2H), 1.51-1.56 (m, 1H), 1.31-1.36 (m, 1H), 1.27 (d, *J* = 7.0 Hz, 3H), 1.23 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (CDCl$_3$, 150 MHz) *δ*: 147.3, 128.3, 127.0, 125.9, 41.4, 40.0, 35.6, 34.4, 22.5, 20.7, 13.1.

MS (EI, 70 eV) m/z (%): 208 (11) $[M^+]$, 118 (100), 105 (42), 91 (17), 75 (18), 41 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3027, 2958, 2918, 1603, 1494, 1451, 1374, 760, 698.

HRMS (EI) *m/z*: calcd for $C_{13}H_{20}S^{+\bullet}$ $[M]^{+\bullet}$: 208.1286, found: 208.1280.



syn-**2-4d**

According to typical procedure *syn*-**2-1d** (166 mg, 0.50 mmol, d.r. = 92:8) as a starting material and PPh_2Cl (224 µL, 1.25 mmol) as an electrophile were used. After 5 min stirring at –100 °C, the resulting mixture was treated with S_8 (1.28 g, 5.0 mmol) and was allowed to warm to room temperature for 12 h. Workup was made as shown in typical procedure and the crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/9 to afford *syn*-**2-4d** (156 mg, 74% yield, d.r. = 91:9) as white solid. The relative configuration was determined by X-ray crystallography of *anti*-**2-4d**.

m.p. = 103-105 °C

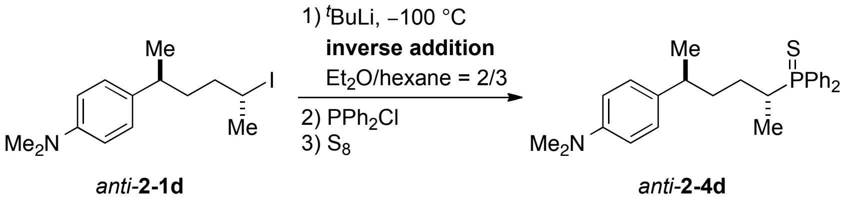
^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 7.81-7.91 (m, 4H), 7.36-7.44 (m, 6H), 6.98 (d, J = 8.5 Hz, 2H), 6.67 (d, J = 8.5 Hz, 2H), 2.93 (s, 6H), 2.56-2.63 (m, 1H), 2.46-2.51 (m, 1H), 1.71-1.81 (m, 1H), 1.46-1.55 (m, 3H), 1.14 (d, J = 7.0 Hz, 3H), 1.13 (dd, J = 19.3 Hz, J = 7.0 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 149.1, 135.6, 132.1 (d, J = 76.1 Hz), 131.8 (d, J = 77.0 Hz), 131.4 (d, J = 9.3 Hz), 131.3 (d, J = 9.3 Hz), 131.2 (d, J = 2.7 Hz), 131.1 (d, J = 2.7 Hz), 128.5 (d, J = 11.5 Hz), 128.4 (d, J = 11.6 Hz), 127.3, 113.0, 40.9, 38.8, 36.2 (d, J = 13.7 Hz), 33.0 (d, J = 55.5 Hz), 27.7, 22.1, 12.5.

MS (EI, 70 eV) m/z (%): 421 (29) $[M]^{+\bullet}$, 218 (7), 183 (6), 161 (6), 149 (10), 148 (100), 108 (3).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2924, 1614, 1519, 1435, 1098, 814, 724, 707, 688.

HRMS (EI) *m/z*: calcd for **$C_{26}H_{32}NPS^{+\bullet}$** $[M]^{+\bullet}$: 421.1993, found: 421.1990.



anti-**2-4d**

According to typical procedure *anti*-**2-1d** (166 mg, 0.50 mmol, d.r. = 96:4) as a starting material and PPh_2Cl (224 µL, 1.25 mmol) as an electrophile were used. After 5 min stirring at

–100 °C, the resulting mixture was treated with S_8 (1.28 g, 5.0 mmol) and was allowed to warm to room temperature for 12 h. Workup was made as shown in typical procedure and the crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/9 to afford *anti*-**2-4d** (160 mg, 76% yield, d.r. = 94:6) as white solid. The relative configuration was determined by X-ray crystallography of *anti*-**2-4d**.

m.p. = 98-100 °C

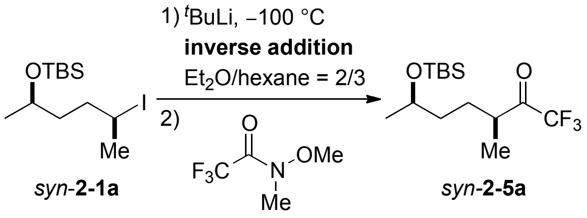
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.74-7.90 (m, 4H), 7.33-7.44 (m, 6H), 7.00 (d, J = 8.6 Hz, 2H), 6.69 (d, J = 8.6 Hz, 2H), 2.94 (s, 6H), 2.65-2.72 (m, 1H), 2.54-2.61 (m, 1H), 1.77-1.81 (m, 1H), 1.43-1.57 (m, 3H), 1.13 (d, J = 6.7 Hz, 3H), 1.12 (dd, J = 19.4 Hz, J = 6.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 149.1, 134.9, 132.3 (d, J = 76.1 Hz), 131.7 (d, J = 77.6 Hz), 131.4 (d, J = 9.2 Hz), 131.2 (d, J = 9.3 Hz), 131.1 (d, J = 2.7 Hz), 131.1 (d, J = 2.7 Hz), 128.4 (d, J = 11.6 Hz), 128.4 (d, J = 11.6 Hz), 127.5, 113.1, 40.9, 38.0, 35.2 (d, J = 13.6 Hz), 32.3 (d, J = 55.6 Hz), 26.9, 23.1, 12.2.

MS (EI, 70 eV) m/z (%): 420 (23) $[M-H]^{+\bullet}$, 218 (8), 186 (7), 161 (8), 149 (11), 148 (100), 108 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2922, 2854, 1614, 1520, 1436, 1099, 816, 724, 706, 690.

HRMS (EI) *m/z*: calcd for **$C_{26}H_{32}NPS^{+\bullet}$** $[M-H]^{+\bullet}$: 420.1915, found: 420.1907.



syn-**2-5a**

According to typical procedure *syn*-**2-1a** (171 mg, 0.50 mmol, d.r. = 97:3) as a starting material and *N*-Methoxy-*N*-methyl-2,2,2-trifluoroacetamide (151 µL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 99/1 to afford *syn*-**2-5a** (101 mg, 65% yield, d.r. = 95:5) as colorless oil. The relative configuration was determined by assuming the reaction with Weinreb-amide proceeds with retention of the configuration from the previous literature.[40]

^{1}H NMR (CDCl$_3$, 400 MHz) δ: 3.73-3.81 (m, 1H), 2.92-3.01 (m, 1H), 1.69-1.79 (m, 1H), 1.54-1.61 (m, 1H), 1.32-1.41 (m, 2H), 1.20 (d, J = 6.9 Hz, 3H), 1.11 (d, J = 6.1 Hz, 3H), 0.87 (s, 9H), 0.03 (d, J = 2.4 Hz, 6H).

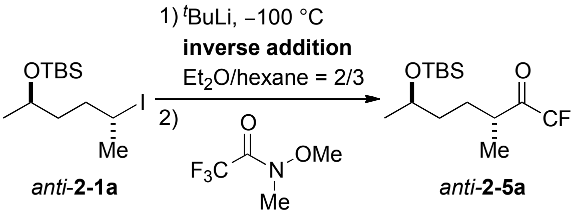
^{13}C NMR (CDCl$_3$, 100 MHz) δ: 195.3 (q, J = 33.4 Hz), 115.7 (q, J = 293.1 Hz), 68.1, 40.9, 36.6, 28.4, 25.8, 23.7, 18.0, 16.0, –4.4, –4.9.

^{19}F NMR (CDCl$_3$, 376 MHz) δ: –78.0.

MS (EI, 70 eV) m/z (%): 311 (1) $[M-H]^{+\bullet}$, 255 (100), 173 (15), 159 (26), 113 (15), 83 (20), 77 (39), 75 (39), 73 (56), 55 (18).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957, 2931, 1758, 1463, 1255, 1200, 1148, 986, 834, 773.

HRMS (EI) *m/z*: calcd for $C_{14}H_{26}F_3O_2Si^{+\bullet}$ $[M-H]^{+\bullet}$: 311.1654, found: 311.1638.



anti-**2-5a**

According to typical procedure *anti*-**2-1a** (171 mg, 0.50 mmol, d.r = 98:2) as a starting material and *N*-Methoxy-*N*-methyl-2,2,2-trifluoroacetamide (151 μL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/99 to afford *anti*-**2-5a** (104 mg, 67% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by assuming the reaction with Weinreb-amide proceeds with retention of the configuration from the previous literature.[40]

^{1}H NMR (CDCl$_3$, 400 MHz) δ: 3.74-3.80 (m, 1H), 2.90-2.99 (m, 1H), 1.86-1.93 (m, 1H), 1.35-1.46 (m, 3H), 1.20 (d, J = 6.9 Hz, 3H), 1.11 (d, J = 6.1 Hz, 3H), 0.88 (s, 9H), 0.04 (d, J = 2.7 Hz, 6H).

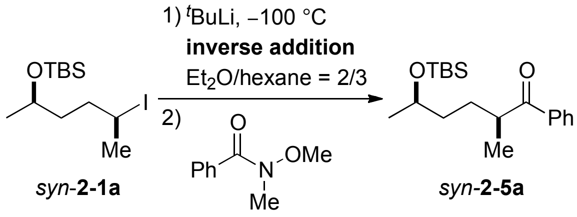
^{13}C NMR (CDCl$_3$, 100 MHz) δ: 195.2 (q, J = 33.3 Hz), 115.7 (q, J = 293.2 Hz), 68.0, 40.8, 36.5, 28.2, 25.8, 23.6, 18.0, 15.8, –4.4, –4.9.

^{19}F NMR (CDCl$_3$, 376 MHz) δ: –78.0.

MS (EI, 70 eV) m/z (%): 311 (1) $[M-H]^{+\bullet}$, 255 (100), 173 (16), 159 (35), 147 (17), 111 (18), 83 (31), 77 (59), 75 (710), 73 (80), 55 (26), 43 (71).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957, 2931, 1758, 1463, 1255, 1200, 1148, 986, 834, 773.

HRMS (EI) *m/z*: calcd for $C_{14}H_{26}F_3O_2Si^{+\bullet}$ $[M-H]^{+\bullet}$: 311.1654, found: 311.1643.



syn-**2-5a**

According to typical procedure *syn*-**2-1a** (171 mg, 0.50 mmol, d.r = 97:3) as a starting material and *N*-Methoxy-*N*-methyl-benzamide (190 µL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/49 to afford *syn*-**2-5a** (109 mg, 68% yield, d.r. = 94:6) as colorless oil. The relative configuration was determined by assuming the reaction with Weinreb-amide proceeds with retention of the configuration from the previous literature.[40]

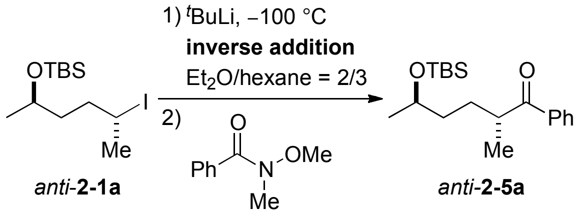
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.95 (d, J = 7.2 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.43-7.48 (m, 2H), 3.74-3.80 (m, 1H), 3.42-3.49 (m, 1H), 1.72-1.82 (m, 1H), 1.53-1.62 (m, 1H), 1.38-1.44 (m, 2H), 1.19 (d, J = 6.9 Hz, 3H), 1.09 (d, J = 6.1 Hz, 3H), 0.86 (s, 9H), 0.02 (s, 6H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 204.4, 136.7, 132.8, 128.6, 128.2, 68.7, 40.7, 37.3, 29.9, 25.9, 23.7, 18.1, 17.4, –4.4, –4.7.

MS (EI, 70 eV) m/z (%): 305 (1) $[M-CH_3]^{+\bullet}$, 263 (43), 221 (22), 171 (11), 159 (11), 145 (100), 131 (17), 105 (38), 75 (44), 55 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956, 2929, 1683, 1252, 1056, 968, 833, 773, 701.

HRMS (EI) *m/z*: calcd for $C_{18}H_{29}O_2Si^{+\bullet}$ $[M-CH_3]^{+\bullet}$: 305.1937, found: 305.1925.



anti-**2-5a**

According to typical procedure *anti*-**2-1a** (171 mg, 0.50 mmol, d.r. = 98:2) as a starting material and *N*-Methoxy-*N*-methyl-benzamide (190 µL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/49 to afford *anti*-**2-5a** (106 mg, 66% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by assuming the reaction with Weinreb-amide proceeds with retention of the configuration from the previous literature.[40]

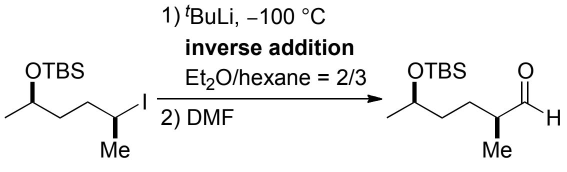
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.94 (d, J = 7.2 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.43-7.47 (m, 2H), 3.72-3.78 (m, 1H), 3.40-3.46 (m, 1H), 1.84-1.91 (m, 1H), 1.36-1.47 (m, 3H), 1.20 (d, J = 6.8 Hz, 3H), 1.10 (d, J = 6.1 Hz, 3H), 0.84 (s, 9H), 0.00 (d, J = 9.8 Hz, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 204.2, 136.7, 132.7, 128.6, 128.2, 68.4, 40.7, 37.2, 29.6, 25.8, 23.6, 18.1, 17.0, –4.4, –4.8.

MS (EI, 70 eV) m/z (%): 319 (1) [M–H]$^{+\bullet}$, 263 (56), 221 (19), 145 (100), 131 (20), 105 (40), 77 (23), 73 (33).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956, 2929, 1683, 1448, 1253, 970, 832, 773, 701.

HRMS (EI) *m/z*: calcd for **C$_{19}$H$_{31}$O$_2$Si$^{+\bullet}$** [M–H]$^{+\bullet}$: 319.2093, found: 319.2098.



syn-**2-1a** *syn*-**2-6a**

syn-**2-6a**

According to typical procedure *syn*-**2-1a** (171 mg, 0.50 mmol, d.r. = 97:3) as a starting material and DMF (97 µL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/49→1/20 to afford *syn*-**2-6a** (85 mg, 70% yield, d.r. = 91:9) as colorless oil. The relative configuration was determined by assuming the reaction with DMF proceeds with retention of the configuration from the previous literature.[15af]

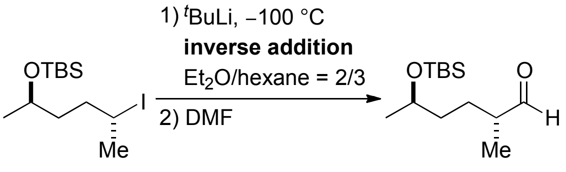
^{1}H NMR (CDCl$_3$, 300 MHz) δ: 9.60 (d, J = 1.9 Hz, 1H), 3.74-3.81 (m, 1H), 2.27-2.34 (m, 1H), 1.65-1.72 (m, 1H), 1.37-1.49 (m, 3H), 1.11 (d, J = 6.1 Hz, 3H), 1.07 (d, J = 7.0 Hz, 3H), 0.87 (s, 9H), 0.03 (d, J = 1.3 Hz, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) δ: 205.1, 68.3, 46.2, 36.7, 26.5, 25.8, 23.7, 18.1, 13.3, –4.4, –4.8.

MS (EI, 70 eV) m/z (%): 243 (1) [M–H]$^{+\bullet}$, 187 (26), 185 (26), 145 (26), 95 (26), 83 (25), 75 (100), 73 (34), 57 (28), 55 (33), 40 (20).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955, 2930, 2858, 1707, 1463, 1253, 1059, 833, 772.

HRMS (EI) *m/z*: calcd for **C$_{13}$H$_{27}$O$_2$Si$^{+\bullet}$** [M–H]$^{+\bullet}$: 243.1780, found: 243.1767.



anti-**2-1a** anti-**2-6a**

anti-**2-6a**

According to typical procedure *anti*-**2-1a** (171 mg, 0.50 mmol, d.r. = 98:2) as a starting material and DMF (97 µL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/49→1/19 to afford *anti*-**2-6a** (98 mg, 80% yield, d.r. = 92:8) as colorless oil. The relative configuration was determined by assuming the reaction with DMF proceeds with retention of the configuration from the previous literature.[15af]

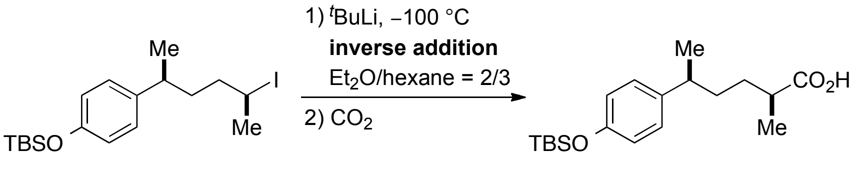
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 9.69 (s, 1H), 3.73-3.81 (m, 1H), 2.27-2.34 (m, 1H), 1.75-1.84 (m, 1H), 1.30-1.45 (m, 3H), 1.11 (d, J = 6.1 Hz, 3H), 1.08 (d, J = 7.0 Hz, 3H), 0.87 (s, 9H), 0.03 (d, J = 1.3 Hz, 6H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 205.1, 68.3, 46.2, 36.7, 26.5, 25.8, 23.6, 18.1, 13.3, –4.4, –4.8.

MS (EI, 70 eV) m/z (%): 243 (1) $[M-H]^{+\bullet}$, 187 (32), 185 (21), 145 (33), 95 (22), 75 (100), 73 (34), 55 (16), 40 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955, 2930, 2858, 1707, 1464, 1253, 1060, 833, 772.

HRMS (EI) *m/z*: calcd for $C_{13}H_{27}O_2Si^{+\bullet}$ $[M-H]^{+\bullet}$: 243.1780, found: 243.1779.



syn-**2-1e** syn-**2-4e**

syn-**2-4e**

According to typical procedure *syn*-**2-1e** (209 mg, 0.50 mmol, d.r. = 98:2) as a starting material and CO_2 dried through P_2O_5 as an electrophile were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 3/7 to afford *syn*-**2-4e** (129 mg, 77% yield, d.r. = 95:5) as white solid. The relative configuration was determined by assuming the reaction with DMF proceeds with retention of the configuration from the previous literature.[15c,15n,36d]

m.p. = 39-42 °C

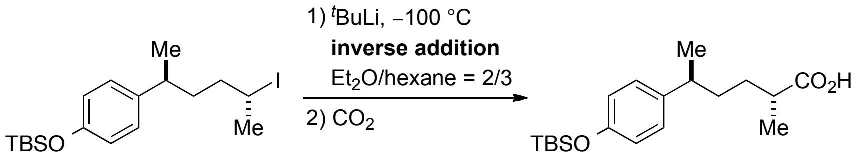
^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 10.28 (s, 1H), 7.02 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 2.60-2.67 (m, 1H), 2.39-2.46 (m, 1H), 1.54-1.61 (m, 3H), 1.41-1.45 (m, 1H), 1.22 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 7.0 Hz, 3H), 0.99 (s, 9H), 0.20 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 183.3, 153.6, 139.8, 127.7, 119.8, 39.3, 39.0, 35.6, 31.5, 25.7, 22.4, 18.2, 16.8, –4.4.

MS (EI, 70 eV) m/z (%): 336 (26) $[M]^{+\bullet}$, 235 (100), 195 (54), 185 (83), 151 (33), 83 (25), 75 (39), 73 (43), 55 (23).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3029, 2957, 2930, 1704, 1608, 1510, 1251, 1171, 912, 834, 779.

HRMS (EI) *m/z*: calcd for $C_{19}H_{32}O_3Si^{+\bullet}$ $[M]^{+\bullet}$: 336.2121, found: 336.2118.



anti-**2-1e** *anti*-**2-4e**

anti-**2-4e**

According to typical procedure in 0.25 mmol scale *anti*-**2-1e** (104 mg, 0.25 mmol, d.r. = 98:2) as a starting material and CO$_2$ dried through P$_2$O$_5$ as an electrophile were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 3/7 to afford *anti*-**2-4e** (66 mg, 79% yield, d.r. = 94:6) as white solid. The relative configuration was determined by assuming the reaction with DMF proceeds with retention of the configuration from the previous literature.[15c,15n,36d]

m.p. = 33-35 °C

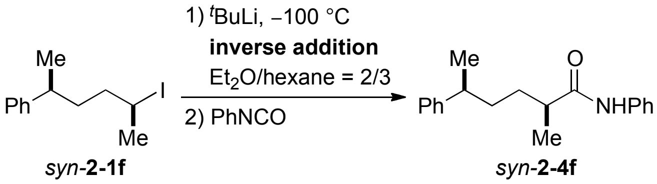
^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 10.31 (s, 1H), 7.01 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.4 Hz, 2H), 2.57-2.64 (m, 1H), 2.35-2.42 (m, 1H), 1.53-1.68 (m, 3H), 1.27-1.30 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H), 1.13 (d, J = 7.0 Hz, 3H), 0.99 (s, 9H), 0.20 (s, 6H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 183.1, 153.6, 139.8, 127.7, 119.839.5, 39.2, 36.0, 31.7, 25.7, 22.5, 18.2, 16.9, –4.4.

MS (EI, 70 eV) m/z (%): 336 (35) $[M]^{+\bullet}$, 235 (100), 195 (54), 185 (94), 151 (36), 83 (28), 75 (41), 73 (45), 55 (24).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956, 2929, 1703, 1608, 1510, 1252, 1171, 919, 832, 778.

HRMS (EI) *m/z*: calcd for $C_{19}H_{32}O_3Si^{+\bullet}$ $[M]^{+\bullet}$: 336.2121, found: 336.2117.



syn-**2-4f**

According to typical procedure 0.40 mmol scale *syn*-**2-1f** (115 mg, 0.40 mmol, d.r. = 92:8) as a starting material and PhNCO (109 μL, 1.00 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/19 to afford *syn*-**2-4f** (90 mg, 80% yield, d.r. = 92:8) as white solid. The relative configuration was determined by assuming the reaction with PhNCO proceeds with retention of the configuration from the previous literature.[15p,22]

m.p. = 45-47 °C

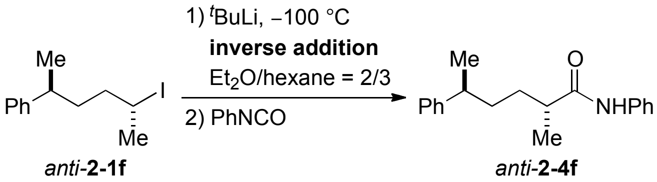
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.51 (d, J = 8.0 Hz, 2H), 7.26-7.33 (m, 4H), 7.16-7.21 (m, 3H), 7.07-7.12 (m, 1H), 2.66-2.73 (m, 1H), 2.26-2.32 (m, 1H), 1.56-1.66 (m, 3H), 1.45-1.49 (m, 1H), 1.25 (d, J = 6.9 Hz, 3H), 1.19 (d, J = 6.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 174.8, 147.1, 138.0, 128.9, 128.4, 126.9, 126.0, 124.1, 119.9, 42.6, 40.0, 35.8, 32.4, 22.2, 17.9.

MS (EI, 70 eV) m/z (%): 281 (46) $[M]^{+\bullet}$, 162 (29), 149 (66), 118 (13), 105 (87), 93 (100), 91 (35), 77 (15).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3294, 3197, 3026, 2962, 2930, 2872, 1658, 1599, 1539, 1493, 1440, 1307, 1248, 1175, 752, 697.

HRMS (EI) *m/z*: calcd for **$C_{19}H_{23}NO^{+\bullet}$** $[M]^{+\bullet}$: 281.1780, found: 281.1771.



anti-**2-4f**

According to typical procedure *anti*-**2-1f** (144 mg, 0.50 mmol, d.r. = 98:2) as a starting material and PhNCO (137 μL, 1.25 mmol) as an electrophile were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/19 to afford *anti*-**2-4f** (113 mg, 80% yield, d.r. = 96:4) as white solid. The relative configuration was determined by assuming the reaction with PhNCO proceeds with retention of the configuration from the previous literature.[15p,22]

m.p. = 77-79 °C

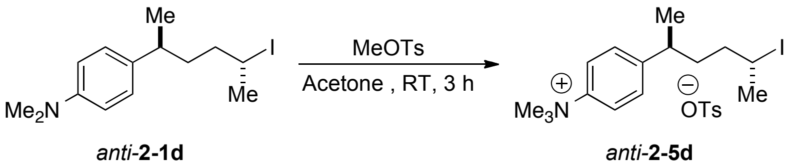
^{1}H NMR (CDCl$_3$, 300 MHz) *δ*: 7.51 (d, *J* = 7.9 Hz, 2H), 7.27-7.34 (m, 4H), 7.17-7.22 (m, 3H), 7.08-7.13 (m, 2H), 2.62-2.72 (m, 1H), 2.20-2.29 (m, 1H), 1.59-1.78 (m, 3H), 1.29-1.38 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (CDCl$_3$, 75 MHz) *δ*: 174.4, 147.2, 138.0, 128.9, 128.4, 127.0, 126.0, 124.1, 119.8, 42.6, 40.2, 36.0, 32.7, 22.5, 17.9.

MS (EI, 70 eV) m/z (%): 281 (22) $[M]^{+\bullet}$, 162 (18), 149 (46), 119 (43), 105 (88), 93 (100), 91 (52), 77 (20), 41 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3294, 3180, 3028, 2961, 2931, 2872, 1718, 1662, 1598, 1541, 1490, 1446, 1210, 1151, 752, 697.

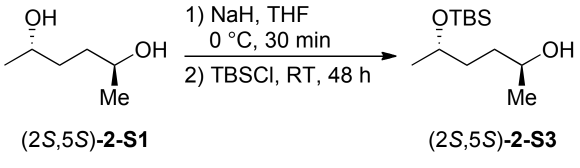
HRMS (EI) *m/z*: calcd for $C_{19}H_{23}NO^{+\bullet}$ $[M]^{+\bullet}$: 281.1780, found: 281.1776.



anti-**2-5d**

A solution of *anti*-**2-1d** (99 mg, 0.30 mmol) in acetone (0.6 mL) was placed into a flame-dried and Ar-flushed *Schlenk*-tube equipped with a stirring bar. MeOTs (48 μL, 0.32 mmol) was added at room temperature and the reaction mixture was stirred for 3 h. After removal of volatile materials under reduced pressure, the resulting crude product was recrystallized from chloroform to obtain a single crystal of *anti*-**2-5d** for X-ray crystallographic analysis.

9.2.3 Determination of the relative configuration



(2S,5S)-**2-3S**

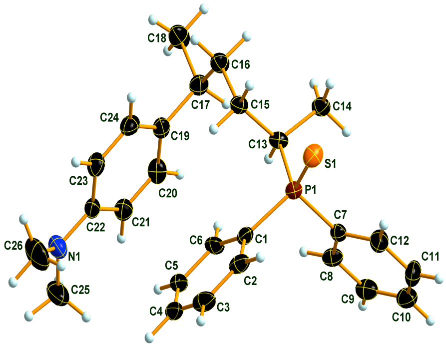
A suspention of NaH (0.22 g, 60 wt%, 5.5 mmol) in THF (50 mL) was placed into a flame-dried and Ar-flushed *Schlenk*-tube equipped with a stirring bar. It was cooled to 0 °C and a solution of commecially available (2*S*,5*S*)-2,5-hexanediol (0.59 g, 5.0 mmol) in THF (5 mL) was added. After 30 min stirring, a solution of TBSCl (0.75 g, 5.0 mmol) in THF (3 mL) was added. The resulting mixture was warmed up to room temperature and stirred overnight. It was quenched with saturated NH_4Cl aqueous solution. The phases were separated, the aqueous phase was extracted with Et_2O three times and the combined organic phase was dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/4 to afford (2S,5S)-**2-3S** (1.02 g, 88% yield) as colorless oil.

9.2.4 Kinetics study

These experiments were carried out according to typical procedure using *syn*-**2-1a** or *anti*-**2-1a** (171 mg, 0.50 mmol) as a starting material and Me_2S_2 (111 µL, 1.25 mmol) as an electrophile except stirring at –100 or –90 °C for different time. The crude products were purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/99 to afford *syn*- or *anti*-**2-3a** with different d.r.

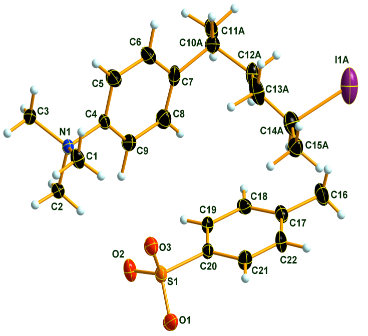
9.2.5 X-ray crystal information

CCDC/963930 (for *anti*-**2-4d**) and CCDC/963929 (for *anti*-**2-5d**) contain supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



anti-**2-4d** (Thermal ellipsoids are drawn at 50 % probability level.)

net formula	$C_{26}H_{32}NPS$
M/g mol^{-1}	421.56
crystal size/mm	0.438 × 0.114 × 0.072
T/K	100(2)
radiation	MoKα
diffractometer	'Xcalibur, Sapphire3'
crystal system	monoclinic
space group	P 21/n
a/Å	16.8176(11)
b/Å	6.5863(4)
c/Å	21.3334(17)
α/°	90.00
β/°	94.595(7)
γ/°	90.00
V/Å^3	2355.4(3)
Z	4
calc. density/g cm^{-3}	1.189
μ/mm^{-1}	0.217
absorption correction	multi-scan
refls. measured	17077
R_{int}	0.0632
mean $\sigma(I)/I$	0.0674
θ range	4.36–26.97
observed refls	2403
x,y (weighting scheme)	0.0484, 1.0642
hydrogen refinement	mixed
refls in refinement	4794
parameters	288
restraints	0
$R(F_{\text{obs}})$	0.0894
$R_{\text{w}}(F^2)$	0.1299
S	1.019
shift/error$_{\text{max}}$	0.001
max electron density/e Å^{-3}	0.671
min electron density/e Å^{-3}	–0.257



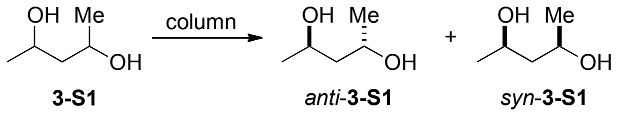
anti-**2-5d** (Thermal ellipsoids are drawn at 50 % probability level.)

net formula	$C_{22}H_{32}INO_3S$
M/g mol^{-1}	517.45
crystal size/mm	0.301 × 0.148 × 0.106
T/K	100(2)
radiation	MoKα
diffractometer	‘Xcalibur, Sapphire3’
crystal system	triclinic
space group	P –1
a/Å	6.5847(4)
b/Å	9.2773(5)
c/Å	19.6376(11)
α/°	101.588(4)
β/°	95.993(5)
γ/°	92.103(4)
V/Å^3	1166.70(12)
Z	2
calc. density/g cm^{-3}	1.437
μ/mm^{-1}	1.483
absorption correction	multi-scan
refls. measured	9728
R_{int}	0.0409
mean σ*(I)*/*I*	0.0721
θ range	4.72–28.96
observed refls	2592
x,y (weighting scheme)	0.0369, 0.0000
hydrogen refinement	mixed
refls in refinement	5759

parameters	321
restraints	0
$R(F_{\text{obs}})$	0.0735
$R_w(F^2)$	0.1086
S	1.027
shift/error$_{\text{max}}$	0.001
max electron density/e Å^{-3}	0.707
min electron density/e Å^{-3}	–0.695

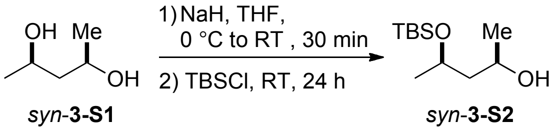
9.3 Stereoconvergent Preparation of Open-Chain Secondary Alkyllithiums Functionalized at 3-Position

9.3.1 Preparation of starting materials



syn-**3-S1** (CAS: 36402-52-5) and *anti*-**3-S1** (CAS: 3950-21-8)

The mixture of diastereomers of **3-S1** (Alfa Aesar, CAS: 625-69-4) was separated by chromatography on silica gel with ether to afford *anti*-**3-S1** as the first fraction and *syn*-**3-S1** as the second fraction. The relative configuration was confirmed by the comparison with (*R*,*R*)-(−)-2,4-pentanediol (Aldrich).



***syn*-4-((*tert*-butyldimethylsilyl)oxy)pentan-2-ol** (*syn*-**3-S2**; CAS: 1599484-67-9)

A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.88 g, 60 wt% in mineral oil, 22.0 mmol) in THF (220 mL) and cooled to 0 °C. A solution of *syn*-**3-S1** (2.1 g, 20.0 mmol, d.r. = 99:1) in THF (20 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then a solution of TBSCl (3.0 g, 20.0 mmol) in THF (10 mL) was added dropwise and the mixture was stirred for 20 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/5 to afford *syn*-**3-S2** (4.2 g, 95% yield, d.r. = 99:1) as yellow oil.

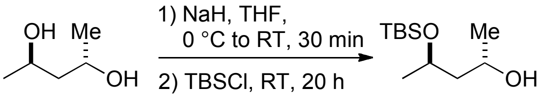
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.23-4.12 (m, 2H), 3.09 (s br, 1H), 1.64 (ddd, J = 14.0, 9.9 and 3.9 Hz, 1H), 1.48 (ddd, J = 14.3, 4.9 and 2.2 Hz, 1H), 1.22 (d, J = 6.3 Hz, 1H), 1.16 (d, J = 6.2 Hz, 1H), 0.88 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 67.9, 64.5, 45.8, 25.9, 23.8, 22.8, 18.1, −4.4, −4.9.

MS (70 eV, EI) *m/z* (%): 203 (1) $[M–Me]^{+•}$, 159 (12), 143 (5), 119 (100), 101 (6), 75 (73), 59 (4).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3418 (br w), 2957 (w), 2928 (w), 2856 (w), 1472 (w), 1463 (w), 1375 (w), 1361 (w), 1255 (w), 1154 (w), 1122 (w), 1058 (m), 1021 (m), 1005 (w), 979 (w), 945 (w), 937 (w), 893 (w), 863 (w), 833 (s), 807 (w), 773 (vs), 725 (w), 678 (w), 657 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{11}H_{27}O_2Si^{+\bullet}}$ $[M+H]^{+\bullet}$: 219,1780, found 219,1811.



anti-**3-S1** *anti*-**3-S2**

anti-**3-S2** (CAS: 1334170-94-3)

A dry and Ar-flushed *Schlenk*-flask was charged with a suspension of NaH (0.88 g, 60 wt% in mineral oil, 22.0 mmol) in THF (220 mL) and cooled to 0 °C. A solution of *anti*-**3-S1** (2.1 g, 20.0 mmol, d.r. = 99:1) in THF (20 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then a solution of TBSCl (3.0 g, 20.0 mmol) in THF (10 mL) was added dropwise and the mixture was stirred for 20 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/5 to afford *anti*-**3-S2** (4.1 g, 93% yield, d.r. = 99:1) as yellow oil.

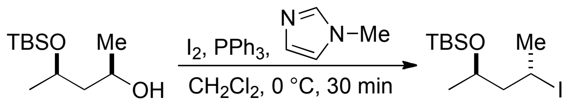
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 4.07 (m, 1H), 3.95 (dqd, J = 9.1, 6.2 and 3.2 Hz, 1H), 3.09 (s br, 1H), 1.62-1.48 (m, 2H), 1.17 (d, J = 6.1 Hz, 3H), 1.15 (d, J = 6.2 Hz, 3H), 0.89 (s, 9H), 0.11 (s, 3H) 0.10 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 70.3, 67.8, 47.6, 25.9, 24.8, 23.6, 18.0, –3.7, –4.7.

MS (70 eV, EI) *m/z* (%): 203 (1) $[M–Me]^{+\bullet}$, 159 (5), 143 (5), 119 (100), 101 (9), 75 (64), 59 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3416 (br w), 2957 (w), 2928 (w), 2856 (w), 1472 (w), 1463 (w), 1375 (w), 1361 (w), 1255 (w), 1154 (w), 1122 (w), 1058 (m), 1021 (m), 1005 (w), 979 (w), 945 (w), 938 (w), 893 (w), 863 (w), 833 (s), 806 (w), 773 (vs), 720 (w), 677 (w), 659 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{11}H_{27}O_2Si^{+\bullet}}$ $[M+H]^{+\bullet}$: 219,1780, found 219,1811.

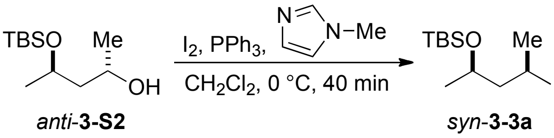


syn-**3-S2** *anti*-**3-3a**

anti-**3-3a**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (24 mL) and cooled to 0 °C. PPh_3 (1.57 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *syn*-**3-S2** (1.1 g, 5.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 40 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *anti*-**3-3a** (1.2 g, 76% yield, d.r. = 99:1) as colorless oil.

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.17 (ddq, J = 7.9, 6.85 and 6.84 Hz, 1H), 3.92 (qt, J = 6.11 and 6.10 Hz, 1H), 2.19 (ddd, J = 14.4, 8.0 and 6.6 Hz, 1H), 1.93 (d, J = 6.8 Hz, 3H), 1.70 (dt, J = 14.1 and 6.5 Hz, 1H), 1.12 (d, J = 6.0 Hz, 3H), 0.89 (s, 9H), 0.074 (s, 3H), 0.068 (s, 3H).
^{13}C-NMR (75 MHz, CDCl$_3$) δ: 68.9, 52.9, 28.9, 26.0, 25.2, 23.1, 18.2, –4.1, –4.6.
MS (70 eV, EI) *m/z* (%): 313 (1) $[\text{M–Me}]^{+\bullet}$, 271 (21), 229 (100), 185 (39), 159 (9), 143 (5), 115 (5), 101 (7), 75 (21), 59 (5).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2927 (w), 2856 (w), 1472 (w), 1462 (w), 1376 (w), 1360 (w), 1255 (w), 1178 (w), 1128 (w), 1107 (m), 1075 (w), 1059 (m), 1019 (w), 1005 (m), 988 (w), 963 (w), 916 (w), 877 (m), 853 (w), 834 (s), 823 (m), 805 (m), 772 (vs), 718 (w), 664 (w).
HRMS (EI) *m/z*: calcd for **$C_{10}H_{22}OISi^{+\bullet}$** $[\text{M–Me}]^{+\bullet}$: 313.0485, found: 313.0420.



syn-**3-3a**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (24 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *anti*-**3-S2** (1.1 g, 5.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 40 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over

$MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *syn*-**3-3a** (1.1 g, 69% yield, d.r. = 99:1) as colorless oil.

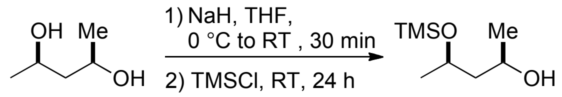
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.28 (dqd, *J* = 11.1, 6.9 and 2.8 Hz, 1H), 3.95 (dqd, *J* = 9.4, 6.1 and 2.4 Hz, 1H), 1.96 (d, *J* = 6.9 Hz, 3H), 1.86 (ddd, *J* = 14.7, 11.1 and 2.4 Hz, 1H), 1.52 (ddd, *J* = 14.7, 9.4 and 2.9 Hz, 1H), 1.18 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 68.9, 52.9, 29.9, 28.9, 26.1, 24.1, 18.2, –3.8, –4.2.

MS (70 eV, EI) *m/z* (%): 313 (1) $[M–Me]^{+\bullet}$, 271 (15), 229 (100), 185 (40), 159 (8), 143 (6), 115 (5), 101 (8), 75 (23), 59 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2927 (w), 2855 (w), 1471 (w), 1462 (w), 1372 (w), 1360 (w), 1251 (w), 1168 (w), 1145 (m), 1127 (m), 1056 (m), 996 (w), 963 (w), 925 (w), 881 (w), 867 (w), 834 (s), 823 (m), 805 (m), 773 (vs), 716 (w), 656 (w).

HRMS (EI) *m/z*: calcd for **$C_{10}H_{22}OISi^{+\bullet}$** $[M–Me]^{+\bullet}$: 313.0485, found: 313.0468.



syn-**3-S1** *syn*-**3-S3**

syn-**3-S3**

A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.37 g, 60 wt% in mineral oil, 9.3 mmol) in THF (10 mL) and cooled to 0 °C. A solution of *syn*-**3-S1** (0.93 g, 8.9 mmol, d.r. = 99:1) in THF (5 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then a solution of TMSCl (1.1 mL, 8.9 mmol) was added dropwise and the mixture was stirred for 24 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were carefully evaporated. The crude product was purified by Kügel distillation (1 mbar, 55 °C) to afford *syn*-**3-S3** (0.35 g, 22% yield) as colorless oil. This compound is not so stable.

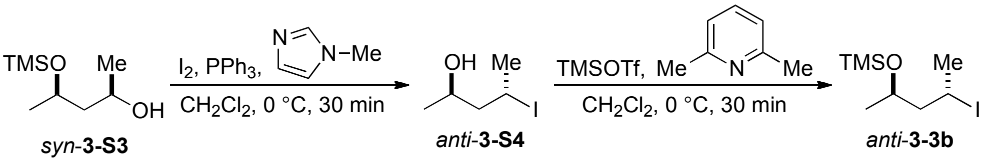
^{1}H-NMR (200 MHz, $CDCl_3$) δ: 4.25-4.00 (m, 2H), 3.10 (s br, 1H), 1.68-1.41 (m, 2H), 1.20 (d, *J* = 6.3 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 0.13 (s, 9H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 66.9, 64.5, 46.1, 23.7, 23.0, 0.0. (with some impurity due to decomposition)

MS (70 eV, EI) *m/z* (%): 161 (5) [M–Me]$^{+\bullet}$, 143 (11), 119 (99), 91 (7), 75 (100), 59 (7).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3426 (w br), 2963 (w), 2930 (w), 1454 (w), 1412 (w), 1375 (w), 1249 (m), 1154 (w), 1121 (m), 1058 (m), 1020 (w), 978 (w), 948 (w), 895 (w), 869 (w), 834 (vs), 748 (m), 711 (w), 682 (w).

HRMS (EI) *m/z*: calcd for **$C_8H_{18}OSi^{+\bullet}$** [M–H$_2$O]$^{+\bullet}$: 158.1127, found: 158.1147.



anti-**3-3b**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I$_2$ (0.61 g, 2.4 mmol) in CH$_2$Cl$_2$ (15 mL) and cooled to 0 °C. PPh$_3$ (0.63 g, 2.4 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.19 mL, 2.4 mmol) was added. After 10 min of further stirring, *syn*-**3-S3** (0.35 g, 2.0 mmol) dissolved in CH$_2$Cl$_2$ (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated (NaHSO$_4$+Na$_2$S$_2$O$_5$) aqueous solution[106] and the mixture was extracted with CH$_2$Cl$_2$ three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated at 30 °C.[107] Unfortunately, TMS group had gone judged from a NMR spectrum of the crude product. It was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/2 to afford *anti*-**3-S4** (0.24 g, 41% yield) as colorless oil. A dry and Ar-flushed *Schlenk*-flask was charged with a solution of *anti*-**3-S4** (0.24 g, 1.1 mmol) in CH$_2$Cl$_2$ (5 mL) and cooled to 0 °C. In another *Schlenk*-flask 2,6-dimethylpyridine (0.19 mL, 1.6 mmol) and TMSOTf (0.24 mL, 1.3 mmol) was mixed in CH$_2$Cl$_2$ (2 mL) and stirred at room temperature for 10 min. This mixture was added to the solution of starting material solution and stirred at 0 °C for 30 min. The reaction mixture was diluted with Et$_2$O and saturated NH$_4$Cl aqueous solutions was added to the reaction mixture. Then it is extracted with Et$_2$O three times and dried over MgSO$_4$. After removal of solvent, the crude product was left under vacuum to remove the remained 2,6-dimethylpyridine and *anti*-**3-3b** was obtained (0.25 g, 80% yield, d.r. = 99:1) as yellow oil.

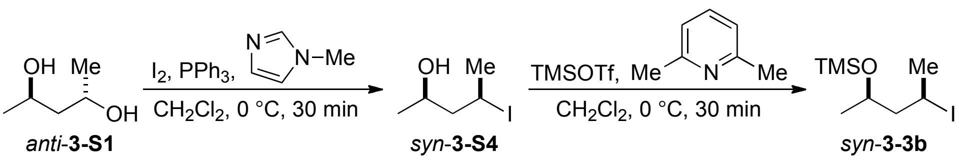
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 4.09 (qt, *J* = 7.0 and 6.9 Hz, 1H), 3.92 (qt, *J* = 6.0 and 5.9 Hz, 1H), 2.17 (dt, *J* = 14.7 and 6.9 Hz, 1H), 1.92 (d, *J* = 6.8 Hz, 3H), 1.69 (dt, *J* = 13.9 and 6.5 Hz, 1H), 1.12 (d, *J* = 6.1 Hz, 3H), 0.13 (s, 9H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 68.4, 52.7, 28.9, 25.2, 23.2, 0.4.

MS (70 eV, EI) *m/z* (%): 271 (4) [M–Me]$^{+•}$, 229 (30), 185 (26), 159 (11), 143 (5), 117 (100), 101 (5), 73 (65), 59 (4).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2925 (w), 1445 (w), 1376 (w), 1359 (w), 1260 (w), 1249 (m), 1178 (w), 1134 (w), 1127 (w), 1105 (w), 1077 (w), 1058 (m), 1019 (w), 989 (w), 964 (w), 917 (w), 888 (w), 878 (w), 867 (w), 834 (vs), 747 (m), 706 (w), 682 (w).

HRMS (EI) *m/z*: calcd for **$C_7H_{16}OISi^{+•}$** [M–Me]$^{+•}$: 271.0015, found: 270.9998.



syn-**3-3b**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I$_2$ (1.65 g, 6.3 mmol) in CH$_2$Cl$_2$ (40 mL) and cooled to 0 °C. PPh$_3$ (1.60 g, 6.3 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.50 mL, 6.3 mmol) was added. After 10 min of further stirring, *anti*-**3-S1** (0.62 g, 6.0 mmol, d.r. = 99:1) dissolved in CH$_2$Cl$_2$ (5 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated (NaHSO$_4$+Na$_2$S$_2$O$_5$) aqueous solution[106] and the mixture was extracted with CH$_2$Cl$_2$ three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated at 30 °C.[107,108] The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/2 to afford *syn*-**3-S4** (0.37 g, 29% yield, CAS:221248-58-4) as colorless oil. A dry and Ar-flushed *Schlenk*-flask was charged with a solution of *syn*-**3-S4** (0.37 g, 1.7 mmol) in CH$_2$Cl$_2$ (7 mL) and cooled to 0 °C. In another *Schlenk*-flask 2,6-dimethylpyridine (0.30 mL, 2.6 mmol) and TMSOTf (0.38 mL, 2.1 mmol) was mixed in CH$_2$Cl$_2$ (3 mL) and stirred at room temperature for 15 min. This mixture was added to the solution of starting material solution and stirred at 0 °C for 30 min. The reaction mixture was diluted with Et$_2$O and saturated NH$_4$Cl aqueous solution was added to the reaction mixture. Then it is extracted with Et$_2$O three times and dried over MgSO$_4$. After removal of solvent, the crude product was left under vacuum to remove the remained 2,6-dimethylpyridine and *syn*-**3-3b** was obtained (0.38 g, 76% yield, d.r. = 99:1) as yellow oil.

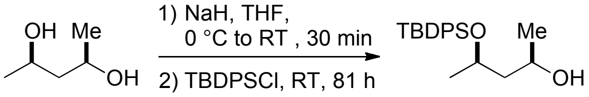
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.26 (dqd, J = 11.1, 6.9 and 2.7 Hz, 1H), 3.95 (dqd, J = 9.4, 6.1 and 2.2 Hz, 1H), 1.95 (d, J = 6.9 Hz, 3H), 1.87 (ddd, J = 14.8, 11.1 and 2.3 Hz, 1H), 1.52 (ddd, J = 14.9, 9.5 and 2.8 Hz, 1H), 1.19 (d, J = 6.1 Hz, 3H), 0.17 (s, 9H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 68.9, 52.5, 29.8, 28.7, 24.1, 0.8.

MS (70 eV, EI) *m/z* (%): 286 (1) [M]$^{+\bullet}$, 271 (6), 229 (51), 185 (39), 159 (23), 143 (6), 117 (100), 101 (6), 73 (67).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2925 (w), 2891 (w), 1446 (w), 1415 (w), 1372 (w), 1358 (w), 1249 (m), 1166 (w), 1145 (m), 1127 (w), 1056 (m), 997 (w), 964 (w), 926 (w), 884 (m), 868 (w), 835 (vs), 748 (m), 705 (w), 683 (w).

HRMS (EI) *m/z*: calcd for **$C_8H_{19}OISi^{+\bullet}$** [M]$^{+\bullet}$: 286.0250, found: 286.0284.



syn-**3-S1** *syn*-**3-S5**

syn-**3-S5**

A dry and N$_2$-flushed *Schlenk*-flask was charged with a suspension of NaH (0.29 g, 60 wt% in mineral oil, 7.4 mmol) in THF (6 mL) and cooled to 0 °C. A solution of *syn*-**3-S1** (0.73 g, 7.0 mmol, d.r. = 99:1) in THF (4 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then a solution of TBDPSCl (1.8 mL, 7.0 mmol) was added dropwise and the mixture was stirred for 81 h at room temperature. The reaction was quenched with saturated NH$_4$Cl aqueous solution at 0 °C and the mixture was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/4 to afford *syn*-**3-S5** (1.7 g, 71% yield, d.r. = 99:1) as colorless oil.

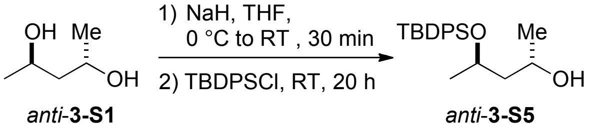
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.75-7.67 (m, 4H), 7.48-7.35 (m, 6H), 4.24-4.11 (m, 2H), 3.15 (s br, 1H), 1.71 (ddd, J = 14.1, 10.0 and 4.0 Hz, 1H), 1.47 (ddd, J = 14.3, 4.9 and 2.3 Hz, 1H), 1.15 (d, J = 6.2 Hz, 3H), 1.11 (d, J = 6.3 Hz, 3H), 1.07 (s, 9H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 136.1, 136.0, 134.0, 133.5, 130.0, 129.9, 127.9, 127.7, 69.0, 64.5, 46.2, 27.1, 23.8, 22.6, 19.3.

MS (70 eV, EI) *m/z* (%): 285 (3) [M–^{t}Bu]$^{+\bullet}$, 243 (28), 199 (100), 181 (8), 139 (29), 121 (3), 105 (3), 77 (4).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3344 (w br), 2963 (w), 2930 (w), 2856 (w), 1472 (w), 1462 (w), 1426 (w), 1375 (w), 1362 (w), 1153 (w), 1110 (m), 1104 (m), 1057 (w), 1018 (w), 1006 (w), 998 (w), 977 (w), 936 (w), 892 (w), 821 (w), 740 (w), 727 (w), 699 (vs), 684 (m).

HRMS (EI) *m/z*: calcd for **$C_{21}H_{29}O_2Si^{+\bullet}$** $[M–H]^{+\bullet}$: 341.1937, found: 341.1923.



anti-**3-S5**

A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.29 g, 60 wt% in mineral oil, 7.4 mmol) in THF (6 mL) and cooled to 0 °C. A solution of *anti*-**3-S1** (0.73 g, 7.0 mmol, d.r. = 99:1) in THF (4 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then a solution of TBDPSCl (1.8 mL, 7.0 mmol) was added dropwise and the mixture was stirred for 20 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/4 to afford *anti*-**3-S5** (1.7 g, 70% yield, d.r. = 99:1) as colorless oil.

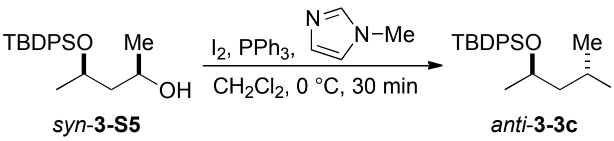
^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.78-7.70 (m, 4H), 7.49-7.35 (m, 6H), 4.12 (dqd, *J* = 8.6, 6.1 and 4.6 Hz, 1H), 4.02 (dqdd, *J* = 9.0, 6.1, 6.0 and 3.1 Hz, 1H), 2.63 (s br, 1H), 1.72 (dt, *J* = 14.2 and 8.7 Hz, 1H), 1.52 ddd, *J* = 14.2, 4.4 and 3.4 Hz, 1H), 1.14 (d, *J* = 6.2 Hz, 3H), 1.06 (s, 9H), 1.00 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 136.01, 135.96, 134.6, 133.7, 129.9, 129.7, 127.9, 127.6, 70.7, 67.1, 48.2, 27.1, 24.3, 23.8, 19.3.

MS (70 eV, EI) *m/z* (%): 285 (2) $[M–^tBu]^{+\bullet}$, 267 (4), 243 (21), 199 (100), 181 (9), 139 (36), 121 (4), 105 (5), 77 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3368 (w br), 2963 (w), 2930 (w), 2856 (w), 1472 (w), 1426 (w), 1376 (w), 1109 (m), 1103 (m), 1056 (w), 1022 (w), 1006 (w), 998 (w), 982 (w), 941 (w), 904 (w), 821 (w), 731 (w), 699 (vs), 685 (m).

HRMS (DEI) *m/z*: calcd for **$C_{21}H_{31}O_2ISi^{+\bullet}$** $[M+H]^{+\bullet}$: 343.2015, found: 343,2094.



anti-**3-3c**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 5.8 mmol) in CH_2Cl_2 (25 mL) and cooled to 0 °C. PPh_3 (1.5 g, 5.8 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.46 mL, 5.8 mmol) was added. After 10 min of further stirring, *syn*-**3-S5** (1.7 g, 4.9 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/200 to afford *anti*-**3-3c** (1.4 g, 64% yield, d.r. = 99:1) as colorless oil.

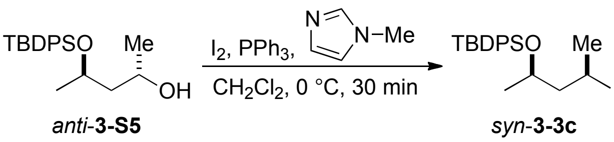
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.72-7.64 (m, 4H), 7.47-7.34 (m, 6H), 4.14 (qt, *J* = 7.0 and 6.9 Hz, 1H), 3.93 (qt, *J* = 6.2 and 6.1 Hz, 1H), 2.28 (ddd, *J* = 14.3, 7.7 and 6.7 Hz, 1H), 1.77 (d, *J* = 6.7 Hz, 3H), 1.76 (ddd, *J* = 14.0, 7.0 and 6.6 Hz, 1H), 1.063 (s, 9H), 1.058 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 136.01, 135.97, 134.6, 134.0, 129.8, 129.7, 127.8, 127.6, 69.6, 52.8, 28.8, 27.2, 24.7, 23.0, 19.4.

MS (70 eV, EI) *m/z* (%): 395 (14) $[M–{}^tBu]^{+\bullet}$, 353 (44), 309 (100), 267 (13), 249 (50), 223 (7), 199 (36), 181 (27), 135 (11), 105 (11), 77 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3069 (w), 2961 (w), 2929 (w), 2856 (w), 1471 (w), 1461 (w), 1426 (w), 1379 (w), 1361 (w), 1241 (w), 1177 (w), 1126 (w), 1103 (s), 1059 (m), 1019 (m), 1006 (w), 988 (w), 961 (w), 917 (w), 878 (w), 850 (w), 821 (w), 763 (w), 737 (w), 728 (w), 699 (vs), 686 (m).

HRMS (EI) *m/z*: calcd for **$C_{21}H_{28}OISi^{+\bullet}$** $[M–H]^{+\bullet}$: 451.0954, found: 451.0943.



syn-**3-3c** (CAS: 219547-21-4)

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.4 g, 5.4 mmol) in CH_2Cl_2 (25 mL) and cooled to 0 °C. PPh_3 (1.4 g, 5.4 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.42 mL, 5.4 mmol) was added. After 10 min of further stirring, *anti*-**3-S5** (1.5 g, 4.5 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/200 to afford *syn*-**3-3c** (1.9 g, 95% yield, d.r. = 99:1) as white solid. The relative configuration was further confirmed by X-ray crystallographic analysis after recrystallization from *n*-pentane.

m.p.: 58.3-60.3 °C

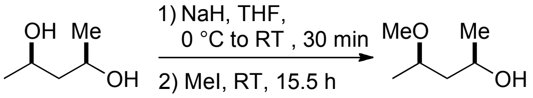
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.28-7.64 (m, 4H), 7.48-7.33 (m, 6H), 4.42 (dqd, *J* = 10.5, 6.9 and 3.7 Hz, 1H), 4.00 (dqd, *J* = 9.1, 6.1 and 3.1 Hz, 1H), 1.92 (d, *J* = 6.9 Hz, 3H), 1.91 (ddd, *J* = 14.5, 10.5 and 3.1 Hz, 1H), 1.75 (ddd, *J* = 14.7, 8.7 and 3.7 Hz, 1H), 1.06 (s, 9H), 1.04 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 136.2, 136.0, 134.9, 133.7, 129.8, 129.6, 127.8, 127.5, 70.1, 53.1, 29.7, 27.8, 27.2, 23.8, 19.5.

MS (70 eV, EI) *m/z* (%): 451 (1) $[M–H]^{+•}$, 395 (14), 353 (56), 309 (100), 267 (11), 249 (43), 223 (6), 199 (25), 181 (19), 135 (6), 105 (6), 77 (4).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3071 (w), 2962 (w), 2927 (w), 2853 (w), 1471 (w), 1461 (w), 1426 (w), 1374 (w), 1361 (w), 1253 (w), 1169 (w), 1142 (w), 1129 (w), 1110 (m), 1046 (m), 1028 (w), 1007 (w), 992 (w), 958 (w), 939 (w), 925 (w), 882 (w), 866 (w), 822 (m), 740 (m), 729 (m), 699 (vs), 682 (w).

HRMS (EI) *m/z*: calcd for **$C_{21}H_{28}OISi^{+•}$** $[M–H]^{+•}$: 451.0954, found: 451.0963.

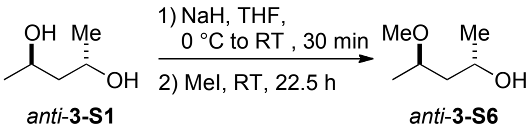


syn-**3-S1** *syn*-**3-S6**

syn-**3-S6** (CAS: 111832-88-3)

A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.61 g, 60 wt% in mineral oil, 15.2 mmol) in THF (150 mL) and cooled to 0 °C. A solution of *syn*-**3-S1** (1.4 g, 13.8 mmol, d.r. = 99:1) in THF (15 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then MeI (0.86 mL, 13.8 mmol) was added and the mixture was stirred for 15.5 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*n*-pentane = 2/1 to afford *syn*-**3-S6** (1.3 g, 82% yield, d.r. = 99:1) as colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: 4.16-4.04 (m, 1H), 3.65 (dqd, *J* = 6.40, 6.36 and 3.8 Hz, 1H), 2.87 (d, *J* = 4.0 Hz, 1H), 3.35 (s, 3H), 1.67 (ddd, *J* = 14.6, 8.3 and 3.8 Hz, 1H), 1.58 (ddd, *J* = 14.6, 6.8 and 3.2 Hz, 1H), 1.20 (d, *J* = 6.2 Hz, 3H), 1.14 (d, *J* = 6.3 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 75.2, 65.0, 56.3, 44.1, 23.6, 18.7.
MS (70 eV, EI) *m/z* (%): 103 (4) $[M–Me]^{+•}$, 85 (8), 59 (100).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3397 (w br), 2966 (w), 2932 (w), 2822 (w), 1457 (w), 1413 (w), 1373 (w), 1354 (w), 1238 (w), 1185 (w), 1155 (m), 1122 (m), 1080 (vs), 1036 (m), 995 (w), 956 (w), 909 (w), 881 (w), 832 (w), 797 (w).
HRMS (ESI) *m/z*: calcd for $C_{12}H_{28}NaO_4^+$ $[2M+Na]^+$: 259.1885, found: 259.1904.



anti-**3-S6** (CAS: 111832-39-4)
A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.84 g, 60 wt% in mineral oil, 21.1 mmol) in THF (220 mL) and cooled to 0 °C. A solution of *anti*-**3-S1** (2.0 g, 19.2 mmol, d.r. = 99:1) in THF (20 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then MeI (1.2 mL, 19.2 mmol) was added and the mixture was stirred for 22.5 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*n*-pentane = 2/1 to afford *anti*-**3-S6** (1.6 g, 70% yield, d.r. = 99:1) as colorless oil.

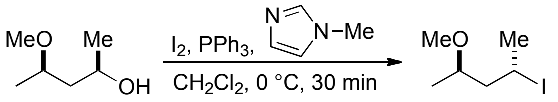
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.97 (dqdd, J = 9.1, 6.2, 2.7 and 1.3 Hz, 1H), 3.67 (s br, 1H), 3.57 (dqd, J = 9.7, 6.1 and 3.7 Hz, 1H), 3.34 (s, 3H), 1.61 (dt, J = 14.6 and 9.3 Hz, 1H), 1.50 (ddd, J = 14.6, 3.5 and 2.8 Hz, 1H), 1.16 (d, J = 6.1 Hz, 3H), 1.15 (d, J = 6.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 78.4, 68.1, 55.9, 45.7, 23.7, 19.2.

MS (70 eV, EI) *m/z* (%): 103 (5) $[M–Me]^{+\bullet}$, 85 (11), 59 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3412 (w br), 2968 (w), 2932 (w), 2822 (w), 1457 (w), 1414 (w), 1373 (w), 1303 (w), 1188 (w), 1169 (w), 1139 (m), 1116 (m), 1079 (vs), 1038 (s), 1000 (w), 951 (w), 915 (w), 883 (w), 845 (w), 816 (w), 792 (w).

HRMS (ESI) *m/z*: calcd for $\mathbf{C_{12}H_{28}NaO_4}^+$ $[2M+Na]^+$: 259.1885, found: 259.1903.



syn-**3-S6** *anti*-**3-3d**

anti-**3-3d**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (25 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *syn*-**3-S6** (1.5 g, 4.5 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*n*-pentane = 1/30 to afford *anti*-**3-3d** (0.82 g, 72% yield, d.r. = 99:1) as colorless oil.

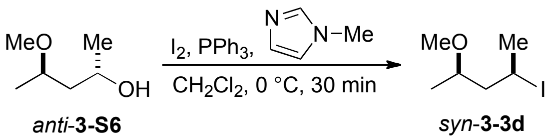
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.22 (tq, J = 7.6 and 6.8 Hz, 1H), 3.43 (tq, J = 6.4 and 6.1 Hz, 1H), 3.32 (s, 3H), 2.27 (ddd, J = 14.5, 7.8 and 6.9 Hz, 1H), 1.94 (d, J = 6.8 Hz, 3H), 1.69 (ddd, J = 14.3, 6.8 and 6.0 Hz, 1H), 1.12 (d, J = 6.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 76.6, 56.1, 49.7, 28.8, 25.0, 18.6.

MS (70 eV, EI) *m/z* (%): 228 (1) $[M]^{+\bullet}$, 127 (5), 101 (15), 85 (7), 59 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2969 (w), 2919 (w), 2819 (w), 1451 (w), 1375 (w), 1246 (w), 1198 (w), 1177 (w), 1139 (w), 1084 (w), 1046 (w), 982 (w), 929 (w), 871 (m), 853 (m), 798 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_6H_{13}OI}^{+\bullet}$ $[M]^{+\bullet}$: 228.0011, found: 228.0005.



syn-**3-3d**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (25 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *anti*-**3-S6** (1.5 g, 4.5 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*n*-pentane = 1/30 to afford *syn*-**3-3d** (0.91 g, 79% yield, d.r. = 99:1) as colorless oil.

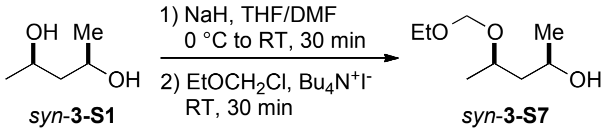
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 4.42 (dqd, *J* = 11.0, 6.9 and 3.2 Hz, 1H), 3.49 (dqd, *J* = 9.5, 6.1 and 2.6 Hz, 1H), 3.37 (s, 3H), 1.94 (d, *J* = 6.9 Hz, 3H), 1.85 (ddd, *J* = 15.0, 11.0 and 2.6 Hz, 1H), 1.54 (ddd, *J* = 15.1, 9.6 and 3.1 Hz, 1H), 1.17 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 76.9, 56.7, 50.6, 29.7, 27.9, 18.7.

MS (70 eV, EI) *m/z* (%): 228 (2) $[M]^{+\bullet}$, 127 (5), 101 (18), 85 (9), 69 (16), 59 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2970 (w), 2927 (w), 2882 (w), 2821 (w), 1444 (w), 1416 (w), 1372 (w), 1352 (w), 1258 (w), 1202 (w), 1165 (w), 1140 (w), 1127 (w), 1083 (m), 1017 (m), 939 (w), 868 (w), 797 (w).

HRMS (EI) *m/z*: calcd for **$C_6H_{13}OI^{+\bullet}$** $[M]^{+\bullet}$: 228.0011, found: 228.0006.



syn-**3-S7**

A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.42 g, 60 wt% in mineral oil, 10.5 mmol) in THF (5 mL) and DMF (5 mL). Then it was cooled to 0 °C. A solution of *syn*-**3-S1** (1.0 g, 10.0 mmol, d.r. = 99:1) in THF (5 mL) was added and the resulting solution was stirred for 40 min at 0 °C to room temperature. Then chloromethyl

ethyl ether (0.93 mL, 10.0 mmol) and $Bu_4N^+I^-$ (0.37 g, 1.0 mmol) was added successively and the mixture was stirred for 30 min at room temperature. The reaction was quenched with water at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*n*-pentane = 2/1 to afford *syn*-**3-S7** (0.97 g, 60% yield, d.r. = 99:1) as colorless oil.

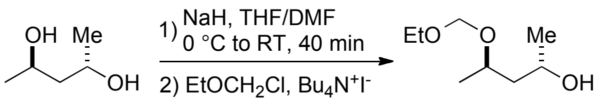
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 4.72 (d, *J* = 6.9 Hz, 1H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.07 (qt, *J* = 6.24 and 6.18 Hz, 1H), 3.98 (qt, *J* = 6.24 and 6.18 Hz, 1H), 3.66 (dq, *J* = 9.4 and 7.1 Hz, 1H), 3.57 (dq, *J* = 9.5 and 7.1 Hz, 1H), 3.04 (s br, 1H), 1.57 (t, *J* = 6.0 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.20 (d, *J* = 6.6 Hz, 3H), 1.18 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 93.9, 71.4, 64.3, 63.8, 45.4, 23.4, 20.3, 15.2.

MS (70 eV, EI) *m/z* (%): 161 (1) $[M–H]^{+\bullet}$, 117 (7), 103 (19), 91 (5), 85 (14), 75 (18), 70 (18), 59 (100), 55 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3426 (w br), 2967 (w), 2932 (w), 2879 (w), 1448 (w), 1391 (w), 1376 (w), 1298 (w), 1179 (w), 1153 (w), 1094 (m), 1032 (vs), 958 (w), 910 (w), 883 (w), 846 (w), 833 (w), 795 (w).

HRMS (ESI) *m/z*: calcd for $\mathbf{C_7H_{18}NaO_3^+}$ $[M+Na]^+$: 185.1154, found: 185.1147.



anti-**3-S1** *anti*-**3-S7**

anti-**3-S7**

A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.42 g, 60 wt% in mineral oil, 10.5 mmol) in THF (5 mL) and DMF (5 mL). Then it was cooled to 0 °C. A solution of *anti*-**3-S1** (1.0 g, 10.0 mmol, d.r. = 99:1) in THF (5 mL) was added and the resulting solution was stirred for 40 min at 0 °C to room temperature. Then chloromethyl ethyl ether (0.93 mL, 10.0 mmol) and $Bu_4N^+I^-$ (0.37 g, 1.0 mmol) was added successively and the mixture was stirred for 30 min at room temperature. The reaction was quenched with water at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*n*-pentane = 2/1 to afford *anti*-**3-S7** (0.85 g, 53% yield, d.r. = 99:1) as colorless oil.

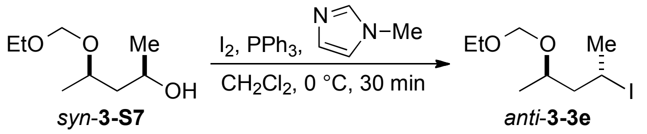
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 4.77 (d, J = 7.1 Hz, 1H), 4.66 (d, J = 7.1 Hz, 1H), 3.95 (dq, J = 15.2 and 8.9 Hz, 1H), 3.94 (dq, J = 15.5 and 8.9 Hz, 1H), 3.64 (dq, J = 9.4 and 7.1 Hz, 1H), 3.56 (dq, J = 9.4 and 7.1 Hz, 1H), 3.01 (s br, 1H), 1.66 (dt, J = 14.5 and 9.3 Hz, 1H), 1.53 (dt, J = 14.5 and 3.3 Hz, 1H), 1.20 (t, J = 7.4 Hz, 3H), 1.17 (d, J = 6.7 Hz, 3H), 1.16 (d, J = 6.4 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 93.1, 73.5, 67.6, 63.8, 46.0, 23.6, 10.5, 15.2.

MS (70 eV, EI) *m/z* (%): 161 (1) $[M{-}H]^{+\bullet}$, 117 (6), 103 (19), 91 (5), 85 (14), 75 (18), 70 (18), 59 (100), 55 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3414 (w br), 2970 (w), 2931 (w), 2880 (w), 1489 (w), 1391 (w), 1376 (w), 1298 (w), 1183 (w), 1139 (w), 1096 (m), 1028 (s), 952 (w), 920 (w), 846 (w).

HRMS (ESI) *m/z*: calcd for **$C_7H_{17}NaO_3^+$** $[M+Na]^+$: 185.1154, found: 185.1148.



anti-**3-3e**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.75 g, 6.9 mmol) in CH_2Cl_2 (30 mL) and cooled to 0 °C. PPh_3 (1.8 g, 6.9 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.54 mL, 6.9 mmol) was added. After 10 min of further stirring, *syn*-**3-S7** (0.81 g, 5.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/18 to afford *anti*-**3-3e** (1.2 g, 77% yield, d.r. = 99:1) as colorless oil.

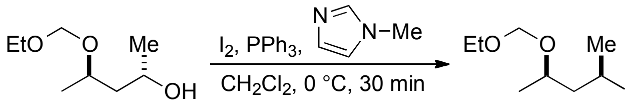
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 4.75 (d, J = 7.1 Hz, 1H), 4.68 (J = 7.1 Hz, 1H), 4.23 (qt, J = 7.1 and 7.0 Hz, 1H), 3.85 (qt, J = 6.1 and 6.0 Hz, 1H), 3.64 (dq, J = 9.4 and 7.1 Hz, 3H), 3.61 (dq, J = 9.5 and 7.1 Hz, 3H), 2.32 (dt, J = 14.6 and 7.4 Hz, 1H), 1.96 (d, J = 6.8 Hz, 3H), 1.78 (ddd, J = 14.1, 7.4 and 6.0 Hz, 1H), 1.23 (t, J = 7.1 Hz, 3H), 1.17 (t, J = 6.1 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 93.4, 72.7, 63.5, 50.5, 28.6, 24.3, 19.8, 15.2.

MS (70 eV, EI) *m/z* (%): 227 (3) $[M–OEt]^{+•}$, 197 (25), 155 (5), 145 (8), 127 (2), 115 (10), 103 (46), 69 (36), 59 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2972 (w), 2928 (w), 2880 (w), 1445 (w), 1416 (w), 1390 (w), 1377 (w), 1247 (w), 1189 (w), 1174 (w), 1136 (w), 1095 (m), 1030 (vs), 982 (w), 931 (w), 846 (w), 796 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_8H_{17}O_2ISi}^{+•}$ $[M–H]^{+•}$: 272.0195, found: 272.0260.



anti-**3-S7** *syn*-**3-3e**

syn-**3-3e**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (25 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *anti*-**3-S7** (0.81 g, 5.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/18 to afford *syn*-**3-3e** (1.1 g, 79% yield, d.r. = 99:1) as colorless oil.

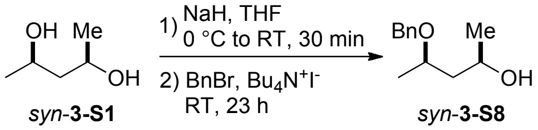
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.76 (d, *J* = 7.0 Hz, 1H), 4.70 (*J* = 6.2 Hz, 1H), 4.34 (dqd, *J* = 13.8, 6.9 and 3.3 Hz, 1H), 3.88 (dqd, *J* = 8.7, 6.1 and 2.5 Hz, 1H), 3.65 (dq, *J* = 9.3 and 7.0 Hz, 3H), 3.59 (dq, *J* = 9.3 and 7.0 Hz, 3H), 1.94 (d, *J* = 6.9 Hz, 3H), 1.88 (ddd, *J* = 13.7, 11.1 and 2.5 Hz, 1H), 1.61 (ddd, *J* = 15.1, 9.7 and 2.9 Hz, 1H), 1.24 (d, *J* = 7.0 Hz, 3H), 1.21 (t, *J* = 6.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 94.0, 73.5, 63.6, 50.8, 29.7, 27.4, 20.4, 15.3.

MS (70 eV, EI) *m/z* (%): 227 (2) $[M–OEt]^{+•}$, 197 (22), 155 (4), 145 (5), 127 (5), 115 (10), 103 (42), 69 (41), 59 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2972 (w), 2929 (w), 2877 (w), 1444 (w), 1416 (w), 1391 (w), 1374 (w), 1255 (w), 1191 (w), 1161 (w), 1139 (w), 1128 (w), 1104 (m), 1095 (m), 1031 (vs), 940 (w), 870 (w), 847 (w), 793 (w).

HRMS (EI) ***m/z*****:** calcd for **$C_8H_{17}O_2ISi^{+\bullet}$** $[M]^{+\bullet}$: 272.0273, found 272.0260.



syn-**3-S8** (CAS: 86272-42-6)

A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.42 g, 60 wt% in mineral oil, 10.6 mmol) in THF (10 mL) and was cooled to 0 °C. A solution of *syn*-**3-S1** (1.1 g, 10.1 mmol, d.r. = 99:1) in THF (5 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then benzyl bromide (1.2 mL, 10.1 mmol) and $Bu_4N^+I^-$ (0.37 g, 1.0 mmol) was added successively and the mixture was stirred for 23 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/4 to afford *syn*-**3-S8** (1.5 g, 77% yield, d.r. = 99:1) as pale yellow oil.

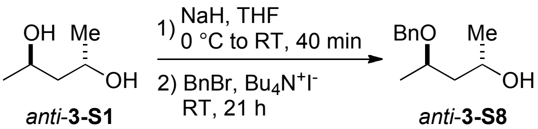
^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.38-7.26 (m, 5H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.42 (d, *J* = 11.6 Hz, 1H), 4.18-4.07 (m, 1H), 3.86 (qt, *J* = 6.3 and 4.2 Hz, 1H), 2.85 (s br, 1H), 1.68 (ddd, *J* = 14.3, 8.0 and 3.9 Hz, 1H), 1.62 (ddd, *J* = 14.5, 6.8 and 3.5 Hz, 1H), 1.26 (d, *J* = 6.2 Hz, 3H), 1.18 (d, *J* = 6.3 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 138.5, 128.5, 127.8, 127.7, 72.8, 70.6, 64.6, 44.5, 23.6, 19.3.

MS (70 eV, EI) ***m/z*** **(%):** 176 (21) $[M–H_2O]^{+\bullet}$, 118 (7), 107 (27), 91 (100), 79 (12), 70 (18).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3424 (w br), 2966 (w), 2929 (w), 2871 (w), 1498 (w), 1453 (w), 1344 (w), 1307 (w), 1207 (w), 1153 (m), 1116 (m), 1088 (m), 1065 (s), 1038 (m), 1027 (m), 958 (w), 916 (w), 883 (w), 829 (w), 733 (s), 696 (vs).

HRMS (EI) ***m/z*****:** calcd for **$C_{12}H_{16}O^{+\bullet}$** $[M–H_2O]^{+\bullet}$: 176.1201, found: 176.1189.



anti-**3-S8** (CAS: 86272-49-3)

A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.48 g, 60 wt% in mineral oil, 12.1 mmol) in THF (5 mL) and was cooled to 0 °C. A solution of *anti*-**3-S1** (1.2 g, 11.5 mmol, d.r. = 99:1) in THF (5 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then benzyl bromide (1.4 mL, 11.5 mmol) and $Bu_4N^+I^-$ (0.55 g, 1.5 mmol) was added successively and the mixture was stirred for 21 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/5→1/4 to afford *anti*-**3-S8** (1.8 g, 81% yield, d.r. = 99:1) as pale yellow oil.

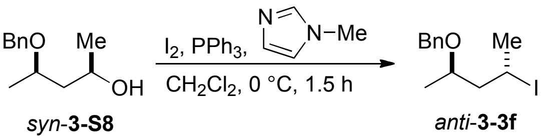
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.37-7.26 (m, 5H), 4.67 (d, *J* = 11.4 Hz, 1H), 4.42 (d, *J* = 11.4 Hz, 1H), 3.98 (dqdd, *J* = 9.4, 6.2, 2.3 and 1.2 Hz, 1H), 3.81 (dqd, *J* = 9.5, 6.0 and 3.4 Hz, 1H), 3.81 (s br, 1H), 1.69 (dt, *J* = 14.6 and 9.7 Hz, 1H), 1.55 (ddd, *J* = 14.6, 3.3 and 2.4 Hz, 1H), 1.24 (d, *J* = 6.0 Hz, 3H), 1.14 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 138.1, 128.6, 127.92, 127.89, 76.2, 70.4, 68.0, 45.8, 23.6, 19.8.

MS (70 eV, EI) *m/z* (%): 176 (1) $[M-H_2O]^{+\bullet}$, 118 (5), 107 (27), 91 (100), 79 (11), 70 (19).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3424 (w br), 2967 (w), 2931 (w), 2869 (w), 1497 (w), 1453 (w), 1373 (w), 1340 (w), 1306 (w), 1207 (w), 1167 (w), 1119 (m), 1083 (m), 1064 (m), 1036 (m), 1027 (s), 1001 (w), 952 (w), 919 (w), 884 (w), 834 (w), 733 (s), 696 (vs).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{16}O^{+\bullet}$** $[M-H_2O]^{+\bullet}$: 176.1201, found: 176.1194.



anti-**3-3f**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (45 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *syn*-**3-S8** (0.97 g, 5.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/60 to afford *anti*-**3-3f** (1.2 g, 77% yield, d.r. = 99:1) as colorless oil.

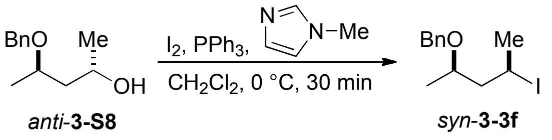
^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.38-7.26 (m, 5H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.44 (*J* = 11.6 Hz, 1H), 4.26 (tq, *J* = 7.2 and 7.0 Hz, 1H), 3.66 (ddq, *J* = 7.2, 6.3 and 6.1 Hz, 1H), 2.37 (dt, *J* = 14.5 and 7.3 Hz, 1H), 1.88 (d, *J* = 6.8 Hz, 3H), 1.79 (ddd, *J* = 14.3, 7.2 and 5.7 Hz, 1H), 1.20 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 138.7, 128.5, 127.9, 127.7, 74.4, 70.5, 50.1, 28.6, 25.0, 19.2.

MS (70 eV, EI) *m/z* (%): 304 (1) $[M]^{+\bullet}$, 135 (21), 91 (100), 65 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2967 (w), 2864 (w), 1495 (w), 1452 (w), 1375 (w), 1344 (w), 1243 (w), 1205 (w), 1178 (w), 1138 (m), 1125 (m), 1086 (w), 1067 (m), 1047 (w), 1027 (w), 984 (w), 933 (w), 910 (w), 854 (w), 798 (w), 733 (s), 695 (vs).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{12}H_{17}OI^{+\bullet}}$ $[M]^{+\bullet}$: 304.0324, found: 304.0310.



syn-**3-3f**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (45 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *anti*-**3-S8** (0.81 g, 5.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/20 to afford *syn*-**3-3f** (1.3 g, 87% yield, d.r. = 99:1) as colorless oil.

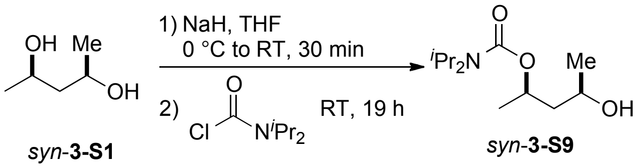
^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.41-7.27 (m, 5H), 4.65 (d, *J* = 11.1 Hz, 1H), 4.48 (dqd, *J* = 11.0, 6.9 and 3.0 Hz, 1H), 4.47 (*J* = 11.1 Hz, 1H), 3.78 (dqd, *J* = 9.7, 6.1 and 2.6 Hz, 1H), 1.96 (d, *J* = 6.9 Hz, 3H), 1.89 (ddd, *J* = 15.0, 11.2 and 2.6 Hz, 1H), 1.64 (ddd, *J* = 15.1, 9.8 and 3.0 Hz, 1H), 1.27 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 138.7, 128.5, 128.1, 127.8, 75.6, 71.4, 50.5, 29.6, 28.1, 19.4.

MS (70 eV, EI) *m/z* (%): 304 (2) $[M]^{+\bullet}$, 177 (5), 159 (5), 135 (19), 91 (100), 65 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2967 (w), 2882 (w), 1495 (w), 1452 (w), 1416 (w), 1395 (w), 1372 (w), 1372 (w), 1342 (w), 1251 (w), 1174 (w), 1145 (s), 1129 (m), 1086 (m), 1064 (s), 1027 (m), 943 (w), 912 (w), 868 (w), 848 (w), 732 (s), 695 (vs).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{17}OI^{+\bullet}$** $[M]^{+\bullet}$: 304.0324, found: 304.0327.



syn-**3-S9**

A dry and N$_2$-flushed *Schlenk*-flask was charged with a suspension of NaH (0.33 g, 60 wt% in mineral oil, 8.3 mmol) in THF (10 mL) and was cooled to 0 °C. A solution of *syn*-**3-S1** (0.8 g, 7.9 mmol, d.r. = 99:1) in THF (5 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then diisopropyl carbamoylchloride (1.3 g, 7.9 mmol) in THF (5 mL) was added and the mixture was stirred for 22.5 h at room temperature. The reaction was quenched with saturated NH$_4$Cl aqueous solution at 0 °C and the mixture was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/1 to afford *syn*-**3-S9** (1.0 g, 56% yield, d.r. = 99:1) as pale yellow oil.

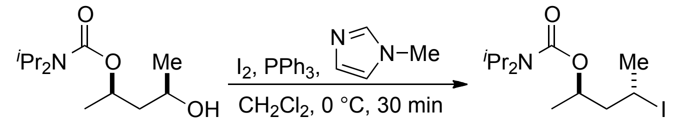
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 5.04-4.92 (m, 1H), 4.26-3.50 (s br, 1H), 3.89 (dddd, *J* = 10.9, 7.7, 6.3 and 4.8 Hz, 1H), 2.63(s br, 1H), 1.84 (dt, *J* = 14.3 and 7.6 Hz, 1H), 1.89 (dt, *J* = 14.2 and 4.9 Hz, 1H), 1.26 (d, *J* = 6.3 Hz, 3H), 1.22-1.15 (m, 15H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 155.7, 69.9, 66.0, 46.3, 45.9 (br), 23.8, 21.3, 21.2 (br).

MS (70 eV, EI) *m/z* (%): 216 (48) $[M{-}Me]^{+\bullet}$, 146 (45), 130 (88), 102 (13), 86 (100), 70 (23), 58 (16).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3443 (w br), 2968 (w), 2931 (w), 1660 (s), 1477 (w), 1437 (m), 1368 (m), 1292 (vs), 1213 (w), 1194 (w), 1133 (w), 1048 (s), 1004 (w), 954 (w), 920 (w), 897 (w), 771 (m).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{25}O_3N^{+\bullet}$** $[M]^{+\bullet}$: 231.1834, found: 231.1853.



anti-**3-3g**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.2 g, 4.8 mmol) in CH_2Cl_2 (30 mL) and cooled to 0 °C. PPh_3 (1.3 g, 4.8 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.38 mL, 4.8 mmol) was added. After 10 min of further stirring, *syn*-**3-S9** (0.93 g, 4.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/7 to afford *anti*-**3-3g** (1.2 g, 85% yield, d.r. = 99:1) as colorless oil.

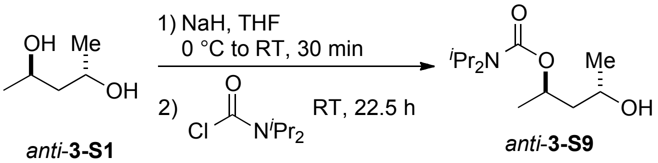
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 4.96 (dqd, *J* = 7.0, 6.2 and 5.2 Hz, 1H), 4.13 (qt, *J* = 6.9, 6.8 and 7.3 Hz, 1H), 3.72 (s br, 1H), 2.42 (ddd, *J* = 14.6, 8.0 and 6.9 Hz, 1H), 1.93 (d, *J* = 6.8 Hz, 3H), 1.94-1.84 (m, 1H), 1.21 (d, *J* = 6.2 Hz, 3H), 1.17 (d, *J* = 6.8 Hz, 12H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 155.2, 70.2, 49.8, 45.8, 28.5, 22.8, 21.3, 20.2.

MS (70 eV, EI) *m/z* (%): 341 (3) $[M]^{+\bullet}$, 326 (72), 282 (9), 214 (100), 197 (54), 146 (41), 130 (64), 102 (14), 86 (50), 69 (95), 55 (16).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2968 (w), 2931 (w), 2874 (w), 1682 (vs), 1475 (w), 1431 (m), 1377 (w), 1367 (m), 1333 (w), 1287 (s), 1247 (w), 1213 (w), 1157 (w), 1133 (s), 1121 (s), 1129 (m), 1086 (m), 1061 (m), 1046 (s), 1008 (w), 984 (w), 935 (w), 910 (w), 768 (m).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{24}ONI^{+\bullet}$** $[M]^{+\bullet}$: 341.0852, found: 341.0836.



anti-**3-S9**

A dry and N_2-flushed *Schlenk*-flask was charged with a suspension of NaH (0.33 g, 60 wt% in mineral oil, 8.3 mmol) in THF (10 mL) and was cooled to 0 °C. A solution of *anti*-**3-S1**

(0.83 g, 7.9 mmol, d.r. = 99:1) in THF (5 mL) was added and the resulting solution was stirred for 30 min at 0 °C to room temperature. Then diisopropyl carbamoylchloride (1.3 g, 7.9 mmol) in THF (5 mL) was added and the mixture was stirred for 19 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/1 to afford *anti*-**3-S9** (1.3 g, 73% yield, d.r. = 99:1) as pale yellow oil.

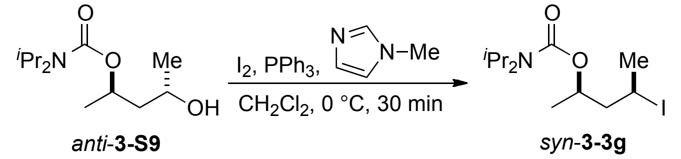
^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 5.14 (dqd, *J* = 9.7, 6.4 and 3.3 Hz, 1H), 4.12 (s br, 1H), 3.73 (s br, 1H), 3.67 (dqd, *J* = 10.0, 6.3 and 3.2 Hz, 1H), 1.60 (ddd, *J* = 14.4, 10.5 and 3.2 Hz, 1H), 1.53 (ddd, *J* = 14.4, 10.2 and 3.3 Hz, 1H), 1.29 (d, *J* = 6.4 Hz, 3H), 1.20 (d, *J* = 6.4 Hz, 12H), 1.17 (d, *J* = 6.3 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 156.8, 68.2, 63.2, 47.7, 46.1 (br), 22.7, 21.2, 21.1 (br).

MS (70 eV, EI) *m/z* (%): 231 (2) $[M]^{+\bullet}$, 216 (54), 146 (45), 130 (100), 102 (13), 86 (81), 69 (21), 58 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3457 (w br), 2969 (w), 2932 (w), 1658 (s), 1477 (w), 1437 (m), 1368 (m), 1347 (w), 1294 (vs), 1212 (w), 1194 (w), 1151 (m), 1134 (w), 1049 (s), 1000 (w), 959 (w), 917 (w), 897 (w), 771 (m).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{25}O_3N^{+\bullet}$** $[M]^{+\bullet}$: 231.1834, found: 231.1822.



syn-**3-3g**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (40 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, *anti*-**3-S9** (1.2 g, 5.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was washed with saturated $NaHCO_3$ aqueous solution[116] and dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/7 to afford *syn*-**3-3g** (0.49 g, 25% yield, d.r. = 99:1) as colorless oil.

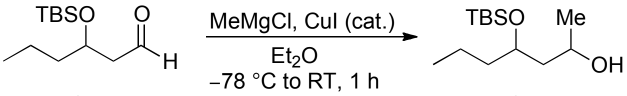
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.97 (dqd, *J* = 8.6, 6.2 and 4.0 Hz, 1H), 4.20 (dqd, *J* = 9.4, 6.9 and 5.1 Hz, 1H), 3.89 (s br, 1H), 2.07 (ddd, *J* = 14.9, 9.4 and 3.9 Hz, 1H), 1.94 (d, *J* = 6.9 Hz, 3H), 1.94 (ddd, *J* = 14.9, 8.7 and 5.1 Hz, 1H), 1.26 (d, *J* = 6.2 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 12H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 155.2, 71.2, 49.8, 45.7 (br), 29.3, 24.7, 21.2 (br), 20.6.

MS (70 eV, EI) *m/z* (%): 326 (25) $[M–Me]^{+\bullet}$, 214 (49), 197 (36), 155 (9), 146 (39), 130 (51), 102 (9), 86 (50), 69 (100), 55 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2968 (w), 2930 (w), 2874 (w), 1682 (vs), 1474 (w), 1431 (m), 1375 (w), 1367 (m), 1327 (w), 1305 (s), 1289 (s), 1252 (w), 1212 (w), 1190 (w), 1171 (w), 1157 (w), 1130 (s), 1046 (s), 984 (w), 943 (w), 901 (w), 874 (w), 769 (m).

HRMS (EI) *m/z*: calcd for $C_{12}H_{24}ONI^{+\bullet}$ $[M]^{+\bullet}$: 341.0852, found: 341.0834.



S10 **S11**

S11

To a suspension of CuI (0.61 g, 3.2 mmol) in Et_2O (80 mL) containing **S10**[117] (3.6 g, 15.6 mmol) was added dropwise MeMgCl (6.9 mL, 2.7 M in THF, 18.7 mmol) at –78°C. The reaction was stirred at room temperature for 1 h. A saturated NH_4OH/NH_4Cl = 2/1 aqueous solution was added and the mixture was extracted twice with Et_2O. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/3 to afford **S11** (2.8 g, 72% yield, d.r. = 64:36) as colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: **Major:** 3.96-3.85 (m, 2H), 3.52 (br s, 1H), 1.63-1.41 (m, 4H), 1.33-1.19 (m, 2H), 1.12 (d, *J* = 6.2 Hz, 3H), 0.86 (s, 9H), 0.85-0.90 (m, 3H), 0.06 (s, 3H), 0.04 (s, 3H). **Minor:** 4.14- 4.06 (m, 2H), 3.34 (br s, 1H), 1.63-1.41 (m, 4H), 1.33-1.19 (m, 2H), 1.12 (d, *J* = 6.2 Hz, 3H), 0.86 (s, 9H), 0.88-0.85 (m, 3H), 0.08 (s, 3H), 0.06 (s, 3H).

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[116] Neutralization led to a low yield.

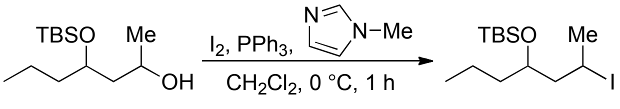
[117] C. Roche, N. Desroy, M. Haddad, P. Phansavath, J. Genet, *Org. Lett.* **2008**, *10*, 3911.

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: Major: 67.4, 67.0, 44.3, 39.8, 25.4, 22.7, 18.4, 17.5, 13.7, –4.9, –5.4. **Minor:** 70.2, 69.2, 45.8, 39.5, 25.4, 24.1, 18.2, 17.5, 13.8, –4.8, –5.2.

MS (70 eV, EI) *m/z* (%): 189 (5) [M–^{t}Bu]$^{+\bullet}$, 159 (29), 119 (100), 97 (32), 75 (79).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3459 (br, w), 2939 (w), 2866 (w), 2823 (w), 1251 (m), 1083 (w), 1057 (m), 1003 (w), 829 (s), 773 (s), 741 (m).

HRMS (EI) *m/z*: calcd for **$C_9H_{21}O_2Si^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 189.1311, found: 189.1303.



S11 **3-3h**

3-3h

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (0.57 g, 2.2 mmol) in CH_2Cl_2 (13 mL) and cooled to 0 °C. PPh_3 (0.59 g, 2.2 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.18 mL, 2.2 mmol) was added. After 10 min of further stirring, **S11** (0.46 g, 1.9 mmol, d.r. = 64:36) dissolved in CH_2Cl_2 (6 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with the mixture of Et_2O/*i*-hexane = 1:4. All organic phase was combined and solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/99 to afford **3-3h** (0.42 g, 63% yield, d.r. = 66:34) as colorless oil. The relative configuration was determined by the analogy of NMR spectrum of *syn*- and *anti*-**3-3a**.

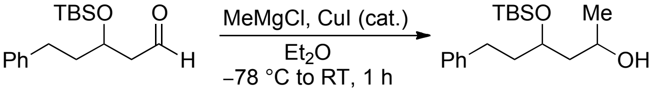
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: ***syn*-3-3h:** 4.27 (dqd, *J* = 11.1, 6.9 and 3.0 Hz, 1H), 3.85-3.79 (m, 1H), 1.96 (d, *J* = 6.9 Hz, 3H), 1.92 (ddd, *J* = 14.7, 11.0 and 2.3 Hz, 1H), 1.55-1.43 (m, 3H), 1.40-1.24 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H), 0.89 (s, 9H), 0.14 (s, 3H), 0.00 (s, 3H). ***anti*-3-3h:** 4.15 (dqd, *J* = 8.2, 6.7 and 6.4 Hz, 1H), 3.80-3.75 (m, 1H), 2.14 (ddd, *J* = 14.3, 8.2 and 6.3 Hz, 1H), 1.93 (d, *J* = 6.7 Hz, 3H), 1.73 (dt, *J* = 14.3 and 6.4 Hz, 1H), 1.44-1.29 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H), 0.89 (s, 9H), 0.067 (s, 3H), 0.069 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: ***syn*-3-3h:** 72.5, 50.0, 40.1, 30.0, 29.3, 26.1, 18.2, 18.1, 14.5, –3.87, –3.92. ***anti*-3-3h:** 72.1, 50.5, 38.7, 29.1, 26.0, 25.4, 18.2, 14.4, –4.1, –4.2.

MS (70 eV, EI) *m/z* (%): 299 (15) [M–^{t}Bu]$^{+\bullet}$, 257 (100), 215 (42), 185 (30), 129 (21), 115 (8), 97 (6), 75 (34).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 2857 (w), 1463 (w), 1255 (w), 1056 (m), 1040 (m), 922 (w), 834 (s), 824 (m), 806 (m), 773 (s), 662 (w)

HRMS (EI) m/z: calcd for **$C_9H_{20}IOSi^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 299.0328, found: 299.0351.



S12 **S13**

S13

To a suspension of CuI (0.67 g, 3.5 mmol) in Et_2O (90 mL) containing **S12**[118] (5.4 g, 17.6 mmol, CAS: 166171-34-2) was added dropwise MeMgCl (8.4 mL, 2.7 M in THF, 22.9 mmol) at –78°C. The reaction was then allowed to stir at room temperature for 1 h. A saturated NH_4OH/NH_4Cl (2:1) aqueous solution was added and the mixture was extracted twice with Et_2O. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/3 to afford **S13** (3.7 g, 67% yield, d.r. = 55:45) as colorless oil.

^{1}H-NMR (400 MHz, CDCl$_3$) δ: **Major:** 7.31-7.26 (m, 2H), 7.21-7.16 (m, 3H), 4.05-3.92 (m, 2H), 3.33 (br s, 1H), 2.71-2.54 (m, 2H), 1.92-1.87 (m, 2H), 1.72-1.63 (m, 2H), 1.13 (d, J = 7.5 Hz, 3H), 0.91 (s, 9H), 0.103 (s, 3H), 0.100 (s, 3H). **Minor:** 7.31-7.26 (m, 2H), 7.21-7.16 (m, 3H), 4.21-4.13 (m, 1H), 4.05-3.92 (m, 1H), 3.11 (br s, 1H), 2.71-2.54 (m, 2H), 1.87-1.78 (m, 2H), 1.72-1.63 (m, 2H), 1.19 (d, J = 7.5 Hz, 3H), 0.92 (s, 9H), 0.11 (s, 3H). 0.08 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: **Major:** 142.1, 128.4, 128.2, 125.9, 71.3, 64.5, 43.2, 37.1, 32.2, 25.8, 23.9, 17.9, –4.6, –4.7. **Minor:** 141.9, 128.4, 128.2, 125.8, 72.6, 67.2, 44.5, 39.8, 30.9, 25.8, 23.7, 17.9, –4.0, –4.8.

MS (70 eV, EI) *m/z* (%): 293 (1) [M–Me]$^{+\bullet}$, 251 (4), 249 (5), 233 (2), 209 (2), 159 (29), 117 (100), 105 (8), 91 (67), 75 (47).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3442 (br, w), 2929 (w), 2857 (w), 1252 (m), 1087 (w), 1062 (m), 1004 (w), 833 (s), 807 (w), 773 (s), 746 (m), 697 (s).

HRMS (EI) m/z: calcd for **$C_{14}H_{23}O_2Si^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 251.1467, found: 251.1428

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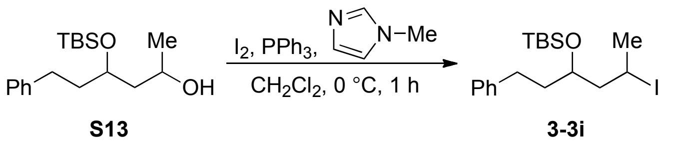
[118] B. D. Cons, A. J. Bunt, C. D. Bailey, C. L. Willis, *Org. Lett.* **2013**, *15*, 2046.



3-3i

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (0.99 g, 3.9 mmol) in CH_2Cl_2 (20 mL) and cooled to 0 °C. PPh_3 (1.0 g, 3.9 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.31 mL, 3.9 mmol) was added. After 10 min of further stirring, **S13** (1.0 g, 3.2 mmol, d.r. = 55:45) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with the mixture of Et_2O/*i*-hexane = 1:4. All organic phase was combined and solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/99 to afford **3-3i** with a little impurity (0.54 g, 40% yield, d.r. = 62:38) as colorless oil. The relative configuration was determined by the analogy of NMR spectrum of *syn*- and *anti*-**3-3a**.

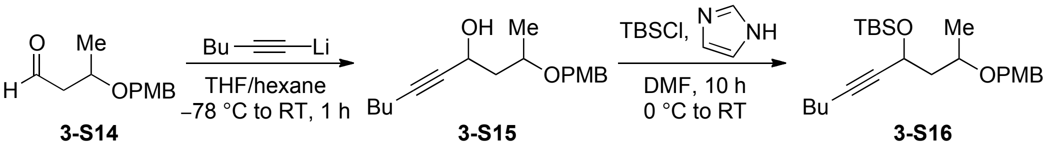
^{1}H-NMR (400 MHz, $CDCl_3$) δ: ***syn*-3-3i:** 7.33-7. 29 (m, 2H), 7.23-7.19 (m, 3H), 4.31 (dqd, *J* = 11.0, 6.9 and 2.7 Hz, 1H), 3.96-3.82 (m, 1H), 2.77-2.56 (m, 2H), 2.08-2.02 (m, 1H), 2.02 (d, *J* = 6.9 Hz, 3H), 1.88-1.76 (m, 2H), 1.74-1.63 (m, 1H), 0.94 (s, 9H), 0.17 (s, 3H), 0.13 (s, 3H). ***anti*-3-3i:** 7.33-7.29 (m, 2H), 7.23-7.19 (m, 3H), 4.16 (dqd, *J* = 8.5, 6.6 and 6.4 Hz, 1H), 3.96-3.82 (m, 1H), 2.77-2.58 (m, 2H), 2.23 (ddd, *J* = 14.3, 8.5 and 5.9 Hz, 1H), 1.95 (d, *J* = 6.7 Hz, 3H), 1.88-1.76 (m, 2H), 1.74-1.63 (m, 1H), 0.95 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: ***syn*-3-3i:** 142.4, 128.5, 128.4, 125.9, 72.2, 50.0, 39.7, 31.2, 28.8, 26.1, 24.8, 18.2, –3.87, –3.90. ***anti*-3-3i:** 142.3, 128.53, 128.46, 125.9, 72.0, 50.3, 38.2, 31.4, 29.2, 26.0, 24.8, 18.2, –4.1, –4.2.

MS (70 eV, EI) *m/z* (%): 361 (14) $[M-{}^tBu]^{+\bullet}$, 319 (12), 249 (17), 233 (21), 191 (56), 159 (100), 117 (43), 91 (71), 75 (60).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 2857 (w), 1472 (w), 1473 (w), 1372 (w), 1255 (m), 1163 (w), 1130 (w), 1056 (m), 1040 (m), 954 (w), 922 (w), 834 (s), 806 (m), 773 (s), 662 (w).

HRMS (EI) m/z: calcd for $C_{14}H_{22}IOSi^{+\bullet}$ $[M-{}^tBu]^{+\bullet}$: 361.0485, found: 361.0480.



3-S16

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of 1-hexyne (3.7 mL, 32.3 mmol) in THF (60 mL) and cooled to –78 °C. Then ^{n}BuLi (12.7 mL, 2.6 M in *n*-hexane, 32.3 mmol) was added dropwise for 10 min. After stirring at –78 °C for 1 h, **3-S14**[119] (5.6 g, 26.9 mmol, CAS: 186743-05-5) in THF (10 mL) was added. The reaction mixture was stirred for 20 min at –78 °C and warmed up to room temperature gradually for 40 min. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated to afford the crude product of **3-S15**. A dry and Ar-flushed *Schlenk*-flask was charged with a solution of this crude **3-S15** in DMF (60 mL). Imidazole (4.4 g, 64.6 mmol) was added and the reaction mixture was cooled down to 0 °C. Then TBSCl (4.5 g, 29.6 mmol) was added and the reaction mixture was warmed up to room temperature and stirred for 10 h. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted three times with Et_2O/*i*-hexane = 1:3. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/9 to afford **3-S16** (6.8 g, 60% yield in two steps, d.r. = 62:38) as yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: **Major:** 7.28-7.22 (m, 2H), 6.86 (d, J = 8.7 Hz, 2H), 4.60-4.50 (m, 1H), 4.49 (d, J = 11.5 Hz, 1H), 4.37 (d, J = 11.3 Hz, 1H), 3.79 (s, 3H), 3.77-3.67 (m, 1H), 2.12-2.00 (m, 2H), 2.00 (ddd, J = 13.4, 7.8 and 6.2 Hz, 1H), 1.68 (ddd, J = 13.2, 7.9 and 4.0 Hz, 1H), 1.52-1.35 (m, 3H), 1.20 (d, J = 6.2 Hz, 3H), 0.93-0.86 (m, 3H), 0.88 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H). **Minor:** 7.28-7.22 (m, 2H), 6.86 (d, J = 8.7 Hz, 2H), 4.60-4.50 (m, 1H), 4.50 (d, J = 10.9 Hz, 1H), 4.33 (d, J = 11.0 Hz, 1H), 3.79 (s, 3H), 3.77-3.67 (m, 1H), 2.12-2.00 (m, 2H), 1.90 (ddd, J = 13.9, 8.5 and 4.0 Hz, 1H), 1.76 (ddd, J = 13.9, 9.1 and 4.1 Hz, 1H), 1.52-1.35 (m, 3H), 1.20 (d, J = 6.2 Hz, 3H), 0.93-0.86 (m, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: **Major:** 159.2, 131.4, 129.3, 113.9, 85.1, 81.7, 72.2, 70.4, 61.1, 55.4, 46.4, 30.9, 22.1, 20.0, 18.5, 18.4, 13.7, –4.3, –4.8. **Minor:** 159.2, 131.4, 129.2,

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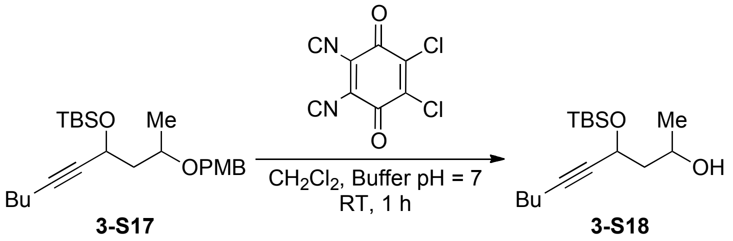
[119] P. A. Hume, D. P. Furkert, M. A. Brimble, *Org. Lett.* **2013**, *15*, 4588.

113.9, 84.7, 82.2, 71.5, 70.2, 60.0, 55.4, 47.0, 30.9, 26.1, 22.1, 20.1, 18.5, 18.4, 13.7, –4.1, –4.8.

MS (70 eV, EI) *m/z* (%): 404 (1) [M]$^{+\bullet}$, 272 (2), 139 (5), 121 (100), 73 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2927 (w), 2855 (w), 1612 (w), 1512 (m), 1426 (w), 1372 (w), 1360 (w), 1342 (w), 1301 (w), 1246 (s), 1179 (w), 1171 (w), 1154 (w), 1132 (w), 1095 (m), 1060 (m), 1038 (m), 1003 (w), 937 (w), 904 (w), 834 (s), 775 (vs), 667 (w).

HRMS (EI) *m/z*: calcd for **$C_{24}H_{40}O_3Si^{+\bullet}$** [M]$^{+\bullet}$: 404.2747, found: 404.2743.



3-S18

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of **3-S17** (1.7 g, 4.0 mmol, d.r. = 60:40) in CH_2Cl_2 (20 mL) and buffer solution (pH = 7, 10 mL). After cooling it down to 0 °C, DDQ (1.8 g, 8.0 mmol) was added to the reaction mixture and it was stirred at room temperature for 1 h. The reaction was quenched with saturated $NaHCO_3$ aqueous solution and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/8 to afford **3-S18** (1.1 g, 93% yield, d.r. = 60:40) as yellow oil.

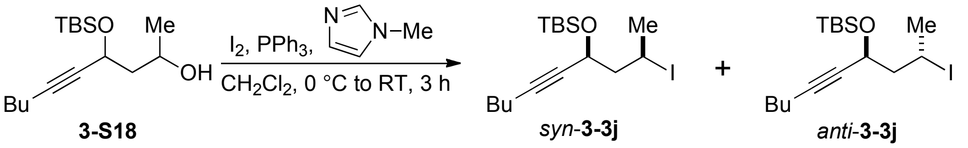
^{1}H-NMR (300 MHz, CDCl$_3$) δ: **Major:** 4.56 (ddt, *J* = 8.8, 4.8 and 2.0 Hz, 1H), 4.03 (dqd, *J* = 8.9, 6.5 and 3.0 Hz, 1H), 3.17 (s br, 1H), 1.84-1.72 (m, 2H), 1.85 (ddd, *J* = 14.2, 8.9 and 8.4 Hz, 1H), 1.84-1.72 (m, 1H), 1.54-1.32 (m, 4H), 1.19 (d, *J* = 6.3 Hz, 3H), 0.94-0.87 (m, 3H), 0.91 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H). **Minor:** 4.68 (tt, *J* = 4.5 and 2.1 Hz, 1H), 4.30 (dqd, *J* = 8.8, 6.4 and 2.3 Hz, 1H), 3.29 (s br, 1H), 1.84-1.72 (m, 2H), 1.84-1.72 (m, 1H), 1.69 (ddd, *J* = 14.2, 4.9 and 2.5 Hz, 1H), 1.54-1.32 (m, 4H), 1.18 (d, *J* = 6.3 Hz, 3H), 0.94-0.87 (m, 3H), 0.90 (s, 9H), 0.16 (s, 3H), 0.13 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: **Major:** 86.0, 81.3, 67.1, 63.4, 47.1, 30.7, 25.9, 23.5, 22.1, 18.5, 18.2, 13.7, –4.0, –4.9. **Minor:** 86.2, 80.7, 65.4, 62.8, 45.9, 30.8, 25.9, 23.5, 22.1, 18.5, 18.2, 13.7, –4.4, –5.1.

MS (70 eV, EI) *m/z* (%): 283 (1) [M]$^{+\bullet}$, 225 (5), 185 (100), 139 (9), 101 (5), 75 (55).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3446 (w br), 2956 (w), 2928 (w), 2856 (w), 1471 (w), 1462 (w), 1360 (w), 1249 (w), 1146 (w), 1125 (w), 1068 (m), 991 (w), 937 (w), 910 (w), 834 (vs), 811 (m), 775 (s), 727 (w), 667 (w).

HRMS (EI) *m/z*: calcd for **$C_{24}H_{40}O_3Si^{+\bullet}$** [M–H]$^{+\bullet}$: 283.2093, found: 283.2032.



syn-**3-3j** and *anti*-**3-3j**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.1 g, 4.3 mmol) in CH_2Cl_2 (35 mL) and cooled to 0 °C. PPh_3 (1.1 g, 4.3 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.34 mL, 4.3 mmol) was added. After 10 min of further stirring, a mixture of the diastereomers of **3-S18** (1.0 g, 4.0 mmol, d.r. = 60:40) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 1.5 h at 0 °C. Then it was warmed up to room temperature and stirred for 1.5 h. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/4. After collecting the organic phase, the remained sticky substance was dissolved in CH_2Cl_2 (5 mL) and it was passed through a pad of silica gel with the mixture of Et_2O/*i*-hexane = 1/4. All organic phase was combined and solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/600 to afford *syn*-**3-3j** (0.28 g, 20% yield, d.r. = 99:1) as the first fraction and a colorless oil and *anti*-**3-3j** (0.68 g, 49% yield, d.r. = 99:1) as the second fraction and colorless oil. The relative configuration was determined by the analogy of NMR spectrum of *syn*- and *anti*-**3-3a**.

syn-**3-3j**

^{1}H-NMR (600 MHz, $CDCl_3$) δ: 4.45 (d, J = 9.6 Hz, 1H), 4.28 (dqd, J = 10.3, 6.9 and 3.2 Hz, 1H), 2.19 (t, J = 7.0 Hz, 2H), 2.08 (ddd, J = 14.2, 10.5 and 3.2 Hz, 1H), 1.96 (d, J = 6.9 Hz, 3H), 1.83 (ddd, J = 14.2, 9.7 and 3.0 Hz, 1H), 1.47 (quint, J = 7.0 Hz 2H), 1.40 (h, J = 7.3 Hz, 2H), 0.92-0.86 (m, 3H), 0.91 (s, 9H), 0.17 (s, 6H).

^{13}C-NMR (150 MHz, CDCl$_3$) *δ*: 85.4, 81.2, 63.4, 51.7, 30.8, 29.3, 26.8, 26.1, 22.1, 18.5, 18.3, 13.7, –4.1, –4.7.

MS (70 eV, EI) *m/z* (%): 379 (1) [M–Me]$^{+•}$, 337 (9), 295 (100), 225 (9), 185 (18), 139 (12), 75 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2927 (w), 2856 (w), 1470 (w), 1462 (w), 1388 (w), 1377 (w), 1360 (w), 1341 (w), 1248 (w), 1236 (w), 1165 (w), 1138 (w), 1101 (m), 1058 (m), 1022 (m), 1004 (w), 967 (w), 938 (w), 918 (w) 902 (w), 834 (s), 809 (m), 776 (vs), 735 (w), 663 (w).

HRMS (EI) *m/z*: calcd for **$C_{16}H_{30}OISi^{+•}$** [M–H]$^{+•}$: 393.1111, found: 393.1085.

anti-**3-3j**

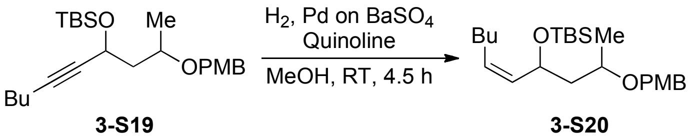
^{1}H-NMR (600 MHz, CDCl$_3$) *δ*: 4.49 (dd, *J* = 7.7 and 6.0 Hz, 1H), 4.27 (dq, *J* = 13.6 and 6.8 Hz, 1H), 2.24 (ddd, *J* = 15.0, 9.1 and 6.0 Hz, 1H), 2.18 (td, *J* = 7.0 and 1.6 Hz, 2H), 1.95 (d, *J* = 6.9 Hz, 3H), 1.89 (ddd, *J* = 13.8, 7.7 and 5.4 Hz, 1H), 1.48 (quint, *J* = 7.0 Hz, 2H), 1.40 (h, *J* = 7.0 Hz, 2H), 0.93-0.87 (m, 3H), 0.90 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H).

^{13}C-NMR (150 MHz, CDCl$_3$) *δ*: 86.0, 80.4, 64.2, 51.4, 30.8, 29.0, 26.0, 24.7, 22.1, 18.5, 18.4, 13.7, –4.3, –4.8.

MS (70 eV, EI) *m/z* (%): 337 (4) [M–^{t}Bu]$^{+•}$, 295 (100), 225 (12), 185 (24), 139 (23), 111 (5), 75 (21).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2927 (w), 2856 (w), 1471 (w), 1462 (w), 1388 (w), 1377 (w), 1360 (w), 1335 (w), 1249 (w), 1226 (w), 1157 (w), 1140 (w), 1074 (s), 1026 (w), 1004 (w), 972 (w), 938 (w), 922 (w), 908 (w) 834 (vs), 810 (w), 775 (s), 726 (w), 667 (w).

HRMS (EI) *m/z*: calcd for **$C_{16}H_{30}OISi^{+•}$** [M–^{t}Bu]$^{+•}$: 337.0485, found: 337.0446.



3-S20

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of **3-S19** (2.8 g, 7.0 mmol, d.r. = 60:40) in MeOH (56 mL) and Pd on BaSO$_4$ (0.28 g, 0.13 mmol, 5% Pd) was added to the reaction mixture. Then H$_2$ was babbled into the reaction mixture for 5 min and stirred at room temperature for 4.5 h. After filtering Pd on BaSO$_4$ the amount of MeOH was reduced by evaporation. The mixture was diluted with Et$_2$O and washed with 1 M aqueous HCl solution. The organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/20 to afford **3-S20** (2.5 g, 89% yield, d.r. = 60:40) as yellow oil.

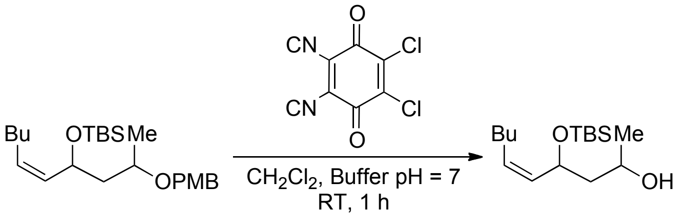
^{1}H-NMR (300 MHz, $CDCl_3$) δ: Major: 7.31-7.23 (m, 2H), 6.90-6.83 (m, 2H), 5.39-5.23 (m, 2H), 4.62-4.53 (m, 1H), 4.48 (d, J = 11.3 Hz, 1H), 4.35 (d, J = 11.2 Hz, 1H), 3.800 (s, 3H), 3.58 (qt, J = 6.3 and 6.0 Hz, 1H), 2.12-1.91 (m, 3H), 1.42 (dt, J = 13.5 and 6.2 Hz, 1H), 1.37-1.26 (m, 4H), 1.21 (d, J = 6.1 Hz, 1H), 0.95-0.84 (m, 3H), 0.86 (s, 9H), 0.02 (s, 6H). **Minor:** 7.31-7.23 (m, 2H), 6.90-6.83 (m, 2H), 5.39-5.23 (m, 2H), 4.69 (td, J = 7.9 and 5.0 Hz, 1H), 4.53 (d, J = 11.1 Hz, 1H), 4.37 (d, J = 11.1 Hz, 1H), 3.803 (s, 3H), 3.70 (dt, J = 12.5 and 6.0 Hz, 1H), 2.12-1.91 (m, 2H), 1.60 (ddd, J = 12.3, 4.8 and 2.3 Hz, 1H), 1.37-1.26 (m, 5H), 1.20 (d, J = 6.2 Hz, 1H), 0.95-0.84 (m, 3H), 0.87 (s, 9H), 0.03 (s, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: Major: 159.1, 133.8, 131.4, 129.6, 129.1, 113.8, 72.1, 69.9, 66.3, 55.4, 45.8, 32.0, 27.7, 26.0, 22.6, 19.8, 18.3, 14.1, –4.0, –4.7. **Minor:** 159.0, 134.2, 131.6, 129.2, 128.9, 113.8, 71.9, 70.1, 65.9, 55.4, 46.7, 31.9, 27.6, 26.1, 22.6, 20.4, 18.3, 14.1, –3.9, –4.6.

MS (70 eV, EI) *m/z* (%): 406 (1) $[M]^{+\bullet}$, 227 (3), 138 (7), 121 (100), 75 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2928 (w), 2855 (w), 1614 (w), 1513 (m), 1462 (w), 1373 (w), 1360 (w), 1341 (w), 1302 (w), 1245 (s), 1180 (w), 1172 (w), 1135 (w), 1039 (s), 1005 (w), 939 (w), 908 (w), 833 (s), 809 (m), 773 (vs), 728 (w), 668 (w).

HRMS (EI) *m/z*: calcd for $C_{24}H_{42}O_3Si^{+\bullet}$ $[M]^{+\bullet}$: 406.2903, found: 406.2883.



3-S20 **3-S21**

3-S21

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of **3-S20** (2.4 g, 6.0 mmol, d.r. = 60:40) in CH_2Cl_2 (30 mL) and buffer solution (pH = 7, 15 mL). After cooling it down to 0 °C, DDQ (2.7 g, 12.0 mmol) was added to the reaction mixture and it was stirred at 0 °C for 30 min. The reaction was quenched with saturated $NaHCO_3$ aqueous solution and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/8 to afford **3-S21** (1.6 g, 95% yield, d.r. = 60:40) as yellow oil.

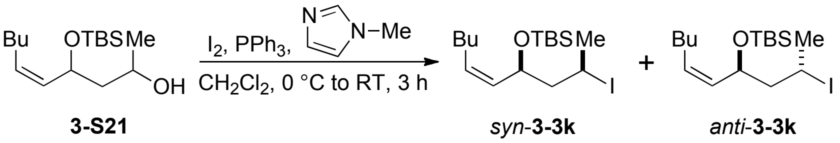
^{1}H-NMR (300 MHz, CDCl$_3$) δ: **Major:** 5.40-5.26 (m, 2H), 4.73-4.65 (m, 1H), 3.99 (dqd, *J* = 9.8, 6.2 and 2.2 Hz, 1H), 2.12-1.94 (m, 2H), 1.72-1.51 (m, 1H), 1.85 (ddd, *J* = 14.2, 8.9 and 8.4 Hz, 0.6H), 1.84-1.72 (m, 1H), 1.44 (ddd, *J* = 14.3, 3.8 and 2.2 Hz, 1H), 1.38-1.25 (m, 4H), 1.17 (d, *J* = 6.2 Hz, 3H), 0.95-0.85 (m, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H). **Minor:** 5.54 (ddt, *J* = 11.4, 8.3 and 1.6 Hz, 1H), 5.40-5.26 (m, 1H), 4.80 (dddd, *J* = 8.5, 5.3, 4.3 and 1.1 Hz, 1H), 4.13 (dqd, *J* = 9.1, 6.0 and 2.8 Hz, 1H), 2.12-1.94 (m, 2H), 3.17 (s br, 0.6H), 1.84-1.72 (m, 2H), 1.72-1.51 (m, 2H), 1.38-1.25 (m, 4H), 1.16 (d, *J* = 6.3 Hz, 3H), 0.95-0.85 (m, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: **Major:** 133.4, 129.8, 70.6, 67.7, 46.1, 31.9, 27.6, 26.0, 23.7, 22.6, 18.1, 14.1, –3.6, –4.8. **Minor:** 132.8, 129.7, 68.4, 65.1, 46.1, 31.9, 27.6, 25.9, 23.8, 22.6, 18.1, 14.1, –4.2, –4.9.

MS (70 eV, EI) *m/z* (%): 229 (8) $[\mathrm{M}-{}^{t}\mathrm{Bu}]^{+\bullet}$, 227 (21), 187 (100), 171 (5), 159 (4), 145 (4), 131 (56), 115 (6), 105 (4), 95 (14), 75 (67), 55 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3436 (w br), 2956 (w), 2927 (w), 2856 (w), 1471 (w), 1462 (w), 1360 (w), 1252 (w), 1128 (w), 1065 (m), 1003 (w), 938 (w), 912 (w), 879 (w), 834 (vs), 809 (m), 773 (s), 726 (w), 666 (w).

HRMS (EI) *m/z*: calcd for **$C_{16}H_{34}O_2Si^{+\bullet}$** $[\mathrm{M}-{}^{t}\mathrm{Bu}]^{+\bullet}$: 229.1624, found: 229.1655.



syn-**3-3k** and *anti*-**3-3k**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (50 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, a mixture of the diastereomers of **3-S21** (1.4 g, 5.0 mmol, d.r. = 60:40) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. Then it was warmed up to room temperature and stirred for 2 h. The reaction mixture was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and it was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with the mixture of Et_2O/*i*-hexane = 1/4. After collecting the organic phase, the remained sticky substance was dissolved in CH_2Cl_2 (5 mL) and it was passed through a pad of silica gel with the mixture of Et_2O/*i*-hexane = 1/4. All organic phase was combined and solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/400 to afford *syn*-**3-3k** (0.98 g, 49% yield, d.r. = 99:1) as the first fraction and colorless oil and *anti*-**3-3k** (0.28 g, 14% yield, d.r. = 99:1) as the second fraction and colorless oil. The relative configuration was determined by the analogy of NMR spectrum of *syn*- and *anti*-**3a**.

syn-**3-3k**

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 5.46-5.26 (m, 2H), 4.59 (ddd, *J* = 9.7, 7.3 and 2.5 Hz, 1H), 4.31 (dqd, *J* = 11.0, 6.9 and 2.9 Hz, 1H), 2.12-2.04 (m, 2H), 1.96 (d, *J* = 6.9 Hz, 3H), 1.77 (ddd, *J* = 14.8, 11.1 and 2.5 Hz, 1H), 1.58 (ddd, *J* = 14.8, 9.6 and 2.9 Hz, 1H), 1.44-1.25 (m, 4H), 0.97-0.86 (m, 3H), 0.88 (s, 9H), 0.13 (s, 3H), 0.06 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 133.4, 130.0, 69.7, 51.3, 31.9, 29.7, 28.7, 27.7, 26.1, 22.6, 18.3, 14.2, –3.8, –4.4.

MS (70 eV, EI) *m/z* (%): 339 (5) $[M-{}^tBu]^{+\bullet}$, 297 (100), 241 (52), 227 (20), 215 (5), 185 (16), 171 (4), 127 (4), 113 (8), 95 (19), 75 (26), 57 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2927 (w), 2856 (w), 1471 (w), 1462 (w), 1360 (w), 1252 (w), 1157 (w), 1124 (w), 1097 (m), 1059 (m), 1049 (m), 1026 (w), 1005 (w), 972 (w), 938 (w), 910 (m), 834 (s), 824 (s), 808 (m), 775 (vs), 728 (w), 667 (w).

HRMS (EI) m/z: calcd for **$C_{12}H_{24}OISi^{+\bullet}$** $[M-{}^tBu]^{+\bullet}$: 339.0641, found: 339.0616.

anti-**3-3k**

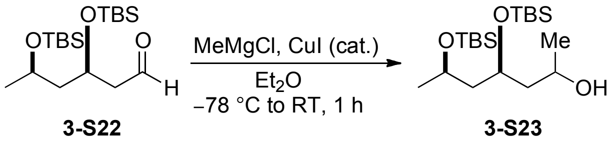
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 5.42 (dtd, *J* = 11.1, 7.4 and 0.9 Hz, 1H), 5.21 (ddt, *J* = 10.5, 8.9 and 1.6 Hz, 1H), 4.57 (dddd, *J* = 8.8, 7.0, 5.9 and 0.9 Hz, 1H), 4.11-3.98 (m, 1H), 2.22 (ddd, *J* = 14.5, 8.7 and 6.0 Hz, 1H), 2.19-2.08 (m, 2H), 1.93 (d, *J* = 6.9 Hz, 3H), 1.71 (ddd, *J* = 14.3, 7.2 and 5.6 Hz, 1H), 1.42-1.30 (m, 4H), 0.96-0.87 (m, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 132.3, 131.6, 68.7, 51.7, 32.2, 29.1, 28.3, 26.0, 25.1, 22.7, 18.3, 14.2, –4.0, –4.6.

MS (70 eV, EI) *m/z* (%): 339 (6) $[M-{}^tBu]^{+\bullet}$, 297 (100), 241 (37), 227 (22), 185 (9), 171 (4), 95 (6), 75 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2953 (w), 2926 (w), 2855 (w), 1471 (w), 1462 (w), 1377 (w), 1360 (w), 1251 (w), 1221 (w), 1159 (w), 1130 (w), 1110 (w), 1065 (s), 1029 (w), 1026 (w), 1005 (w), 912 (w), 859 (w), 834 (s), 809 (w) 774 (vs), 726 (w), 666 (w).

HRMS (EI) m/z: calcd for **$C_{12}H_{24}OISi^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 339.0641, found: 339.0610.



3-S23

To a suspension of CuI (0.12 g, 0.63 mmol) in Et_2O (16 mL) containing **3-S22**[120] (1.1 g, 3.2 mmol) was added dropwise MeMgCl (1.4 mL, 2.73 M in THF, 3.8 mmol) at –78°C. The reaction was then allowed to stir at room temperature for 1 h. Then saturated NH_4OH/NH_4Cl (2:1) aqueous solution was added and the mixture was extracted twice with Et_2O. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/3 to afford **3-S23** (0.84 g, 71% yield, d.r. = 94:6) as colorless oil.

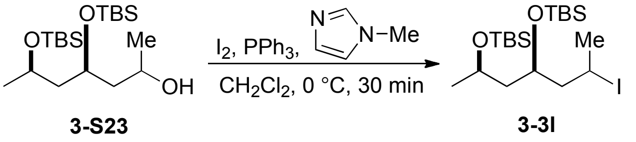
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 4.08 (tt, *J* = 9.4 and 3.7 Hz, 1H), 3.94 (dqd, *J* = 9.2, 6.3 and 2.3 Hz, 1H), 3.81 (dqd, *J* = 9.3, 6.0 and 3.3 Hz, 1H), 3.39 (br s, 1H), 1.78-1.66 (m, 2H), 1.53-1.43 (m, 2H), 1.16 (d, *J* = 6.2 Hz, 3H), 1.13 (d, *J* = 6.0 Hz, 3H), 0.90 (s, 3H), 0.12 (s, 6H), 0.05 (s, 3H), 0.03 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 70.9, 67.3, 65.6, 48.4, 44.5, 25.8, 25.7, 24.6, 23.6, 17.9, 17.8, –4.0, –4.1, –4.8, –4.9.

MS (70 eV, EI) *m/z* (%): 319 (4) [M–^{t}Bu]$^{+\bullet}$, 233 (33), 187 (74), 159 (100), 145 (83), 119 (65), 103 (23), 73 (48).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3420 (br w), 2957 (w), 2930 (w), 2858 (w), 1472 (w), 1254 (m), 1122 (w), 1068 (w), 1004 (w), 834 (s), 806 (m), 773 (s), 664 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{35}O_3Si_2^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 319.2125, found: 319.2128.



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[120] T. C. Judd, A. Bischoff, Y. Kishi, S. Adusumilli, P. L. C. Small, *Org. Lett.* **2004**, *6*, 4901.

3-3l

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.3 g, 5.2 mmol) in CH_2Cl_2 (35 mL) and cooled to 0 °C. PPh_3 (1.4 g, 5.2 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.41 mL, 5.2 mmol) was added. After 10 min of further stirring, **3-S23** (1.6 g, 4.4 mmol, d.r. = 94:6) dissolved in CH_2Cl_2 (15 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with the mixture of Et_2O/*i*-hexane = 1/4. All organic phase was combined and solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with diethyl Et_2O/*i*-hexane = 1/200 to afford **3-3l** with a little triphenyl phosphine (0.76 g, 36% yield, d.r. = 63:37) as colorless oil.

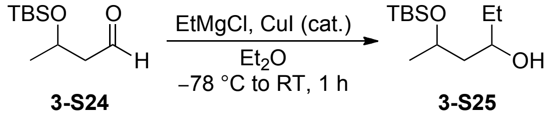
^{1}H-NMR (400 MHz, $CDCl_3$) δ: **<u>Major:</u>** 4.31-4.22 (m, 1H), 3.97-3.88 (m, 2H), 2.15-2.03 (m, 1H), 1.95 (d, J = 6.8 Hz, 3H), 1.67-1.58 (m, 1H), 1.55-1.47 (m, 2H), 1.16-1.13 (m, 3H), 0.90-0.87 (m, 18H), 0.15 (s, 3H), 0.08 (s, 3H), 0.064 (s, 3H), 0.057 (s, 3H). **<u>Minor:</u>** 4.20-4.13 (m, 1H), 3.87-3.80 (m, 2H), 2.15-2.03 (m, 1H), 1.91 (d, J = 6.8 Hz, 3H), 1.85-1.80 (m, 1H), 1.77-1.71 (m, 1H), 1.47-1.42 (m, 1H), 1.20-1.13 (m, 3H), 0.90-0.87 (m, 18H), 0.10 (s, 3H), 0.09 (s, 3H), 0.053 (s, 3H), 0.048 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: **<u>Major:</u>** 69.9, 65.4, 50.5, 48.1, 29.8, 28.0, 25.99, 25.97, 25.7, 24.6, 18.01, 17.96, –3.91, –3.93, –4.0, –4.3. **<u>Minor:</u>** 69.9, 65.5, 50.5, 46.7, 29.8, 28.9, 25.9, 25.8, 24.7, 23.8, 18.1, 17.9, –3.6, –4.26, –4.31, –4.7.

MS (70 eV, EI) *m/z* (%): 429 (10) $[M{-}^tBu]^{+\bullet}$, 387 (69), 297 (12), 259 (33), 229 (88), 185 (37), 159 (100), 147 (71), 133 (29), 73 (52).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2929 (w), 2857 (w), 1472 (w), 1253 (m), 1122 (w), 1061 (m), 1005 (w), 833 (s), 806 (m), 772 (s), 722 (w), 667 (w).

HRMS (EI) *m/z*: calcd for $C_{15}H_{34}IO_2Si_2^{+\bullet}$ $[M{-}^tBu]^{+\bullet}$: 429.1142, found: 429.1116.



3-S25

To a suspension of CuI (0.34 g, 1.8 mmol) in Et_2O (45 mL) containing **3-S24**[121] (1.7 g, 9.0 mmol, CAS: 92775-37-6) was added dropwise EtMgCl (4.0 mL, 2.7 M in THF, 10.9 mmol) at –78°C. The reaction was then allowed to stir at room temperature for 1 h. A saturated NH_4OH/NH_4Cl (2:1) aqueous solution was added and the mixture was extracted twice with Et_2O. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/3 to afford **3-S25** (1.8 g, 85% yield, d.r. = 64:36) with some starting material as colorless oil.

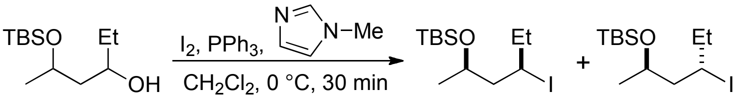
^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: **Major:** 4.25-4.15 (m, 1H), 3.89-3.83 (m, 1H), 3.45 (d, *J* = 2.2 Hz, 1H), 1.63-1.35 (m, 4H), 1.21 (d, *J* = 6.3 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 3H), 0.87 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H). **Minor:** 4.12-4.01 (m, 1H), 3.68-3.62 (m, 1H), 3.48 (d, *J* = 1.1 Hz, 1H), 1.63-1.35 (m, 4H), 1.16 (d, *J* = 6.0 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H), 0.88 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: **Major:** 69.6, 67.7, 43.5, 30.5, 25.7, 22.6, 17.9, 9.9, –4.6, –5.1. **Minor:** 72.8, 70.2, 45.2, 30.2, 25.7, 24.6, 17.8, 9.6, –3.9, –4.9.

MS (70 eV, EI) *m/z* (%): 175 (7) [M–^{t}Bu]$^{+\bullet}$, 159 (31), 133 (9), 119 (94), 101 (14), 83 (42), 75 (100)

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3439 (br w), 2958 (w), 2930 (w), 2858 (w), 1376 (w), 1255 (w), 1152 (w), 1122 (w), 1072 (m), 1002 (w), 910 (w), 833 (s), 806 (m), 773 (s), 721 (w).

HRMS (EI) *m/z*: calcd for **$C_8H_{19}O_2Si^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 175.1154, found: 175.1103.



3-S25 *syn*-**3-3m** *anti*-**3-3m**

syn-**3-3m** and *anti*-**3-3m**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (3.2 g, 12.5 mmol) in CH_2Cl_2 (70 mL) and cooled to 0 °C. PPh_3 (3.3 g, 12.5 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.98 mL, 12.5 mmol) was added. After 10 min of further stirring, a mixture of the diastereomers of **3-S25** (2.4 g, 12.5 mmol, d.r. = 64:36) dissolved in CH_2Cl_2 (20 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated

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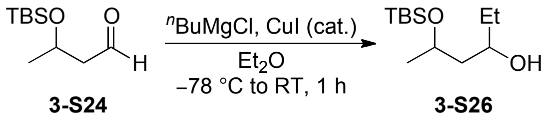
[121] Q. Liang, J. K. D. Brabander, *Tetrahedron* **2011**, *67*, 5046.

($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with the mixture of Et_2O/*i*-hexane = 1/4. All organic phase was combined and solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *syn*-**3-3m** (0.85 g, 24% yield, d.r. = 97:3) as the first fraction and colorless oil, and *anti*-**3-3m** (0.70 g, 20% yield, d.r. = 98:2) as the second fraction and colorless oil. The relative configuration was determined by the analogy of NMR spectrum of *syn*- and *anti*-**3a**.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: *syn*-3-3m: 4.21 (dddd, *J* = 11.0, 7.6, 5.0 and 2.6 Hz, 1H), 4.01 (dqd, *J* = 9.6, 6.0 and 2.3 Hz, 1H), 1.93-1.76 (m, 3H), 1.60 (ddd, *J* = 14.8, 9.6 and 2.5 Hz, 1H), 1.17 (d, *J* = 7.2 Hz, 3H), 1.03 (t, *J* = 7.2 Hz, 3H), 0.89 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H). ***anti*-3-3m:** 4.07-3.96 (m, 2H), 2.19 (ddd, *J* = 14.2, 8.7 and 6.2 Hz, 1H), 1.82-1.74 (m, 3H), 1.11 (d, *J* = 6.0 Hz, 3H), 1.02 (t, *J* = 7.2 Hz, 3H), 0.86 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: *syn*-3-3m: 68.3, 50.1, 40.1, 34.5, 25.9, 24.1, 18.0, 14.0, –4.0, –4.3. ***anti*-3-3m:** 68.3, 50.5, 41.1, 38.0, 31.5, 25.9, 24.0, 21.8, 17.9, 14.0, –3.9, –4.4.
MS (70 eV, EI) *m/z* (%): 285 (11) $[M-{}^{t}Bu]^{+\bullet}$, 243 (6), 229 (90), 185 (57), 159 (28), 115 (12), 101 (14), 83 (100).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 2857 (w), 1463 (w), 1255 (w), 1130 (w), 1056 (m), 1039 (w), 922 (w), 833 s), 824 (s), 805 (m), 772 (s), 661 (w).
HRMS (EI) *m/z*: calcd for **$C_{11}H_{24}OISi^{+\bullet}$** $[M-Me]^{+\bullet}$: 327.0641, found: 327.0630.



3-S26

To a suspension of CuI (0.34 g, 1.8 mmol) in Et_2O (45 mL) containing **3-S24**[121] (1.7 g, 9.0 mmol, CAS: 92775-37-6) was added dropwise ^{n}BuMgCl (8.4 mL, 1.3 M in THF, 10.7 mmol) at –78°C. The reaction was then allowed to stir at room temperature for 1 h. A saturated NH_4OH/NH_4Cl (2:1) aqueous solution was added and the mixture was extracted twice with Et_2O. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/3 to afford **3-S26** (2.1 g, 88% yield, d.r. = 62:38) as colorless oil.

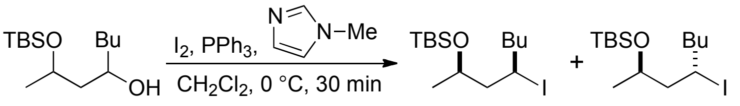
^{1}H-NMR (400 MHz, CDCl$_3$) δ: **Major:** 4.22-4.15 (m, 1H), 3.97-3.90 (m, 1H), 3.42 (d, *J* = 2.3 Hz, 1H), 1.57-1.64 (ddd, *J* = 13.9, 9.8 and 3.8 Hz, 1H), 1.53-1.44 (m, 2H), 1.41-1.25 (m, 5H), 1.20 (d, *J* = 6.3 Hz, 3H), 0.89-0.84 (m, 12H), 0.07 (s, 3H), 0.06 (s, 3H). **Minor:** 4.09-4.01 (m, 1H), 3.75-3.69 (m, 1H), 3.47 (d, *J* = 1.2 Hz, 1H), 1.53-1.44 (m, 3H), 1.29-1.25 (m, 5H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.89-0.84 (m, 12H), 0.10 (s, 3H), 0.08 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: **Major:** 71.5, 68.2, 44.0, 37.5, 27.8, 25.7, 22.73, 22.66, 17.9, 14.1, –4.6, –5.1. **Minor:** 70.2, 67.7, 45.7, 37.3, 27.5, 25.8, 24.6, 22.8, 17.8, 14.1 –3.9, –4.9.

MS (70 eV, EI) *m/z* (%): 203 (7) [M–^{t}Bu]$^{+\bullet}$, 185 (6), 159 (23), 119 (100), 111 (17), 101 (14), 75 (88).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3447 (br w), 2958 (w), 2930 (w), 2858 (w), 1464 (w), 1376 (w), 1255 (m), 1152 (w), 1122 (w), 1072 (m), 1002 (w), 939 (w), 834 (s), 806 (m), 773 (s), 721 (w).

HRMS (EI) *m/z*: calcd for $C_{14}H_{31}O_2Si^{+\bullet}$ [M–H]$^{+\bullet}$: 259.2093, found: 259.2085.



3-S26 *syn*-**3-3n** *anti*-**3-3n**

syn-**3-3n** and *anti*-**3-3n**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I$_2$ (2.5 g, 9.6 mmol) in CH$_2$Cl$_2$ (60 mL) and cooled to 0 °C. PPh$_3$ (2.4 g, 9.6 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.76 mL, 9.6 mmol) was added. After 10 min of further stirring, a mixture of the diastereomers of **3-S26** (2.1 g, 8.0 mmol, d.r. = 62:38) dissolved in CH$_2$Cl$_2$ (10 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated (NaHSO$_3$+Na$_2$S$_2$O$_5$) aqueous solution[106] and the mixture was extracted with CH$_2$Cl$_2$ three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with the mixture of Et$_2$O/*i*-hexane = 1/4. All organic phase was combined and solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/250 to afford *syn*-**3-3n** (0.42 g, 14% yield, d.r. = 99:1) as the first fraction and colorless oil and *anti*-**3-3n** (0.71 g, 24% yield, d.r. = 99:1) as the second fraction and colorless oil. The relative configuration was determined by the analogy of NMR spectrum of *syn*- and *anti*-**3a**.

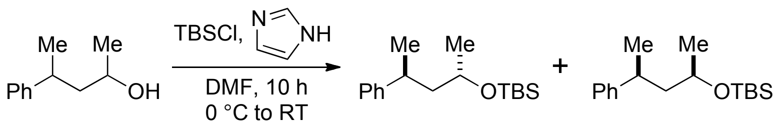
^{1}H-NMR (400 MHz, CDCl$_3$) δ: ***syn*-3-3n:** 4.24 (dddd, *J* = 11.1, 7.9, 5.1 and 2.5 Hz, 1H), 4.02 (dqd, *J* = 9.5, 6.2 and 2.0 Hz, 1H), 1.97-1.85 (m, 2H), 1.74 (ddd, *J* = 14.5, 9.4 and 5.3 Hz, 1H), 1.63 (ddd, *J* = 14.8, 9.5 and 2.5 Hz, 1H), 1.54-1.26 (m, 4H), 1.17 (d, *J* = 6.1 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.89 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H). ***anti*-3-3n:** 4.10-3.96 (m, 2H), 2.19 (ddd, *J* = 14.5, 8.7 and 6.1 Hz, 1H), 1.85-1.68 (m, 3H), 1.58-1.45 (m, 1H), 1.42-1.25 (m, 3H), 1.11 (d, *J* = 6.0 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: ***syn*-3-3n:** 68.3, 50.1, 40.1, 34.5, 25.9, 24.1, 18.0, 14.0, –4.0, –4.3. ***anti*-3-3n:** 68.3, 50.5, 41.1, 38.0, 31.5, 25.9, 24.0, 21.8, 17.9, 14.0, –3.9, –4.4.

MS (70 eV, EI) *m/z* (%): 313 (11), 271 (6), 229 (100), 215 (6), 185 (55), 159 (34), 111 (87), 69 (71).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 1472 (w), 1254 (w), 1129 (w), 1056 (m), 1039 (w), 922 (w), 833 (s), 806 (m), 772 (s), 662 (w).

HRMS (EI) *m/z*: calcd for **$C_{13}H_{28}OISi^{+\bullet}$** [M–Me]$^{+\bullet}$: 355.0954, found: 355.0969.



3-S27 *anti*-**3-S28** *syn*-**3-S28**

anti-**3-S28** and *syn*-**3-S28**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of **3-S27**[122] (1.6 g, 10.0 mmol, CAS: 77614-49-4) in DMF (20 mL). Imidazole (1.7 g, 25.0 mmol) was added and the reaction mixture was cooled down to 0 °C. Then TBSCl (1.8 g, 12.0 mmol) was added and the reaction mixture was warmed up to room temperature and stirred for 15 h. The reaction mixture was quenched with saturated NH$_4$Cl aqueous solution at 0 °C and was extracted three times with Et$_2$O:*i*-hexane = 1:4. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et$_2$O:*i*-hexane = 1/600 to afford *anti*-**3-S28** (1.6 g, 53% yield, d.r. = 99:1) as the first fraction and yellow oil and *syn*-**3-S28** (1.2 g, 38% yield, d.r. = 99:1) as the second fraction and yellow oil.

syn-**3-S28**

^{1}H-NMR (600 MHz, CDCl$_3$) δ: 7.31-7.25 (m, 2H), 7.20-7.16 (m, 3H), 3.70 (qt, *J* = 6.2 and 6.1 Hz, 1H), 2.82 (tq, *J* = 7.1 and 7.0 Hz, 1H), 1.81 (dt, *J* = 13.9 and 7.1 Hz, 1H), 1.57 (dt, *J* =

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[122] B. Holscher, U.S. Pat. Appl. Publ., 20080064625, 13 Mar 2008

13.6 and 6.9 Hz, 1H), 1.24 (d, *J* = 6.9 Hz, 3H), 1.13 (d, *J* = 6.0 Hz, 3H), 0.87 (s, 9H), 0.02 (s, 3H), –0.01 (s, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$) *δ*: 147.9, 128.5, 127.0, 126.0, 66.6, 48.7, 36.4, 26.1, 23.9, 22.3, 18.3, –4.2, –4.6.

MS (70 eV, EI) *m/z* (%): 263 (2) $[M–Me]^{+\bullet}$, 221 (100), 145 (5), 131 (6), 103 (81), 91 (7), 75 (39).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2927 (w), 2856 (w), 1494 (w), 1472 (m), 1461 (w), 1452 (w), 1372 (w), 1360 (w), 1255 (w), 1128 (w), 1102 (w), 1085 (w), 1064 (m), 1047 (w), 1029 (w), 1005 (w), 987 (w), 971 (w), 927 (w), 859 (w), 833 (s), 807 (m), 772 (s), 762 (s), 698 (vs), 663 (w).

HRMS (EI) *m/z*: calcd for **$C_{17}H_{29}O_1Si^{+\bullet}$** $[M–H]^{+\bullet}$: 277.1988, found: 277.1981.

anti-**3-S28**

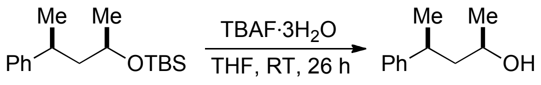
^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: 7.32-7.25 (m, 2H), 7.21-7.14 (m, 3H), 3.65 (tq, *J* = 6.1 and 6.0 Hz, 1H), 2.89 (hex, *J* = 7.1 Hz, 1H), 1.72 (dd, *J* = 7.3 and 6.1 Hz, 2H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.09 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 9H), –0.02 (s, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 147.7, 128.4, 127.3, 126.0, 67.0, 48.4, 36.7, 26.2, 24.5, 23.7, 18.3, –3.9, –4.5.

MS (70 eV, EI) *m/z* (%): 263 (1) $[M–Me]^{+\bullet}$, 221 (2), 159 (5), 131 (5), 115 (5), 103 (100), 91 (10), 75 (65), 59 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 2927 (w), 2855 (w), 1494 (w), 1472 (m), 1462 (w), 1374 (w), 1143 (w), 1086 (w), 1064 (m), 1047 (w), 1029 (w), 1005 (w), 968 (w), 937 (w), 878 (w), 833 (m), 806 (m), 772 (s), 761 (s), 698 (vs).

HRMS (EI) *m/z*: calcd for **$C_{16}H_{27}OSi^{+\bullet}$** $[M–Me]^{+\bullet}$: 263.1831, found: 263.1808.



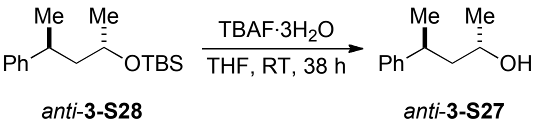
syn-**3-S28** *syn*-**3-S27**

syn-**3-S27** (CAS: 82481-52-5)

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of *syn*-**3-S28** (1.1 g, 4.0 mmol, d.r. = 99:1) in THF (12 mL) and it was cooled to 0 °C. TBAF·3H_2O (3.2 g, 10.0 mmol) was added and the reaction mixture was warmed to room temperature. After stirring at room temperature for 26 h, the reaction was quenched with saturated NH_4Cl

aqueous solution and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O:*i*-hexane = 2/1 to afford *syn*-**3-S27** (0.64 g, 98% yield, d.r. = 99:1) as colorless oil. The relative configuration was determined by the comparison with *anti*-**3-S27'** described below.

^{1}H-NMR (600 MHz, CDCl$_3$) δ: 7.32-7.28 (m, 2H), 7.23-7.17 (m, 3H), 3.77 (qt, J = 6.6 and 6.0 Hz, 1H), 2.87 (hex, J = 7.2 Hz, 1H), 1.83 (dt, J = 13.8 and 7.8 Hz, 1H), 1.65 (ddd, J = 13.6, 7.1 and 5.4 Hz, 1H), 1.30 (s br, 1H), 1.27 (d, J = 6.9 Hz, 3H), 1.19 (d, J = 6.2 Hz, 3H).
^{13}C-NMR (150 MHz, CDCl$_3$) δ: 147.4, 128.7, 127.0, 126.3, 66.6, 48.0, 37.1, 23.9, 22.5.
MS (70 eV, EI) *m/z* (%): 164 (4) $[M]^{+\bullet}$, 146 (36), 131 (97), 115 (6), 105 (100), 91 (51), 77 (21), 51 (7).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3338 (w br), 2961 (w), 2925 (w), 1602 (w), 1493 (w), 1451 (w), 1375 (w), 1129 (w), 1082 (w), 1059 (w), 1033 (w), 1001 (w), 947 (w), 907 (w), 838 (w), 760 (m), 697 (vs).
HRMS (EI) *m/z*: calcd for $C_{11}H_{16}O^{+\bullet}$ $[M]^{+\bullet}$: 164.1201, found: 164.1178.



anti-**3-S27** (CAS: 82481-53-6)
A dry and Ar-flushed *Schlenk*-flask was charged with a solution of *anti*-**3-S28** (1.5 g, 5.5 mmol, d.r. = 99:1) in THF (15 mL) and it was cooled to 0 °C. TBAF·$3H_2O$ (3.2 g, 10.1 mmol) was added and the reaction mixture was warmed to room temperature. After stirring at room temperature for 38 h, the reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O:*i*-hexane = 2/1 to afford *anti*-**3-S27** (0.73 g, 81% yield, d.r. = 99:1) as colorless oil. The relative configuration was determined by the comparison with *anti*-**3-S27'** described below.

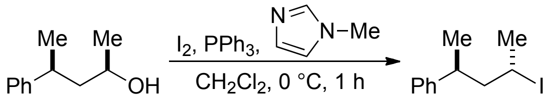
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.34-7.27 (m, 2H), 7.24-7.16 (m, 3H), 3.61-3.49 (m, 1H), 2.97 (dqd, *J* = 8.8, 7.0 and 6.8 Hz, 1H), 1.71 (t, *J* = 7.0 Hz, 1H), 1.70 (dd, *J* = 9.2 and 4.8 Hz, 1H), 1.33 (s br, 1H), 1.27 (d, *J* = 7.0 Hz, 3H), 1.13 (d, *J* = 6.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 147.0, 128.6, 127.3, 126.2, 66.1, 47.8, 36.8, 24.3, 23.2.

MS (70 eV, EI) *m/z* (%): 164 (4) $[M]^{+\bullet}$, 149 (35), 131 (97), 115 (5), 105 (100), 91 (49), 77 (22), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3337 (w br), 2960 (w), 2925 (w), 1493 (w), 1452 (w), 1372 (w), 1138 (w), 1083 (w), 1054 (w), 1034 (w), 1024 (w), 951 (w), 899 (w), 829 (w), 761 (m), 697 (vs).

HRMS (EI) *m/z*: calcd for $C_{11}H_{16}O^{+\bullet}$ $[M]^{+\bullet}$: 164.1201, found: 164.1196.



syn-**3-S27** *anti*-**3-20**

anti-**3-20**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.2 g, 4.8 mmol) in CH_2Cl_2 (20 mL) and cooled to 0 °C. PPh_3 (1.3 g, 4.8 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.38 mL, 4.8 mmol) was added. After 10 min of further stirring, a mixture of the diastereomers of *anti*-**3-S27** (0.66 g, 4.0 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with the mixture of Et_2O/*n*-pentane = 1/4. After collecting the organic phase, the remained sticky substance was dissolved in CH_2Cl_2 (5 mL) and it was passed through a pad of silica gel with the mixture of Et_2O/*n*-pentane = 1/4. All organic phase was combined and solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/1000 to afford *anti*-**3-20** (0.88 g, 81% yield, dr = 98:2) as colorless oil.

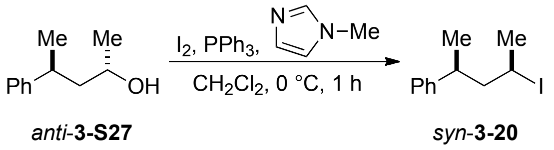
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.35-7.29 (m, 2H), 7.28-7.20 (m, 3H), 3.71 (dqd, *J* = 10.2, 6.8 and 3.4 Hz, 1H), 2.99 (dqd, *J* = 11.0, 7.0 and 4.1 Hz, 1H), 2.12 (ddd, *J* = 14.9, 11.0 and 4.1. Hz, 1H), 1.88 (d, *J* = 6.8 Hz, 3H), 1.70 (ddd, *J* = 14.8, 10.3 and 3.5 Hz, 1H), 1.32 (d, *J* = 7.0 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 145.6, 128.7, 127.3, 126.6, 51.3, 40.5, 30.0, 29.7, 22.6.

MS (70 eV, EI) *m/z* (%): 274 (5) $[M]^{+\bullet}$, 147 (22), 131 (4), 115 (5), 105 (100), 91 (30), 77 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3027 (w), 2959 (w), 2913 (w), 1602 (w), 1494 (w), 1452 (w), 1377 (w), 1231 (w), 1149 (w), 1123 (w), 1064 (w), 1012 (w), 908 (w), 869 (w), 762 (m), 698 (vs).

HRMS (EI) *m/z*: calcd for **$C_{11}H_{15}I^{+\bullet}$** $[M]^{+\bullet}$: 274.0218, found: 274.0199.



syn-**3-20**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (25 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, a mixture of the diastereomers of *anti*-**3-S27** (0.82 g, 5.0 mmol) dissolved in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with the mixture of Et_2O/*n*-pentane = 1/4. After collecting the organic phase, the remained sticky substance was dissolved in CH_2Cl_2 (5 mL) and it was passed through a pad of silica gel with the mixture of Et_2O/*n*-pentane = 1/4. All organic phase was combined and solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/1000 to afford *syn*-**3-20** (1.0 g, 76% yield, d.r. = 98:2) as colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.35-7.28 (m, 2H), 7.25-7.18 (m, 3H), 4.09 (ddq, *J* = 7.8, 6.8 and 6.6 Hz, 1H), 2.93 (tq, *J* = 7.1 and 7.0 Hz, 1H), 2.30 (ddd, *J* = 14.9, 7.8 and 6.6. Hz, 1H), 1.93 (d, *J* = 6.8 Hz, 3H), 1.85 (dt, *J* = 14.3 and 7.2 Hz, 1H), 1.24 (d, *J* = 6.9 Hz, 3H).

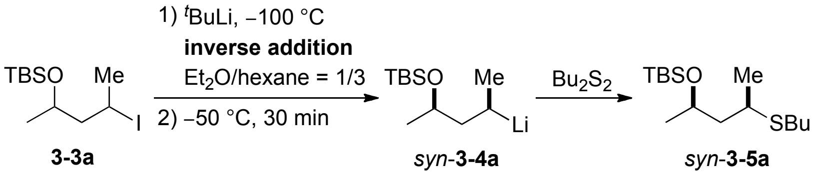
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 146.2, 128.7, 127.1, 126.4, 51.6, 40.0, 28.7, 27.8, 21.3.

MS (70 eV, EI) *m/z* (%): 274 (5) $[M]^{+}$, 147 (17), 131 (5), 115 (5), 105 (100), 91 (25), 77 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3025 (w), 2959 (w), 2914 (w), 2868 (w), 1602 (w), 1492 (w), 1451 (w), 1376 (w), 1234 (w), 1204 (w), 1149 (w), 1120 (w), 1060 (w), 1038 (w), 1025 (w), 1002 (w), 997 (w), 976 (w), 907 (w), 853 (w), 760 (m), 697 (vs).
HRMS (EI) *m/z*: calcd for $C_{11}H_{15}I^{+\bullet}$ [M]$^{+\bullet}$: 274.0218, found: 274.0211.

9.3.2 I/Li exchange and subsequent trapping reaction

[General procedure]
A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (1.7 mL) and Et_2O (0.4 mL) and cooled to –100 °C. ^{t}BuLi (1.83 M in *n*-pentane, 0.41 mL, 0.75 mmol) was added to the reaction mixture. Then, a solution of an alkyl iodide (0.30 mmol) in *n*-hexane (0.4 mL) and Et_2O (0.3 mL) was added dropwise in 10 min. After stirring at –100 °C for 10 min, the reaction mixture was warmed up to –50 °C and stirred for 30 min. Electrophile (0.54–0.75 mmol) was adeded to the reaction mixture and it was stirred at –50 °C for 30 min to 1 h. The reaction was quenched with 7 drops of saturated NH_4Cl aqueous solution and after an addition of $MgSO_4$ this mixture was passed through a pad of silica gel with EtOAc. Solvents were evaporated and the crude product was purified by column chromatography.



***syn*-3-5a**

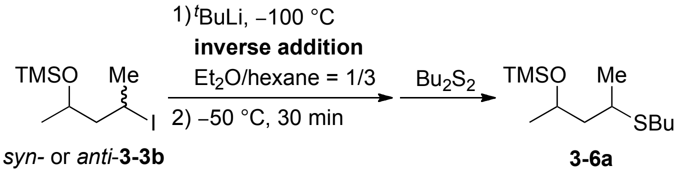
According to general procedure, diastereomeric mixture of **3-3a** (99 mg, 0.30 mmol, d.r. = 50:50) as a starting material and Bu_2S_2 (103 μL, 0.54 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *syn*-**3-5a** (65 mg, 75% yield, d.r. = 93:7) as colorless oil. The relative configuration was determined by the comparison with *syn*-**3-5a**' described below.

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.04 (dqd, *J* = 8.4, 6.1 and 4.1 Hz, 1H), 2.84 (dqd, *J* = 8.9, 6.7 and 5.1 Hz, 1H), 2.49 (td, *J* = 7.5 and 2.6 Hz, 2H), 1.65-1.30 (m, 6H), 1.27 (d, *J* = 6.7 Hz, 3H), 1.11 (d, *J* = 6.1 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).
^{13}C-NMR (75 MHz, CDCl$_3$) δ: 66.4, 47.4, 37.0, 32.1, 29.7, 26.1, 24.4, 22.8, 22.4, 18.2, 13.9, –4.0, –4.5.

MS (70 eV, EI) *m/z* (%): 275 (3) $[M–Me]^{+•}$, 233 (100), 191 (29), 159 (6), 147 (84), 135 (6), 115 (6), 103 (6), 91 (14), 75 (29), 57 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2927 (w), 2856 (w), 1472 (w), 1462 (w), 1373 (w), 1255 (w), 1146 (w), 1126 (w), 1067 (w), 1050 (m), 1024 (w), 1005 (w), 970 (w), 935 (w), 874 (w), 834 (s), 824 (m), 806 (m), 773 (vs), 722 (w), 660 (w).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{31}OSSi^{+•}$** $[M–Me]^{+•}$: 275.1865, found: 275.1851.



3-6a

According to general procedure, *syn*-**3-3b** (86 mg, 0.30 mmol, d.r. = 99:1) or *anti*-**3-3b** (86 mg, 0.30 mmol, d.r. = 99:1) as a starting material and Bu_2S_2 (103 μL, 0.54 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/50 to afford **3-6a** (From *syn*-**S3**: 48 mg, 64% yield, d.r. = 85:15, From *anti*-**S3**: 48 mg, 64% yield, d.r. = 85:15) as colorless oil. The relative configuration was determined by S_N2 reactions of *syn*- and *anti*-**3-3b** with NaSBu.

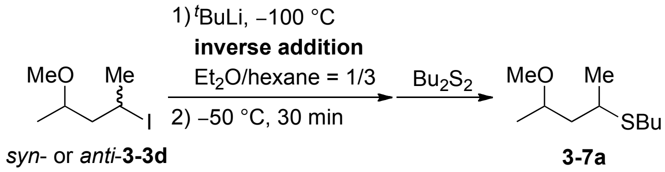
^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: ***syn*-3-3b:** 4.05 (dqd, *J* = 8.4, 6.2 and 3.4 Hz, 1H), 2.82 (dqd, *J* = 9.3, 6.7 and 4.7 Hz, 1H), 2.57-2.42 (m, 2H), 1.63-1.33 (m, 6H), 1.28 (d, *J* = 6.7 Hz, 3H), 1.12 (d, *J* = 6.1 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H), 0.12 (s, 9H). ***anti*-3-3b:** 3.98-3.88 (m, 1H), 2.87-2.75 (m, 1H), 2.57-2.42 (m, 2H), 1.77 (ddd, *J* = 13.8, 8.0 and 5.8 Hz, 1H), 1.63-1.33 (m, 5H), 1.24 (d, *J* = 6.7 Hz, 3H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.83 (t, *J* = 7.2 Hz, 3H), 0.10 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: ***syn*-3-3b:** 66.4, 47.0, 37.1, 32.2, 29.7, 24.4, 22.8, 22.4, 13.8, 0.5. ***anti*-3-3b:** 66.2, 47.2, 36.3, 32.0, 29.9, 24.1, 22.4, 22.3, 13.9, 0.44.

MS (70 eV, EI) *m/z* (%): 248 (9) $[M]^{+•}$, 233 (9), 191 (4), 158 (66), 143 (100), 130 (12), 117 (38), 101 (31), 91 (9), 73 (46), 61 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2926 (w), 1454 (w), 1374 (w), 1250 (w), 1147 (w), 1049 (w), 1006 (w), 970 (w), 906 (m), 877 (w), 838 (w), 729 (vs).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{28}OSSi^{+•}$** $[M]^{+•}$: 248.1630, found: 248.1604.



3-7a

According to general procedure, *syn*-**3-3d** (68 mg, 0.30 mmol, d.r. = 99:1) or *anti*-**3-3d** (68 mg, 0.30 mmol, d.r. = 99:1) as a starting material and Bu_2S_2 (103 µL, 0.54 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/50 to afford **3-7a** (From *syn*-**3-3d**: 44 mg, 77% yield, d.r. = 56:44, From *anti*-**3-3d**: 37 mg, 65% yield, d.r. = 52:48) as colorless oil. The relative configuration was determined by S_N2 reactions of *syn*- and *anti*-**3-3d** with NaSBu.

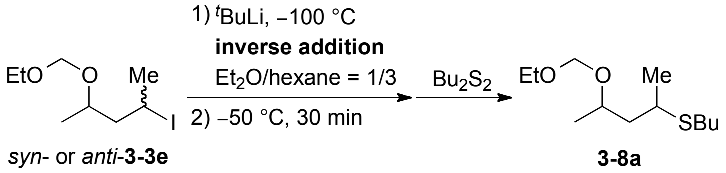
^{1}H-NMR (300 MHz, CDCl$_3$) δ: *syn*-3-7a: 3.56 (dqd, *J* = 8.6, 6.2 and 3.4 Hz, 1H), 3.32 (s, 3H), 2.95-2.81 (m, 1H), 2.56-2.44 (m, 2H), 1.65 (dqd, *J* = 14.4, 8.9 and 5.0 Hz, 1H), 1.60-1.32 (m, 5H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 6.1 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H). ***anti*-3-7a:** 3.45 (dqd, *J* = 7.9, 6.1 and 5.2 Hz, 1H), 3.29 (s, 3H), 2.95-2.81 (m, 1H), 2.56-2.44 (m, 2H), 1.85 (ddd, *J* = 14.0, 7.9 and 6.1 Hz, 1H), 1.60-1.32 (m, 5H), 1.26 (d, *J* = 6.7 Hz, 3H), 1.13 (d, *J* = 6.1 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: *syn*-3-7a: 74.6, 56.0, 45.0, 37.0, 32.1, 30.1, 22.9, 22.2, 21.4, 19.2. ***anti*-3-7a:** 74.4, 56.3, 44.2, 36.4, 32.0, 30.0, 22.9, 22.3, 21.4, 19.2.

MS (70 eV, EI) *m/z* (%): 190 (27) $[M]^{+\bullet}$, 131 (5), 117 (6), 100 (60), 85 (100), 75 (14), 59 (61).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2959 (m), 2927 (m), 2873 (w), 1457 (w), 1373 (m), 1304 (w), 1273 (w), 1213 (w), 1179 (w), 1146 (m), 1121 (w), 1086 (vs), 1037 (w), 990 (w), 877 (w), 800 (w), 748 (w), 700 (w).

HRMS (EI) *m/z*: calcd for **$C_{10}H_{22}OS^{+\bullet}$** $[M]^{+\bullet}$: 190.1391, found: 190.1383.



3-8a

According to general procedure, *syn*-**3-3e** (82 mg, 0.30 mmol, d.r. = 99:1) or *anti*-**3-3e** (82 mg, 0.30 mmol, d.r. = 99:1) as a starting material and Bu_2S_2 (103 µL, 0.54 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/20 to afford **3-8a** (From *syn*-**3-3e**: 43 mg, 61% yield, d.r. = 64:36, From *anti*-**3-3e**: 43 mg, 61% yield, d.r. = 64:36) as colorless oil. The relative configuration was determined by S_N2 reactions of *syn*- and *anti*-**3-3e** with NaSBu.

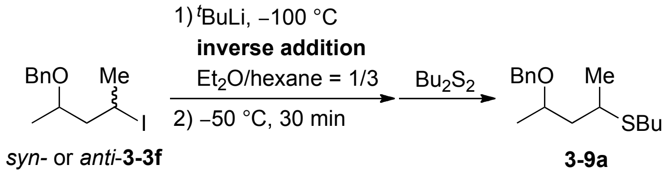
^{1}H-NMR (300 MHz, CDCl$_3$) δ: *syn*-3-8a: 4.74 (d, J = 6.9 Hz, 1H), 4.70 (d, J = 6.9 Hz, 1H), 3.95 (dqd, J = 8.6, 6.2 and 4.2 Hz, 1H), 3.66-3.51 (m, 2H), 2.93-2.81 (m, 1H), 2.49 (t, J = 7.5 Hz, 2H), 1.67 (ddd, J = 14.1, 8.8 and 5.1 Hz, 1H), 1.60-1.32 (m, 5H), 1.28 (d, J = 6.7 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H), 1.16 (d, J = 6.2 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H). ***anti*-3-8a:** 4.72 (d, J = 7.1 Hz, 1H), 4.63 (d, J = 7.1 Hz, 1H), 3.84 (dqd, J = 8.3, 6.1 and 4.9 Hz, 1H), 3.66-3.51 (m, 2H), 2.93-2.81 (m, 1H), 2.51 (t, J = 7.5 Hz, 2H), 1.87 (ddd, J = 14.0, 8.3 and 5.7 Hz, 1H), 1.60-1.32 (m, 5H), 1.27 (d, J = 6.7 Hz, 3H), 1.19 (t, J = 7.1 Hz, 3H), 1.16 (d, J = 6.2 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: *syn*-3-8a: 94.0, 71.4, 63.3, 45.1, 36.8, 32.1, 29.7, 22.7, 22.3, 20.9, 15.2, 13.8. ***anti*-3-8a:** 93.5, 70.8, 63.3, 44.9, 36.2, 32.1, 30.0, 22.3, 21.2, 20.3, 15.2, 13.8.

MS (70 eV, EI) *m/z* (%): 234 (5) $[M]^{+\bullet}$, 207 (21), 175 (12), 159 (9), 131 (47), 117 (44), 98 (14), 86 (37), 75 (36), 59 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2927 (w), 2873 (w), 1456 (w), 1375 (m), 1272 (w), 1201 (w), 1174 (w), 1143 (w), 1095 (m), 1035 (vs), 1013 (m), 989 (w), 847 (w).

HRMS (EI) *m/z*: calcd for $C_{12}H_{26}O_2S^{+\bullet}$ $[M]^{+\bullet}$: 234.1654, found: 234.1650.



3-9a

According to general procedure, *syn*-**3-3f** (91 mg, 0.30 mmol, d.r. = 99:1) or *anti*-**3-3f** (91 mg, 0.30 mmol, d.r. = 99:1) as a starting material and Bu_2S_2 (103 µL, 0.54 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/20 to afford **3-9a** (From *syn*-**3-3f**: 45 mg, 56% yield, d.r. = 66:34, From *anti*-**3-3f**: 46 mg, 58% yield, d.r. = 66:34) as a colorless oil. The relative configuration was determined by S_N2 reactions of *syn*- and *anti*-**3-3f** with NaSBu.

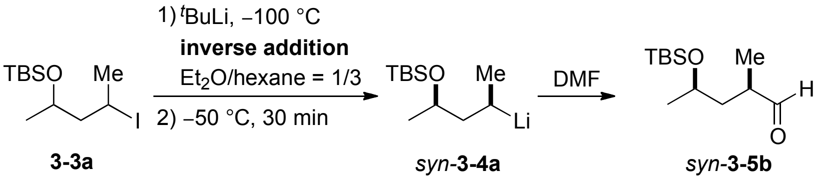
^{1}H-NMR (600 MHz, CDCl$_3$) δ: **<u>*syn*-3-9a:</u>** 7.36-7.23 (m, 5H), 4.60 (d, J = 11.4 Hz, 1H), 4.45 (d, J = 11.4 Hz, 1H), 3.84 (dqd, J = 9.6, 6.2 and 3.8 Hz, 1H), 2.97 (dqd, J = 9.6, 6.8 and 4.7 Hz, 1H), 2.49 (t, J = 7.4 Hz, 2H), 1.76 (ddd, J = 14.2, 9.0 and 4.8 Hz, 1H), 1.60-1.43 (m, 3H), 1.39 (hex, J = 7.3 Hz, 2H), 1.29 (d, J = 6.8 Hz, 3H), 1.20 (d, J = 6.1 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H). **<u>*anti*-3-9a:</u>** 7.36-7.23 (m, 5H), 4.59 (d, J = 11.3 Hz, 1H), 4.41 (d, J = 11.7 Hz, 1H), 3.67 (tq, J = 7.4 and 6.0 Hz, 1H), 2.91 (tq, J = 7.0 and 6.5 Hz, 1H), 2.51 (t, J = 7.3 Hz, 2H), 1.95 (ddd, J = 14.1, 7.9 and 6.0 Hz, 1H), 1.60-1.43 (m, 3H), 1.39 (hex, J = 7.3 Hz, 2H), 1.22 (d, J = 6.8 Hz, 6H), 0.90 (t, J = 7.4 Hz, 3H).

^{13}C-NMR (150 MHz, CDCl$_3$) δ: **<u>*syn*-3-9a:</u>** 139.1, 128.4, 127.9, 127.6, 73.1, 71.0, 45.1, 37.1, 32.2, 30.0, 22.3, 21.3, 20.0, 13.8. **<u>*anti*-3-9a:</u>** 139.0, 128.4, 127.8, 127.6, 72.5, 70.4, 44.6, 36.4, 32.1, 30.0, 22.9, 22.3, 19.8, 13.8.

MS (70 eV, EI) *m/z* (%): 266 (5) $[M]^{+\bullet}$, 207 (14), 175 (17), 160 (21), 143 (4), 131 (14), 117 (49), 107 (8), 91 (100), 75 (15), 59 (8).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 2926 (w), 2870 (w), 1731 (w), 1496 (w), 1453 (w), 1373 (w), 1343 (w), 1270 (w), 1205 (w), 1146 (m), 1127 (w), 1086 (m), 1068 (s), 1028 (w), 950 (w), 911 (w), 877 (w) 816 (w), 733 (s), 695 (vs).

HRMS (EI) *m/z*: calcd for **$C_{16}H_{26}OS^{+\bullet}$** $[M]^{+\bullet}$: 226.1704, found: 226.1697.



3-3a *syn*-**3-4a** *syn*-**3-5b**

syn-**3-5b**

According to general procedure, diastereomeric mixture of **3-3a** (99 mg, 0.30 mmol, d.r. = 50:50) as a starting material and DMF (42 µL, 0.54 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/100→1/50 to afford *syn*-**3-5b** (51 mg, 74% yield, d.r. = 92:8) as a colorless oil. The relative configuration was determined by the comparison of NMR spectra with the literature value.[123] Our previous paper shows the retentive quenching of unstabilized secondary lithium reagents with DMF.[30]

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[123] The literature values are identical to the minor diastereomer of *syn*-**3-5d.** S. Wattanasereekul, M. E. Maier, *Adv. Synth. Catal.* **2004**, *346*, 855.

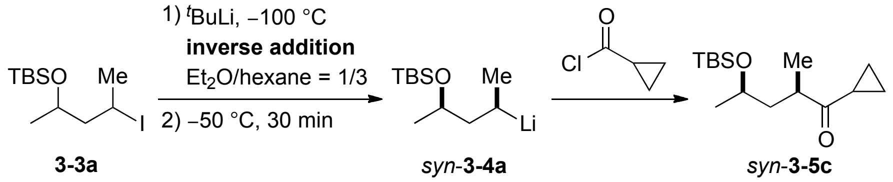
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: <u>*syn*-3-5b:</u> 9.61 (d, *J* = 2.0 Hz, 1H), 3.92 (dqd, *J* = 7.5, 6.0 and 4.2 Hz, 1H), 2.52 (dqdd, *J* = 8.6, 7.0, 4.8 and 1.9 Hz, 1H), 1.83 (ddd, *J* = 14.0, 8.5 and 4.2 Hz, 1H), 1.51 (ddd, *J* = 14.0, 7.6 and 4.7 Hz, 1H), 1.14 (d, *J* = 6.1 Hz, 3H), 1.09 (d, *J* = 7.1 Hz, 3H), 0.86 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H). **<u>*anti*-3-5b:</u>** 9.61 (d, *J* = 2.0 Hz, 1H), 3.96-3.83 (m, 1H), 2.57-2.45 (m, 1H), 1.92 (ddd, *J* = 13.9, 8.9 and 5.5 Hz, 1H), 1.28 (ddd, *J* = 13.9, 8.0 and 3.7 Hz, 1H), 1.16 (d, *J* = 5.8 Hz, 3H), 1.07 (d, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: <u>*syn*-3-5b:</u> 205.0, 66.4, 42.9, 41.0, 26.0, 24.0, 18.2, 14.4, –4.2, –4.6. **<u>*anti*-3-5b:</u>** 205.3, 66.2, 43.6, 40.5, 26.0, 24.5, 18.2, 13.6, –4.0, –4.7.

MS (70 eV, EI) *m/z* (%): 229 (1) $[M–H]^{+•}$, 215 (5), 173 (100), 155 (23), 129 (61), 115 (13), 103 (16), 87 (5), 81 (8), 75 (99), 59 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 2930 (w), 2858 (w), 1728 (m), 1472 (w), 1463 (w), 1375 (w), 1362 (w), 1255 (w), 1140 (w), 1109 (w), 1056 (m), 1006 (w), 989 (w), 940 (w), 900 (w), 875 (w), 834 (s), 806 (m), 773 (vs), 717 (w), 661 (w).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{25}OSi^{+•}$** $[M–H]^{+•}$: 229.1624, found: 229.1624.



syn-**3-5c**

According to general procedure, diastereomeric mixture of **3-3a** (99 mg, 0.30 mmol, d.r. = 50:50) as a starting material and cyclopropanecarbonyl chloride (49 μL, 0.54 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/33 to afford *syn*-**3-5c** (54 mg, 67% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by the analogy of NMR spectra with *syn*-**3-5a** and *syn*-**3-5d**, and by assuming the reaction with acid chloride proceeds with retention of the configuration from the previous literature.[47]

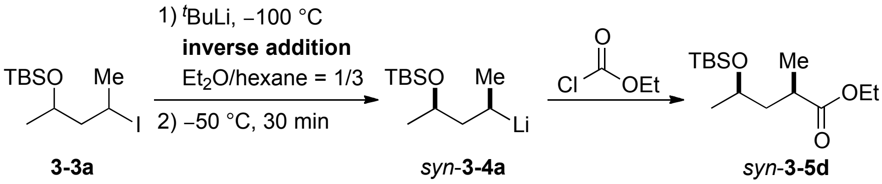
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 3.76 (dqd, *J* = 8.4, 6.1 and 4.3 Hz, 1H), 2.89 (dqd, *J* = 8.8, 7.2 and 4.7 Hz, 1H), 1.95 (tt, *J* = 7.9 and 4.6 Hz, 1H), 1.87 (ddd, *J* = 13.5, 8.9 and 4.2 Hz, 1H), 1.33 (ddd, *J* = 13.6, 8.4 and 4.7 Hz, 1H), 1.14 (d, *J* = 7.3 Hz, 3H), 1.12 (d, *J* = 6.1 Hz, 3H), 0.99 (dd, *J* = 9.1 and 4.2 Hz, 1H), 0.87 (s, 9H), 0.83 (dd, *J* = 7.7 and 4.1 Hz, 1H), 0.02 (s, 3H), 0.01 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 214.0, 66.6, 43.6, 42.2, 25.6, 24.0, 19.2, 17.8, 17.5, 10.8, 10.5, –4.5, –5.1.

MS (70 eV, EI) *m/z* (%): 255 (5) [M–Me]$^{+\bullet}$, 213 (100), 195 (4), 173 (7), 159 (11), 145 (9), 127 (5), 119 (11), 103 (5), 93 (14), 75 (59), 59 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2929 (w), 2856 (w), 1698 (w), 1472 (w), 1462 (w), 1378 (w), 1361 (w), 1254 (w), 1147 (w), 1111 (w), 1082 (w), 1046 (m), 1010 (w), 972 (w), 939 (w), 892 (w), 864 (w), 834 (s), 806 (w), 772 (w), 757 (w).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{27}O_2Si^{+\bullet}$** [M–Me]$^{+\bullet}$: 255.1780, found: 255.1784.



syn-**3-5d**

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (17.0 mL) and Et$_2$O (4.0 mL) and cooled to –100 °C. ^{t}BuLi (5.0 mL, 1.5 M in *n*-pentane, 7.5 mmol) was added to the reaction mixture. Then, a solution of diastereomeric mixture of **3-3a** (0.98 g, 0.30 mmol, d.r. = 50:50) in *n*-hexane (4.0 mL) and Et$_2$O (3.0 mL) was added dropwise in 20 min. After stirring at –100 °C for 10 min, the reaction mixture was warmed up to –50 °C and stirred for 30 min. ClCO$_2$Et (0.52 mL, 5.4 mmol) was adeded to the reaction mixture and it was stirred at –50 °C for 30 min. The reaction was quenched with saturated NH$_4$Cl aqueous solution and the mixture was extracted with Et$_2$O three times. The combined organic solution was dried over MgSO$_4$. Solvents were evaporated and the crude product was purified by column chromatography with Et$_2$O/*i*-hexane = 1/20 to afford *syn*-**3-5d** (0.57 g, 70% yield, d.r. = 97:3) as colorless oil. The relative configuration was determined by the further transformation to *trans*-**3-17**, which is written below, and its comparison with the literature value.

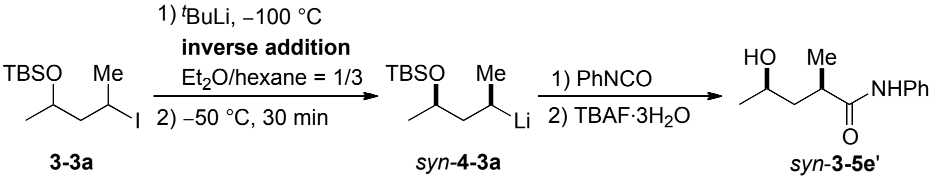
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.11 (q, *J* = 6.9 Hz, 2H), 3.80 (dqd, *J* = 8.0, 6.2 and 3.7 Hz, 1H), 2.63 (dqd, *J* = 9.9, 7.2 and 4.3 Hz, 1H), 1.78 (ddd, *J* = 13.6, 9.9 and 3.7 Hz, 1H), 1.40 (ddd, *J* = 13.6, 8.9 and 4.3 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.14 (d, *J* = 7.2 Hz, 3H), 1.10 (d, *J* = 6.1 Hz, 3H), 0.87 (s, 9H), 0.022 (s, 3H), 0.018 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 177.1, 66.9, 60.2, 43.9, 36.3, 26.0, 24.4, 18.7, 18.2, 14.4, –4.1, –4.8.

MS (70 eV, EI) *m/z* (%): 259 (4) $[M–Me]^{+•}$, 229 (22), 217 (100), 189 (8), 171 (72), 159 (13), 143 (5), 127 (14), 115 (12), 103 (25), 87 (5), 75 (84), 59 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 2929 (w), 2857 (w), 1733 (m), 1472 (w), 1463 (w), 1372 (w), 1347 (w), 1252 (w), 1178 (m), 1150 (m), 1132 (m), 1093 (m), 1052 (m), 1030 (w), 1006 (w), 975 (w), 950 (w), 898 (w), 834 (s), 806 (m), 773 (vs), 718 (w), 661 (w).

HRMS (EI) *m/z*: calcd for **$C_{13}H_{27}O_3Si^{+•}$** $[M–Me]^{+•}$: 259.1729, found: 259.1738.



syn-**3-5e'**

According to general procedure, diastereomeric mixture of **3-3a** (99 mg, 0.30 mmol, d.r. = 50:50) as a starting material and PhNCO (76 µL, 0.60 mmol) as an electrophile were used. Before deprotection d.r. is equal to 96:4 from GC analysis. After work up written in general procedure, the crude product was placed in *Schlenk*-flask and it was solved in THF (10 mL). TBAF·3H_2O (0.79 g, 0.75 mmol) was added to the reaction mixture and it was stirred at room temperature for 1 h. The reaction was quenched aqueous HCl solution (0.25 M) and the mixture was extracted with Et_2O three times. The organic phase was washed with saturated aqueous $NaHCO_3$ solution and dried over $MgSO_4$. Solvents were evaporated and the crude product was purified by column chromatography with Et_2O/*i*-hexane = 4:1→1:0 to afford *syn*-**3-5e'** (43 mg, 69% yield, d.r. = 99:1) as colorless oil.

The relative configuration was determined by the analogy of NMR spectra with *syn*-**3-5b** and *syn*-**3-5d**. Our previous paper shows the retentive quenching of unstabilized secondary lithium reagents with phenyl isocyanate.[30]

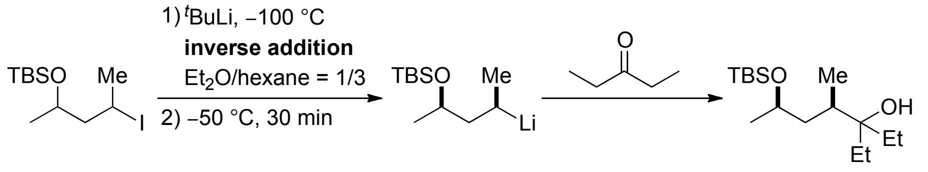
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 8.15 (s br, 1H), 7.50 (d, J = 7.8 Hz, 2H), 7.27 (d, J = 7.8 Hz, 2H), 7.07 (d, J = 7.4 Hz, 1H), 3.80 (dqd, J = 9.1, 6.2 and 3.7 Hz, 1H), 2.90 (s br, 1H), 2.72 (dqd, J = 10.6, 6.9 and 3.8 Hz, 1H), 1.82 (ddd, J = 13.7, 10.7 and 2.8 Hz, 1H), 1.51 (ddd, J = 14.0, 10.1 and 3.7 Hz, 1H), 1.21 (d, J = 6.9 Hz, 3H), 1.18 (d, J = 6.2 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 175.5, 138.0, 129.0, 124.4, 120.2, 65.7, 43.5, 38.7, 24.2, 18.3.

MS (70 eV, EI) *m/z* (%): 99 (12), 93 (100), 70 (39), 55 (61).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3293 (w br), 2966 (w), 2930 (w), 1661 (m), 1599 (s), 1538 (s), 1499 (m), 1491 (m), 1440 (s), 1373 (w), 1307 (m), 1249 (m), 1177 (w), 1147 (w), 1118 (w), 1090 (m), 1039 (w), 1009 (w), 962 (w), 931 (w), 895 (w), 835 (w), 725 (vs), 691 (s).

HRMS (ESI) *m/z*: calcd for $C_{12}H_{16}O_2N^-$ [M–H]$^-$: 206.1181, found: 206.1186.



3-3a *syn*-**3-4a** *syn*-**3-5f**

syn-**3-5f**

According to general procedure, diastereomeric mixture of **3-3a** (99 mg, 0.30 mmol, d.r. = 50:50) as a starting material and 3-pentenone (63 μL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/19 to afford *syn*-**3-5f** (79 mg, 55% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by the analogy of NMR spectra with *syn*-**3-5b** and *syn*-**3-5d**, and by assuming the reaction with ketone proceeds with retention of the configuration from the previous literature.[48]

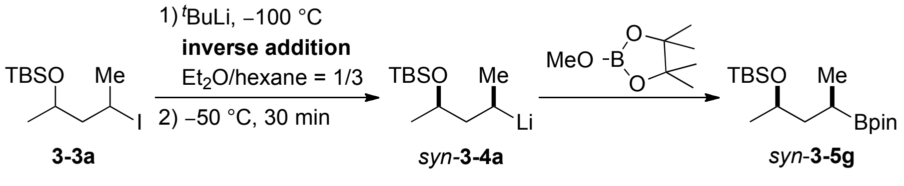
^{1}H-NMR (600 MHz, CDCl$_3$) δ: 3.98-3.84 (m, 1H), 1.77-1.17 (m, 7H), 1.15 (d, J = 6.1 Hz, 3H), 0.94-0.81 (m, 18H), 0.06 (s, 6H).

^{13}C-NMR (150 MHz, CDCl$_3$) δ: 75.6, 68.3, 41.0, 35.7, 28.11, 27.6, 25.9, 22.8, 18.1, 15.6, 7.5, 7.3, –4.6, –4.7.

MS (70 eV, EI) *m/z* (%): 231 (2) [M+H]$^{+\bullet}$, 213 (11), 159 (19), 139 (14), 127 (51), 119 (62), 97 (77), 75 (94), 69 (88), 57 (69).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2962 (s), 1928 (s), 1857 (m), 1462 (m), 1377 (m), 1254 (s), 1126 (m), 1083 (m), 1041 (m), 984 (m), 907 (m), 835 (s), 807 (m), 835 (s), 773 (s), 734 (s).

HRMS (ESI) *m/z*: calcd for $C_{16}H_{37}O_2Si^+$ [M+H]$^+$: 289.2563, found: 289.2557.

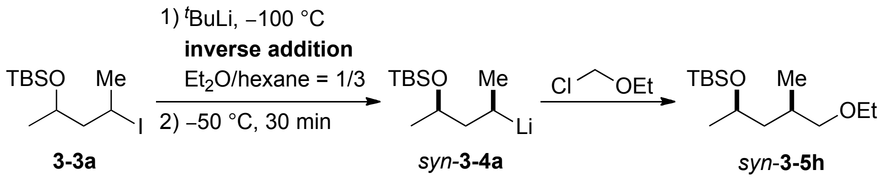


3-3a *syn*-**3-4a** *syn*-**3-5g**

syn-**3-5g**

According to general procedure, diastereomeric mixture of **3-3a** (99 mg, 0.30 mmol, d.r. = 50:50) as a starting material and MeOBpin (93 µL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/50 to afford *syn*-**3-5g** (72 mg, 73% yield, d.r. = 97:3) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*- and *anti*-*syn*-**3-5a**, and by assuming the reaction with boronic acid pinacol ester proceeds with retention of the configuration from the previous literature.[49]

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.82 (dqd, J = 7.3, 6.2 and 6.0 Hz, 1H), 1.53 (ddd, J = 13.5, 8.6 and 5.6 Hz, 1H), 1.37 (dq, J = 13.3 and 6.2 Hz, 1H), 1.22 (s, 12H), 1.15-1.05 (m, 1H), 1.10 (d, J = 6.0 Hz, 1H), 0.95 (d, J = 7.3 Hz, 3H), 0.87 (s, 9H), 0.038 (s, 3H), 0.034 (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 82.9, 68.5, 43.5, 26.1, 25.0, 24.8, 24.2, 18.3, 16.3, –4.2, –4.5.
^{11}B-NMR (128 MHz, $CDCl_3$) δ: 34.4.
MS (70 eV, EI) *m/z* (%): 327 (1) $[M]^{+\bullet}$, 271 (12), 243 (5), 213 (7), 171 (100), 153 (17), 143 (12), 129 (18), 117 (6), 101 (13), 83 (14), 73 (23), 59 (5).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2928 (w), 2856 (w), 1462 (w), 1406 (w), 1386 (w), 1379 (m), 1370 (m), 1316 (w), 1251 (w), 1214 (w), 1191 (w), 1142 (s), 1126 (w), 1058 (m), 1005 (w), 968 (w), 938 (w), 882 (w), 860 (w), 834 (s), 772 (vs), 722 (w), 686 (w), 670 (w).
HRMS (EI) *m/z*: calcd for **$C_{13}H_{28}O_3BSi^{+\bullet}$** $[M–Bu]^{+\bullet}$: 271.1901, found: 271.1835.

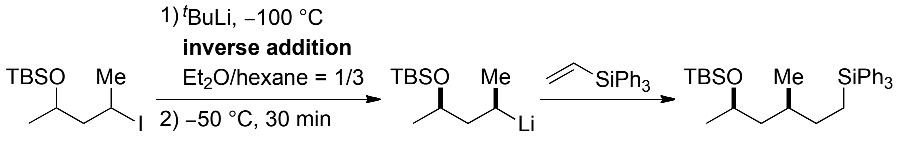


syn-**3-5h**

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (22.7 mL) and Et_2O (5.3 mL) and cooled to –100 °C. ^{t}BuLi (5.5 mL, 1.8 M in *n*-pentane, 10.0 mmol) was added to the reaction mixture. Then, a solution of diastereomeric mixture of **3-3a** (1.31 g, 4.0 mmol, d.r. = 50:50) in *n*-hexane (5.3 mL) and Et_2O (4.0 mL) was added dropwise in 20 min. After stirring at –100 °C for 10 min, the reaction mixture was warmed up to –50 °C and stirred for 30 min. Then $ClCH_2OEt$ (0.67 mL, 7.2 mmol) was added to the reaction mixture and it was stirred at –50 °C for 50 min. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with Et_2O three times. The combined organic solution was dried over

$MgSO_4$. Solvents were evaporated and the crude product was purified by column chromatography with Et_2O/*i*-hexane = 1/40 to afford *syn*-**3-5h** (0.62 g, 60% yield, d.r. = 99:1) as colorless oil. The relative configuration was determined by the transformation of its similar compound *syn*-**3-S31**.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.90 (h, J = 6.3 Hz, 1H), 3.45 (dq, J = 7.1 and 0.9 Hz, 2H), 3.29 (dd, J = 9.3 and 5.5 Hz, 1H), 3.15 (dd, J = 9.2 and 7.2 Hz, 1H), 1.81 (dq, J = 13.2 and 6.6 Hz, 1H), 1.44 (dt, J = 13.6 and 6.6 Hz, 1H), 1.29 (dt, J = 13.9 and 7.1 Hz, 1H), 1.18 (t, J = 7.0 Hz, 3H), 1.12 (d, J = 6.0 Hz, 1H), 0.92 (d, J = 6.7 Hz, 1H), 0.89 (s, 9H), 0.05 (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 76.3, 67.1, 66.4, 44.0, 30.6, 26.1, 23.4, 18.3, 18.0, 15.3, –4.2, –4.6.
MS (70 eV, EI) *m/z* (%): 259 (1) $[M–H]^{+\bullet}$, 203 (3), 159 (11), 147 (82), 129 (4), 115 (5), 103 (100), 83 (11), 75 (23), 55 (9).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2928 (w), 2856 (w), 1472 (w), 1462 (w), 1378 (w), 1360 (w), 1254 (w), 1116 (m), 1069 (m), 1037 (w), 1005 (w), 991 (w), 958 (w), 896 (w), 834 (s), 806 (m), 772 (s), 719 (w), 662 (w).
HRMS (EI) *m/z*: calcd for **$C_{10}H_{23}O_2Si^{+\bullet}$** $[M–Bu]^{+\bullet}$: 203,1467, found: 203,1407.



3-3a *syn*-**3-4a** *syn*-**3-5i**

syn-**3-5i**

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (28.3 mL) and Et_2O (6.7 mL) and cooled to –100 °C. ^{t}BuLi (6.8 mL, 1.8 M in *n*-pentane, 12.5 mmol) was added to the reaction mixture. Then, a solution of diastereomeric mixture of **3-3a** (1.6 g, 5.0 mmol, d.r. = 50:50) in *n*hexane (6.7 mL) and Et_2O (5.0 mL) was added dropwise in 30 min. After stirring at –100 °C for 10 min, the reaction mixture was warmed up to –50 °C and stirred for 30 min. Triphenylvinylsilane (2.6 g, 9.0 mmol) dissolved in Et_2O (10.0 mL) was added to the reaction mixture and it was stirred at –50 °C for 1 h. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with Et_2O three times. The combined organic solution was dried over $MgSO_4$. Solvents were evaporated and the crude product was purified by column chromatography with Et_2O/*i*-hexane = 1/100 to afford *syn*-**3-5i** (1.6 g, 65% yield, d.r. = 99:1) as colorless oil. The relative configuration was determined by the further transformation to *syn*-**3-S33**.

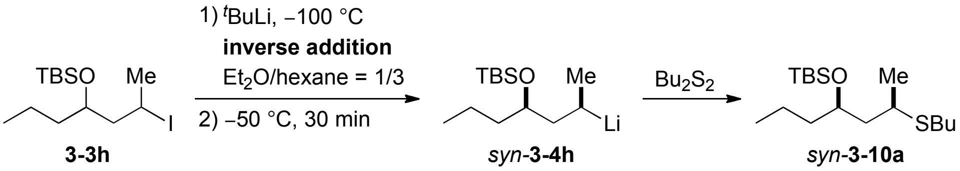
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.61-7.54 (m, 6H), 7.49-7.36 (m, 9H), 3.84 (qt, *J* = 6.4 and 6.0 Hz, 1H), 1.70-1.28 (m, 5H), 1.13 (d, *J* = 6.0 Hz, 1H), 0.95 (dt, *J* = 6.4 Hz, 1H), 0.92 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 135.8, 135.4, 129.5, 128.0, 66.9, 46.8, 32.5, 30.8, 26.1, 24.0, 19.8, 18.3, 10.0, –4.2, –4.6.

MS (70 eV, EI) *m/z* (%): 487 (1) $[M–H]^{+\bullet}$, 333 (61), 259 (100), 197 (5), 181 (8), 157 (5), 75 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2925 (w), 2853 (w), 1476 (w), 1427 (w), 1375 (w), 1255 (w), 1150 (w), 1127 (w), 1110 (m), 1074 (w), 1028 (w), 997 (w), 985 (w), 956 (w), 884 (w), 834 (m), 805 (w), 772 (m), 754 (w), 732 (m), 714 (w), 697 (vs), 666 (m).

HRMS (EI) *m/z*: calcd for **$C_{31}H_{44}OSi_2^{+\bullet}$** $[M]^{+\bullet}$: 488.2931, found: 488.2928.



***syn*-3-10a**

According to general procedure, diastereomeric mixture of **3-3h** (128 mg, 0.36 mmol, d.r. = 66:34) as a starting material and Bu$_2$S$_2$ (137 µL, 0.72 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/99 to afford *syn*-**3-10a** (67 mg, 58% yield, d.r. = 94:6) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*- and *anti*-**3-5a**, and by assuming the reaction sequence proceeds with retention of the configuration from *syn*-**3-5a** and other reactions with disulfide.

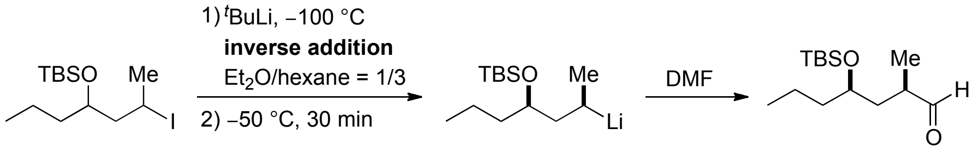
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 3.90 (ddt, *J* = 6.9, 5.6 and 5.5 Hz, 1H), 2.84 (qt, *J* = 7.1 and 6.6 Hz, 1H), 2.53-2.46 (m, 2H), 1.60-1.52 (m, 4H), 1.45-1.38 (m, 4H), 1.37-1.31 (m, 2H), 1.29 (d, J = 6.8 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.1 Hz, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 69.9, 44.5, 40.0, 36.8, 32.0, 29.4, 26.0, 22.6, 22.2, 18.1, 14.3, 13.7, –4.2, –4.4.

MS (70 eV, EI) *m/z* (%): 317 (6) $[M–H]^{+•}$, 303 (17), 261 (9), 203 (21), 229 (41), 188 (100), 131 (28).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2928 (w), 2857 (w), 1455 (w), 1256 (m), 1056 (m), 1005 (m), 834 (s), 806 (m), 773 (s), 746 (m), 697 (s).

HRMS (EI) *m/z*: calcd for **$C_{13}H_{29}OSSi^{+•}$** $[M–tBu]^{+•}$: 261.1708, found: 261.1703.



3-3h *syn*-**3-4h** *syn*-**3-10b**

syn-**3-10b**

According to general procedure, diastereomeric mixture of **3-3h** (107 mg, 0.30 mmol, d.r. = 66:34) as a starting material and DMF (58 μL, 0.75 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *syn*-**3-10b** (47 mg, 61% yield, d.r. = 91:9) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*- and *anti*-**5b**, and by assuming the reaction with DMF with retention of the configuration from *syn*-**3-5b**.

The peaks of the major diastereomer are given.

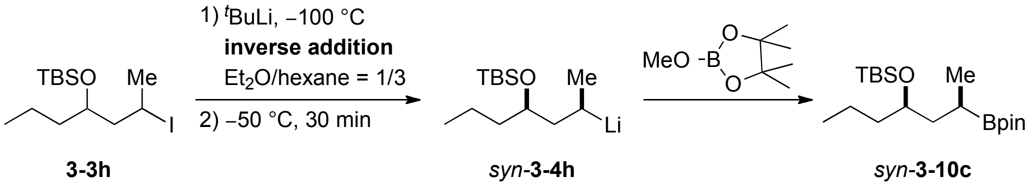
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 9.61 (d, *J* = 2.2 Hz, 1H), 3.77 (dtd, *J* = 6.6, 6.1 and 4.5 Hz, 1H), 2.52 (dtdd, *J* = 8.6, 7.2, 4.9 and 2.2 Hz, 1H), 1.89 (ddd, *J* = 14.2, 8.4 and 4.5 Hz, 1H), 1.51-1.41 (m, 3H), 1.36-1.28 (m, 2H), 1.09 (d, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 204.9, 70.0, 42.6, 39.4, 38.2, 25.9, 18.4, 18.0, 14.5, 14.2, 1.0, –4.4, –4.5.

MS (70 eV, EI) *m/z* (%): 215 (23), 201 (100) $[M–{}^tBu]^{+•}$, 187 (18), 145 (25), 129 (65), 109 (17), 75 (89).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2930 (w), 2856 (w), 1728 (m), 1254 (m), 1134 (w), 1115 (w), 1098 (m), 1006 (m), 832 (s), 810 (m), 774 (s).

HRMS (EI) *m/z*: calcd for **$C_{10}H_{21}O_2SSi^{+•}$** $[M–{}^tBu]^{+•}$: 201.1311, found: 201.1326.



syn-**3-10c**

According to general procedure, diastereomeric mixture of **3-3h** (107 mg, 0.30 mmol, d.r. = 66:34) as a starting material and MeOBpin (99 µL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/50 to afford *syn*-**3-10c** (45 mg, 65% yield, d.r. = 97:3) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*-**3-5g** and by assuming the reaction with boronic acid pinacol ester proceeds with retention of the configuration from the previous literature.[49].

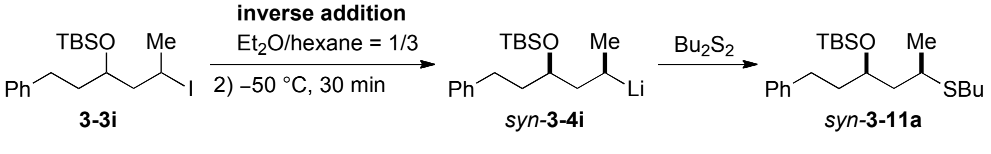
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.71-3.63 (m, 1H), 1.65-1.56 (m, 1H), 1.44-1.27 (m, 5H), 1.22 (s, 12H), 1.16-1.07 (m, 1H), 0.96 (d, J = 7.3 Hz, 3H), 0.91-0.88 (m, 12H), 0.05 (s, 3H), 0.03 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 82.9, 72.2, 41.1, 40.0, 26.2, 25.0, 24.9, 18.5, 18.3, 16.4, 14.4, –4.1.

MS (70 eV, EI) *m/z* (%): 313 (12), 299 (31), 241 (15), 199 (91), 187 (54), 171 (15), 157 (99), 143 (92), 131 (25), 117 (100), 101 (36), 73 (90).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2977 (w), 2952 (w), 2928 (m), 2855 (w), 1744 (w), 1461 (w), 1380 (m), 1370 (m), 1316 (m), 1253 (m), 1215 (w), 1097 (w), 1060 (m), 834 (s), 774 (s), 747 (w), 698 (m).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{32}BO_3Si^{+\bullet}$** $[M{-}^t Bu]^{+\bullet}$: 299.2214, found: 299.2237.



syn-**3-11a**

According to general procedure, diastereomeric mixture of **3-3i** (126 mg, 0.30 mmol, d.r. = 62:38) as a starting material and Bu_2S_2 (114 µL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/99 to afford *syn*-**3-11a** (71 mg, 62% yield, d.r. = 93:7) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*- and *anti*-**5a** and by assuming the reaction sequence proceeds with retention of the configuration from *syn*-**3-5a** and other reactions with disulfide.

The peaks of the major diastereomer are given.

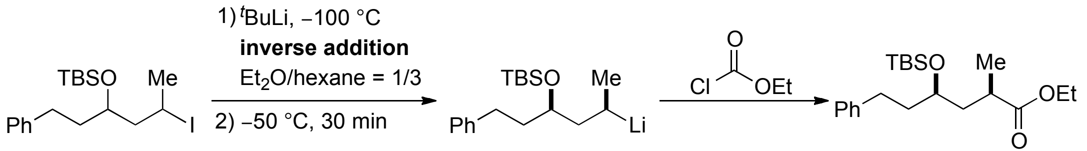
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.30-7.25 (m, 2H), 7.19-7.16 (m, 3H), 4.02-3.96 (m, 1H), 2.89-2.81 (m, 1H), 2.64 (t, J = 8.4 Hz, 2H), 2.50 (td, J = 7.5 Hz and 2.2 Hz, 2H), 1.80-1.72 (m, 2H), 1.67-1.63 (m, 2H), 1.58-1.52 (m, 2H), 1.46-1.36 (m, 2H), 1.31 (d, J = 6.8 Hz, 3H), 0.94-0.90 (m, 12H), 0.086 (s, 3H), 0.084 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 142.6, 128.33, 128.31, 125.7, 69.6, 44.4, 39.6, 36.8, 31.9, 31.2, 29.5, 25.9, 22.5, 22.2, 18.1, 13.7, –4.2, –4.4.

MS (70 eV, EI) *m/z* (%): 323 (100) $[\mathrm{M}-{}^t\mathrm{Bu}]^{+\bullet}$, 249 (5), 233 (8), 191 (21), 147 (17), 117 (21), 91 (24), 75 (28).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2928 (w), 2857 (w), 1455 (w), 1256 (m), 1056 (m), 1005 (m), 834 (s), 806 (m), 773 (s), 746 (m), 697 (s).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{18}H_{31}OSSi^{+\bullet}}$ $[\mathrm{M}-{}^t\mathrm{Bu}]^{+\bullet}$: 323.1865, found: 323.1851.



3-3i *syn*-**3-4i** *syn*-**3-11b**

syn-**3-11b**

According to general procedure, diastereomeric mixture of **3-3i** (126 mg, 0.30 mmol, d.r. = 62:38) as a starting material and ClCO$_2$Et (72 µL, 0.75 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/20 to afford *syn*-**3-11b** (70 mg, 64% yield, d.r. = 93:7) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*-**5d**, and by assuming the reaction sequence proceeds with retention of the configuration from *syn*-**5d** and other reactions with chloroformate.

The peaks of the major diastereomer are given.

^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.30-7.26 (m, 2H), 7.19-7.16 (m, 3H), 4.13 (qd, J = 7.1 Hz and 0.9 Hz, 2H), 3.75 (dtd, J = 8.7, 5.4 and 3.4 Hz, 1H), 2.68-2.60 (m, 3H), 1.95 (ddd, J =

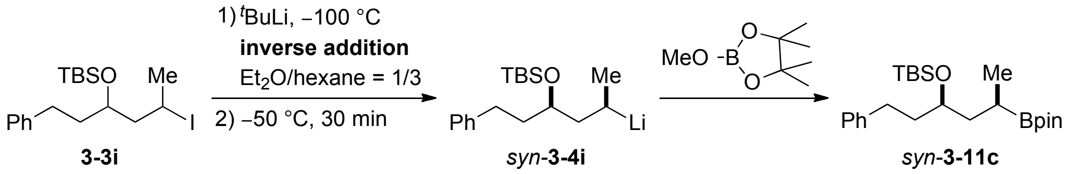
13.8, 9.5 and 3.9 Hz, 1H), 1.80-1.74 (m, 2H), 1.49 (ddd, *J* = 13.7, 8.4 and 4.5 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.19 (d, *J* = 7.1Hz, 3H), 0.91 (s, 9H), 0.040 (s, 3H), 0.035 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 176.8, 142.5, 128.32, 128.31, 125.7, 70.1, 60.2, 40.9, 39.6, 36.1, 31.1, 25.9, 18.6, 18.1, 14.2, –4.3, –4.7.

MS (70 eV, EI) *m/z* (%): 349 (3) $[M–Me]^{+•}$, 319 (13), 307 (100), 261 (54), 169 (9), 117 (14), 91 (28), 75 (19).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 2930 (w), 1738 (m), 1376 (w), 1300 (w), 1253 (m), 1190 (m), 1138 (w), 1081 (s), 1034 (w), 1001 (m), 940 (w), 829 (s), 810 (m), 774 (s), 658 (w).

HRMS (EI) *m/z*: calcd for $C_{17}H_{21}O_3Si^{+•}$ $[M–{}^tBu]^{+•}$: 307.1729, found: 307.1736.



***syn*-3-11c**

According to general procedure, diastereomeric mixture of **3-3i** (126 mg, 0.30 mmol, d.r. = 62:38) as a starting material and MeOBpin (99 μL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/50 to afford *syn*-**3-11c** (87 mg, 69% yield, d.r. = 97:3) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*-**3-5g**, and by assuming the reaction with boronic acid pinacol ester proceeds with retention of the configuration from the previous literature.[49].

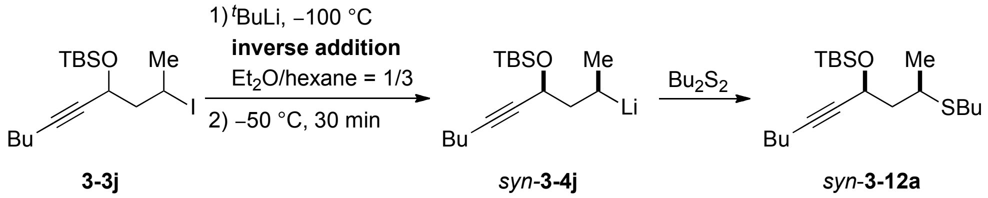
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.29-7.25 (m, 2H), 7.20-7.14 (m, 3H), 3.75 (dtd, *J* = 6.5, 5.9 and 4.9 Hz, 1H), 2.70 (ddd, *J* = 14.2, 11.0 and 6.5 Hz, 1H), 2.62 (ddd, *J* = 13.7, 11.1 and 5.8 Hz, 1H), 1.83-1.66 (m, 3H), 1.41 (dt, *J* = 13.6 and 6.8 Hz, 1H), 1.21 (s, 12H), 1.15 (qt, *J* = 7.6 and 7.1 Hz, 1H), 0.99 (d, *J* = 7.4 Hz, 3H), 0.91 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 143.0, 128.4, 128.2, 125.5, 82.8, 71.7, 40.7, 39.5, 31.5, 26.0, 24.8, 24.7, 18.2, 16.2, –4.27, –4.30.

MS (70 eV, EI) *m/z* (%): 313 (12), 299 (31), 241 (15), 199 (91), 187 (54), 171 (15), 157 (99), 143 (92), 131 (25), 117 (100), 101 (36), 73 (90).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2977 (w), 2952 (w), 2928 (m), 2855 (w), 1744 (w), 1461 (w), 1380 (m), 1370 (m), 1316 (m), 1253 (m), 1215 (w), 1097 (w), 1060 (m), 834 (s), 774 (s), 747 (w), 698 (m).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{15}H_{32}BO_3Si^{+\bullet}}$ [M–^{t}Bu]$^{+\bullet}$: 299.2214, found: 299.2237.



syn-**3-12a**

According to general procedure, diastereomeric mixture of **3-3j** (118 mg, 0.30 mmol, d.r. = 50:50) as a starting material and Bu_2S_2 (103 µL, 0.54 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/170 to afford *syn*-**3-12a** (62 mg, 58% yield, d.r. = 90:10) as colorless oil. The relative configuration was determined by S_N2 reactions of *syn*- and *anti*-**3-3j** with NaSBu.

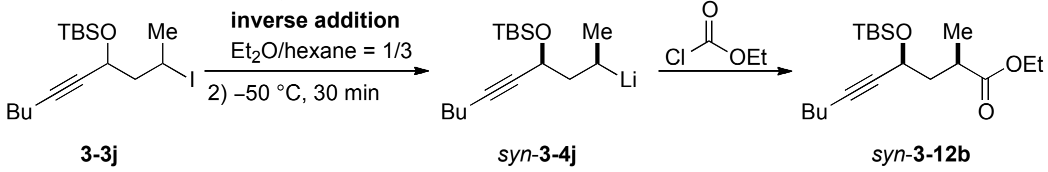
^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: ***syn*-3-12a:** 4.57 (ddt, *J* = 7.9, 5.9 and 2.0 Hz, 1H), 2.91 (tq, *J* = 7.5 and 6.8 Hz, 1H), 2.50 (td, *J* = 7.2 and 3.1 Hz, 2H), 2.18 (tq, *J* = 6.9 and 2.0 Hz, 2H), 1.80 (ddd, *J* = 7.7, 6.0 and 2.4 Hz, 1H), 1.62-1.33 (m, 8H), 1.29 (d, *J* = 6.8 Hz, 1H), 0.94-0.87 (m, 6H), 0.90 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H). ***anti*-3-12a:** 4.57-4.49 (m, 1H), 2.98-2.88(m, 1H), 2.58-2.42 (m, 2H), 2.22-2.14 (m, 2H), 2.00-1.85 (m, 1H), 1.80-1.67 (m, 1H), 1.62-1.33 (m, 8H), 1.28 (d, *J* = 6.8 Hz, 1H), 0.94-0.87 (m, 6H), 0.90 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: ***syn*-3-12a:** 85.0, 81.7, 61.1, 46.4, 36.4, 32.2, 30.8, 29.7, 26.0, 22.4, 22.2, 22.1, 18.5, 18.4, 13.9, 13.7, –4.2, –4.8. ***anti*-3-12a:** 85.2, 81.5, 61.1, 46.4, 36.4, 32.1, 30.9, 30.1, 26.0, 22.4, 22.3, 22.1, 18.5, 18.4, 13.9, 13.7, –4.3, –4.9.

MS (70 eV, EI) *m/z* (%): 356 (5) [M]$^{+\bullet}$, 299 (100), 257 (14), 224 (12), 201 (15), 168 (14), 139 (12), 117 (7), 91 (8), 75 (36).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2928 (w), 2857 (w), 1463 (w), 1378 (w), 1361 (w), 1249 (w), 1144 (w), 1098 (w), 1040 (w), 1005 (w), 975 (w), 933 (w), 902 (w), 834 (s), 810 (m), 775 (vs), 738 (w), 666 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{20}H_{40}OSSi^{+\bullet}}$ [M]$^{+\bullet}$: 356.2569, found: 356.2574.



syn-**3-12b**

According to general procedure, diastereomeric mixture of **3-3i** (118 mg, 0.30 mmol, d.r. = 50:50) as a starting material and $ClCO_2Et$ (57 µL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/40 to afford *syn*-**3-12b** (58 mg, 57% yield, d.r. = 98:2) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*-**3-5d**, and by assuming the reaction sequence proceeds with retention of the configuration from *syn*-**3-5d** and other reactions with chloroformate.

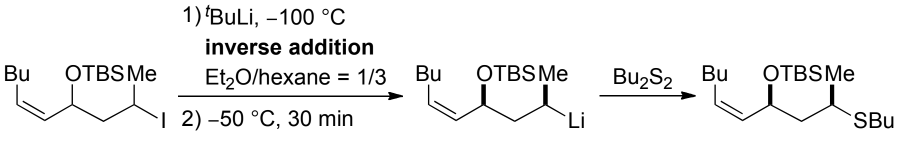
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.37 (ddt, J = 8.6, 4.9 and 1.9 Hz, 1H), 4.11 (qd, J = 7.1 and 1.2 Hz, 2H), 2.70 (dqd, J = 8.7, 7.1 and 5.2 Hz, 1H), 2.17 (td, J = 6.9 and 1.9 Hz, 2H), 2.05 (ddd, J = 13.8, 8.9 and 5.0 Hz, 1H), 1.69 (ddd, J = 13.6, 8.4 and 5.1 Hz, 1H), 1.63-1.32 (m, 4H), 1.25 (td, J = 7.0 and 0.9 Hz, 3H), 1.17 (d, J = 7.2 Hz, 1H), 0.94-0.85 (m, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.08 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 176.6, 85.0, 81.5, 61.5, 60.3, 42.8, 36.0, 30.8, 26.0, 22.1, 18.3, 18.4, 18.1, 14.4, 13.7, –4.4, –5.0.

MS (70 eV, EI) *m/z* (%): 339 (1) $[M–H]^{+\bullet}$, 325 (3), 295 (12), 283 (100), 237 (12), 225 (7), 209 (4), 173 (12), 139 (5), 75 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 2857 (w), 1732 (s), 1463 (w), 1378 (w), 1361 (w), 1343 (w), 1249 (w), 1228 (w), 1177 (m), 1146 (m), 1098 (m), 1053 (m), 1005 (w), 986 (w), 939 (w), 913 (w), 835 (s), 811 (m), 667 (w).

HRMS (EI) *m/z*: calcd for **$C_{18}H_{33}O_3Si^{+\bullet}$** $[M–Me]^{+\bullet}$: 325.2199, found: 325.2218.



3-3k *syn*-**3-4k** *syn*-**3-13a**

syn-**3-13a**

According to general procedure, diastereomeric mixture of **3-3k** (119 mg, 0.30 mmol, d.r. = 50:50) as a starting material and Bu_2S_2 (103 µL, 0.54 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/250 to afford *syn*-**3-13a** (72 mg, 67% yield, d.r. = 95:5) as colorless oil. The relative configuration was determined by S_N2 reactions of *syn*- and *anti*-**3-3k** with NaSBu.

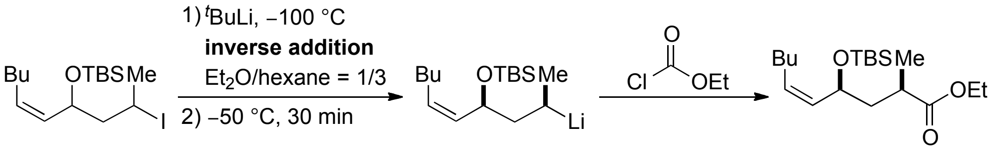
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 5.37-5.24 (m, 2H), 4.70 (dddd, *J* = 9.0, 6.0, 4.0 and 1.6 Hz, 1H), 2.86 (dqd, *J* = 9.2, 6.8 and 5.1 Hz, 1H), 2.50 (t, *J* = 7.4 Hz, 2H), 2.10-1.97 (m, 2H), 1.66 (ddd, *J* = 13.9, 8.9 and 4.9 Hz, 1H), 1.60-1.25 (m, 9H), 1.29 (d, *J* = 6.8 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 6H), 0.88 (s, 9H), 0.07 (s, 3H), 0.04 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 134.0, 129.5, 66.8, 45.9, 36.7, 32.2, 32.0, 29.5, 27.7, 26.1, 22.8, 22.6, 22.4, 18.3, 14.2, 13.9, –4.0, –4.6.

MS (70 eV, EI) *m/z* (%): 358 (1) $[M]^{+\bullet}$, 301 (100), 259 (10), 239 (5), 227 (10), 211 (50), 169 (20), 147 (14), 131 (5), 117 (13), 91 (5), 75 (25), 57 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2926 (m), 2856 (w), 1471 (w), 1462 (w), 1378 (w), 1360 (w), 1251 (w), 1092 (m), 1047 (m), 1005 (w), 918 (w), 834 (s), 826 (s), 809 (m), 774 (vs), 729 (w), 667 (w).

HRMS (EI) *m/z*: calcd for **$C_{16}H_{33}OSSi^{+\bullet}$** $[M–Bu]^{+\bullet}$: 301.2021, found: 301.1934.



3-3k *syn*-**3-4k** *syn*-**3-13b**

syn-**3-13b**

According to general procedure, diastereomeric mixture of **3-3k** (119 mg, 0.30 mmol, d.r. = 50:50) as a starting material and ClCO$_2$Et (57 μL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/40 to afford *syn*-**3-13b** (79 mg, 77% yield, d.r. = 97:3) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*-**3-5d**, and by assuming the reaction sequence proceeds with retention of the configuration from *syn*-**3-5d** and other reaction with chloroformate.

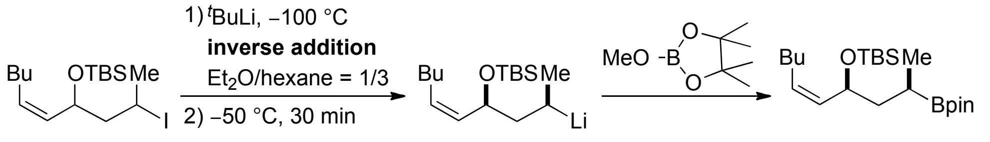
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 5.36-5.24 (m, 2H), 4.46 (ddd, *J* = 9.0, 7.2 and 4.1 Hz, 1H), 4.12 (qd, *J* = 7.1 and 0.8 Hz, 1H), 2.63 (dqd, *J* = 9.7, 7.2 and 4.5 Hz, 1H), 2.11-1.95 (m, 2H), 1.75 (ddd, *J* = 13.8, 9.7 and 4.1 Hz, 1H), 1.49 (ddd, *J* = 13.7, 9.1 and 4.4 Hz, 1H), 1.40-1.25 (m, 4H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.16 (d, *J* = 7.2 Hz, 3H), 0.90 (t, *J* = 6.9 Hz, 1H), 0.87 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 176.8, 134.0, 129.6, 67.3, 60.2, 42.5, 35.9, 31.9, 27.6, 26.0, 22.6, 18.6, 18.3, 14.4, 14.1, –4.1, –4.8.

MS (70 eV, EI) *m/z* (%): 341 (1) $[M]^{+\bullet}$, 297 (5), 285 (100), 239 (36), 227 (20), 183 (5), 171 (5), 137 (5), 109 (6), 95 (8), 75 (32), 57 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2928 (m), 2856 (w), 1732 (m), 1463 (w), 1378 (w), 1360 (w), 1251 (m), 1174 (m), 1137 (w), 1094 (m), 1053 (m), 1005 (w), 939 (w), 914 (w), 835 (s), 811 (m), 774 (vs), 728 (w), 669 (w).

HRMS (EI) *m/z*: calcd for $C_{15}H_{29}O_3Si^{+\bullet}$ $[M–Bu]^{+\bullet}$: 285.1886, found: 285.1882.



3-3k *syn*-**3-4k** *syn*-**3-13c**

syn-**3-13c**

According to general procedure, diastereomeric mixture of **3-3k** (119 mg, 0.30 mmol, d.r. = 50:50) as a starting material and MeOBpin (93 μL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/50 to afford *syn*-**3-13c** (71 mg, 60% yield, d.r. = 99:1) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*-**3-5g**, and by assuming the reaction with boronic acid pinacol ester proceeds with retention of the configuration from the previous literature.[49].

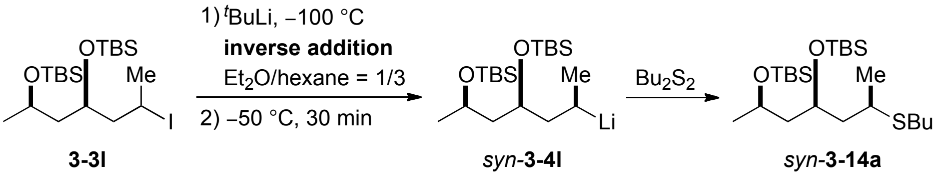
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.34-5.23 (m, 2H), 4.49 (dtd, *J* = 8.0, 5.3 and 2.4 Hz, 1H), 2.13-1.98 (m, 2H), 1.52 (ddd, *J* = 13.4, 9.2 and 5.3 Hz, 1H), 1.42 (ddd, *J* = 13.3, 8.0 and 5.9 Hz, 1H), 1.36-1.28 (m, 4H), 1.23 (s, 12H), 1.23-1.09 (m, 1H), 0.97 (d, *J* = 7.5 Hz, 3H), 0.90 (t, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 134.6, 129.3, 82.9, 68.9, 42.3, 32.1, 27.7, 26.1, 25.0, 24.9, 22.7, 18.4, 16.4, 14.2, –4.0, –4.6.

MS (70 eV, EI) *m/z* (%): 396 (1) $[M]^{+\bullet}$, 339 (22), 239 (32), 227 (100), 201 (9), 171 (12), 159 (11), 137 (33), 117 (14), 101 (8), 75 (23), 55 (7).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2926 (m), 2855 (w), 1461 (w), 1385 (w), 1378 (w), 1370 (w), 1360 (w), 1311 (m), 1250 (m), 1213 (w), 1165 (w), 1143 (s), 1089 (m), 1043 (m), 1004 (w), 967 (w), 933 (w), 908 (w), 877 (w), 862 (w), 834 (s), 809 (w), 773 (vs), 727 (w), 683 (w), 667 (w).

HRMS (EI) *m/z*: calcd for $C_{22}H_{45}O_3BSi^{+\bullet}$ $[M–{}^tBu]^{+\bullet}$: 396.3231, found: 396.3234.



syn-**3-14a** (Table 2, entry 12)

According to general procedure, diastereomeric mixture of **3-3l** (146 mg, 0.30 mmol, d.r. = 63:37) as a starting material and Bu_2S_2 (114 µL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 0/1→1/700 to afford *syn*-**3-14a** (93 mg, 69% yield, d.r. = 91:9) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*- and *anti*-**3-5a**, and by assuming the reaction sequence proceeds with retention of the configuration from *syn*-**3-5a** and other reactions with disulfide.

The peaks of the major diastereomer are given.

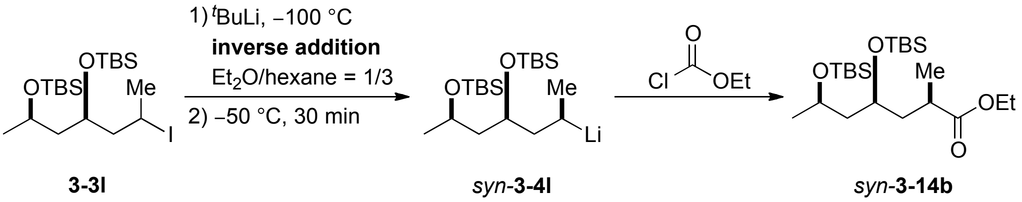
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 3.98-3.87 (m, 2H), 2.84 (dqd, J = 8.3, 6.6 and 6.3 Hz, 1H), 2.56-2.44 (m, 2H), 1.72-1.63 (m, 2H), 1.59-1.35 (m, 6H), 1.28 (d, J = 6.7 Hz, 3H), 1.13 (d, J = 6.0 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H), 0.88 (s, 9H), 0.87 (s, 9H), 0.08 (s, 3H), 0.07 (s, 6H), 0.05 (m, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 67.7, 65.7, 48.1, 45.2, 36.6, 31.9, 29.7, 25.9, 24.0, 22.4, 22.2, 18.1, 18.0, 13.7, –4.2, –4.3, –4.4, –4.6.

MS (70 eV, EI) *m/z* (%): 391 (6) $[M–{}^tBu]^{+\bullet}$, 301 (4), 259 (8), 233 (16), 185 (29), 147 (33), 117 (100), 73 (28).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 2857 (w), 1462 (w), 1254 (w), 1114 (w), 1041 (w), 1004 (w), 833 (s), 805 (m), 771 (w).

HRMS (EI) *m/z*: calcd for **$C_{19}H_{43}O_2SSi_2^{+\bullet}$** $[M–{}^tBu]^{+\bullet}$: 391.2522, found: 391.2536.

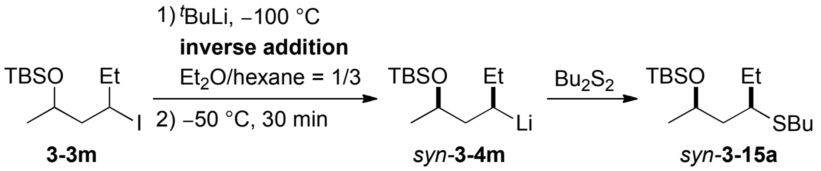


syn-**3-14b**

According to general procedure, diastereomeric mixture of **3-3l** (146 mg, 0.30 mmol, d.r. = 63:37) as a starting material and $ClCO_2Et$ (57 µL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane =

1/50 to afford *syn*-**3-14b** (92 mg, 71% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of **3-5d**, and by assuming the reaction sequence proceeds with retention of the configuration from *syn*-**3-5d** and other reaction with chloroformate.

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.10 (qd, *J* = 7.1 and 1.8 Hz, 2H), 3.89 (dqd, *J* = 7.2, 6.1 and 5.7 Hz, 1H), 3.79-3.73 (m, 1H), 2.61 (dqd, *J* = 8.6, 7.1 and 5.1 Hz, 1H), 1.95 (ddd, *J* = 13.7, 9.1 and 4.4 Hz, 1H), 1.69 (ddd, *J* = 13.7, 7.1 and 5.3 Hz, 1H), 1.46 (ddd, *J* = 13.9, 6.3 and 5.0 Hz, 1H), 1.40 (ddd, *J* = 13.9, 7.9 and 5.0 Hz, 1H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.15 (d, *J* = 7.2 Hz, 3H), 1.12 (d, *J* = 6.1 Hz, 1H), 0.87 (s, 9H), 0.05 (s, 6H), 0.040 (s, 3H), 0.036 (s, 3H).
^{13}C-NMR (75 MHz, CDCl$_3$) δ: 176.9, 68.3, 65.8, 60.3, 48.2, 41.6, 36.0, 26.0, 24.3, 18.7, 18.2, 14.4, –4.1, –4.5, –4.6.
MS (70 eV, EI) *m/z* (%): 375 (46) $[M-{}^tBu]^{+\bullet}$, 333 (23), 259 (47), 233 (23), 201 (32), 169 (59), 159 (68), 147 (93), 95 (54), 75 (100).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 2930 (w), 2858 (w), 1730 (m), 1473 (w), 1376 (w), 1254 (m), 1184 (w), 1136 (w), 1097 (m), 1029 (m), 1004 (m), 833 (s), 810 (m), 774 (s).
HRMS (EI) *m/z*: calcd for **$C_{21}H_{45}O_4Si_2$**$^{+\bullet}$ $[M-Me]^{+\bullet}$: 417.2856, found: 417.2844.



syn-**3-15a**

According to general procedure, diastereomeric mixture of **3-3m** (107 mg, 0.30 mmol, d.r. = 50:50) as a starting material and Bu$_2$S$_2$ (114 μL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/99 to afford *syn*-**3-15a** (59 mg, 65% yield, d.r. = 86:14) as colorless oil. The relative configuration was determined by S$_N$2 reactions of *syn*- and *anti*-**3-3m** with NaSBu.

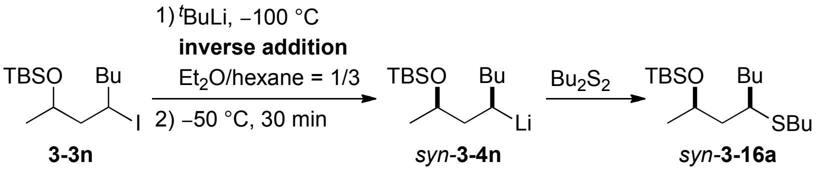
^{1}H-NMR (400 MHz, CDCl$_3$) δ: ***syn*-3-15a:** 4.08 (dqd, *J* = 9.3, 6.1 and 3.3 Hz, 1H), 2.67 (dtd, *J* = 10.1, 6.2 and 4.1 Hz, 1H), 2.51-2.40 (m, 2H), 1.67-1.49 (m, 5H), 1.45-1.35 (m, 3H), 1.13 (d, *J* = 6.2 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). ***anti*-3-15a:** 3.97 (ddq, *J* = 7.3, 6.0 and 5.7 Hz, 1H), 2.67 (dtd, *J* = 10.1, 6.2 and 4.1 Hz, 1H), 2.51-2.40 (m, 2H), 1.73 (dt, *J* = 13.8 and 6.9 Hz, 1H), 1.67-1.49 (m, 5H), 1.49-1.35 (m, 3H), 1.14 (d, *J* = 5.9 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: *syn*-3-15a: 66.3, 45.0, 44.0, 32.0, 29.4, 28.4, 25.9, 24.4, 22.2, 18.0, 13.7, 11.0, –4.0, –4.7. ***anti*-3-15a:** 66.2, 44.5, 43.5, 32.0, 29.7, 27.1, 25.9, 23.8, 22.2, 18.0, 14.1, 11.0, –4.2, –4.8.

MS (70 eV, EI) *m/z* (%): 247 (94) [M–^{t}Bu]$^{+•}$, 191 (46), 157 (44), 147 (100), 129 (9), 115 (16), 103 (17), 91 (27), 83 (33), 75 (91).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 2857 (w), 1472 (w), 1463 (w), 1255 (m), 1132 (w), 1041 (m), 1004 (w), 939 (w), 833 (s), 805 (m), 771 (s), 663 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{33}OSSi^{+•}$** [M–Me]$^{+•}$: 289.2021, found: 289.2018.



syn-3-16a

According to general procedure, diastereomeric mixture of **3-3n** (111 mg, 0.30 mmol, d.r. = 50:50) as a starting material and Bu$_2$S$_2$ (114 µL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/99 to afford *syn*-**3-16a** (63 mg, 63% yield, d.r. = 86:14) as colorless oil. The relative configuration was determined by S$_N$2 reactions of *syn*- and *anti*-**3-3n** with NaSBu.

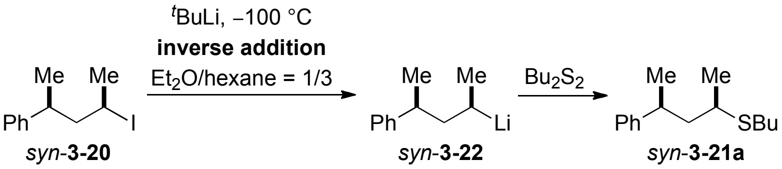
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: *syn*-3-16a: 4.09 (dqd, *J* = 9.2, 6.0 and 3.2 Hz, 1H), 2.71 (dtd, *J* = 10.0, 6.4 and 3.8 Hz, 1H), 2.51-2.40 (m, 2H), 1.67-1.25 (m, 12H), 1.13 (d, *J* = 6.1 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.1 Hz, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). ***anti*-3-16a:** 3.98 (dqd, *J* = 7.3, 5.8 and 5.4 Hz, 1H), 2.63 (dtd, *J* = 7.3, 7.0 and 5.1 Hz, 1H), 2.51-2.40 (m, 2H), 1.74 (dt, *J* = 13.9 and 6.9 Hz, 1H), 1.67-1.25 (m, 11H), 1.14 (d, *J* = 6.0 Hz, 3H), 0.92-0.87 (m, 6H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: *syn*-3-16a: 66.3, 44.9, 42.3, 35.5, 32.0, 29.2, 28.8, 25.9, 24.4, 22.6, 22.2, 18.0, 13.7, –4.0, –4.7. ***anti*-3-16a:** 66.2, 45.6, 42.1, 34.3, 31.9, 29.7, 28.9, 25.9, 23.8, 22.8, 22.2, 18.0, 14.1, –4.3, –4.8.

MS (70 eV, EI) *m/z* (%): 275 (90) [M–^{t}Bu]$^{+•}$, 191 (50), 185 (53), 147 (100), 115 (20), 91 (33), 75 (95).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 1255 (m), 1041 (m), 1004 (w), 939 (w), 833 (s), 805 (m), 772 (s), 663 (w).

HRMS (EI) *m/z*: calcd for **$C_{17}H_{37}OSSi^{+\bullet}$** [M–Me]$^{+\bullet}$: 317.2334, found: 317.2347.



syn-**3-21a**

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (1.7 mL) and Et$_2$O (0.4 mL) and cooled to –100 °C. ^{t}BuLi (0.41 mL, 1.8 M in *n*-pentane, 0.75 mmol) was added to the reaction mixture. A solution of *syn*-**3-20** (82 mg, 0.30 mmol, d.r. = 98:2) in *n*-hexane (0.4 mL) and Et$_2$O (0.3 mL) was added dropwise in 10 min. After stirring at –100 °C for 30 sec, Bu$_2$S$_2$ (102 µL, 0.54 mmol) was added and the mixture was stirred at –100 °C for 30 min. The reaction was quenched with 7 drops of saturated NH$_4$Cl aqueous solution and after an addition of MgSO$_4$ this mixture was passed through a pad of silica gel with EtOAc. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/150→1/75 to afford *syn*-**3-21a** (38 mg, 54% yield, d.r. = 97:3) as colorless oil. The relative configuration was determined by S$_N$2 reactions of *syn*- and *anti*-**3-20** with NaSBu.

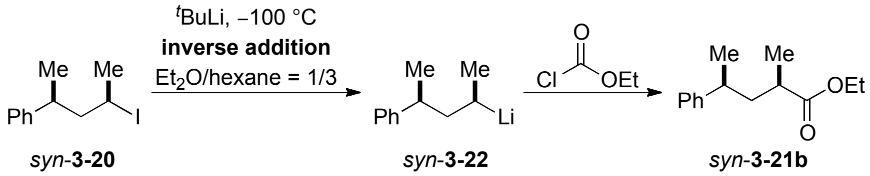
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.34-7.25 (m, 2H), 7.23-7.16 (m, 3H), 2.92 (dq, *J* = 8.9 and 6.8 Hz, 1H), 2.54 (dq, *J* = 8.5 and 6.5 Hz, 1H), 2.45 (t, *J* = 7.2 Hz, 2H), 1.94 (ddd, *J* = 14.3, 8.9 and 5.8 Hz, 1H), 1.64 (ddd, *J* = 14.0, 8.6 and 6.3 Hz, 1H), 1.52-1.28 (m, 4H), 1.26 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 146.9, 128.6, 127.1, 126.2, 45.8, 37.6, 37.4, 32.1, 29.8, 22.8, 22.3, 21.3, 13.8.

MS (70 eV, EI) *m/z* (%): 236 (17) [M]$^{+\bullet}$, 146 (32), 131 (100), 117 (5), 105 (23), 91 (11), 77 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3025 (w), 2958 (w), 2911 (m), 2867 (w), 1601 (w), 1493 (w), 1451 (w), 1376 (w), 1358 (w), 1267 (w), 1231 (w), 1148 (w), 1122 (w), 1063 (w), 1030 (w), 1011 (w), 934 (w), 907 (w), 869 (w), 761 (m), 697 (vs).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{24}S^{+\bullet}$** [M]$^{+\bullet}$: 236.1599, found: 236.1603.



syn-**3-21b**

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (1.7 mL) and Et_2O (0.4 mL) and cooled to –100 °C. ^{t}BuLi (0.41 mL, 1.8 M in *n*-pentane, 0.75 mmol) was added to the reaction mixture. Then, a solution of *syn*-**3-20** (82 mg, 0.30 mmol, d.r. = 98:2) in *n*-hexane (0.4 mL) and Et_2O (0.3 mL) was added dropwise in 10 min. After stirring at –100 °C for 30 sec, $ClCO_2Et$ (57 µL, 0.60 mmol) was added and the mixture was stirred at –100 °C for 30 min. The reaction was quenched with 7 drops of saturated NH_4Cl aqueous solution and after an addition of $MgSO_4$ this mixture was passed through a pad of silica gel with EtOAc. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/50 to afford *syn*-**3-21b** (33 mg, 51% yield, d.r. = 98:2) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*-**3-5d** and by assuming the reaction sequence proceeds with retention of the configuration from *syn*-**3-5d** and other reaction with chloroformate.

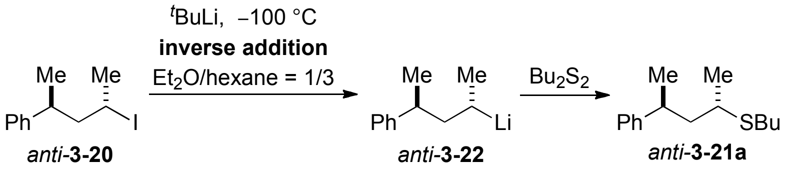
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.34-7.24 (m, 2H), 7.23-7.14 (m, 3H), 4.05 (dq, J = 7.1 and 1.2 Hz, 1H), 2.76 (dqd, J = 9.0, 6.8 and 6.5 Hz, 1H), 2.33 (dqd, J = 7.9, 6.8 and 6.7 Hz, 1H), 2.06 (ddd, J = 13.7, 8.6 and 6.9 Hz, 1H), 1.61 (ddd, J = 14.1, 7.6 and 6.6 Hz, 1H), 1.27 (d, J = 6.9 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H), 1.14 (d, J = 6.9 Hz, 3H).

^{13}C-NMR (150 MHz, CDCl$_3$) δ: 176.9, 146.6, 128.6, 127.1, 126.3, 60.3, 42.0, 37.7, 22.7, 17.2, 14.4.

MS (70 eV, EI) *m/z* (%): 220 (4) $[M]^{+\bullet}$, 205 (12), 175 (11), 119 (51), 105 (81), 102 (100), 91 (27), 74 (56).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3026 (vw), 2966 (w), 2931 (w), 1730 (vs), 1602 (vw), 1493 (w), 1452 (m), 1375 (m), 1271 (w), 1251 (w), 1174 (s), 1130 (m), 1071 (m), 1030 (m), 908 (w), 860 (w), 760 (m), 699 (s).

HRMS (EI) *m/z*: calcd for $C_{14}H_{20}O_2^{+\bullet}$ $[M]^{+\bullet}$: 220.1463, found: 220.1463.



anti-**3-21a**

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (1.7 mL) and Et_2O (0.4 mL) and cooled to –100 °C. ^{t}BuLi (0.41 mL, 1.8 M in *n*-pentane, 0.75 mmol) was added to the reaction mixture. Then, a solution of *anti*-**3-20** (82 mg, 0.30 mmol, d.r. = 98:2) in *n*-hexane (0.4 mL) and Et_2O (0.3 mL) was added dropwise in 10 min. After stirring at –100 °C for 30 sec, Bu_2S_2 (102 µL, 0.54 mmol) was added and the mixture was stirred at –100 °C for 30 min. The reaction mixture was quenched with 7 drops of saturated NH_4Cl aqueous solution and after an addition of $MgSO_4$ this mixture was passed through a pad of silica gel with EtOAc. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/150→1/100 to afford *anti*-**3-21a** (41 mg, 58% yield, d.r. = 95:5) as colorless oil. The relative configuration was determined by S_N2 reactions of *syn*- and *anti*-**3-20** with NaSBu.

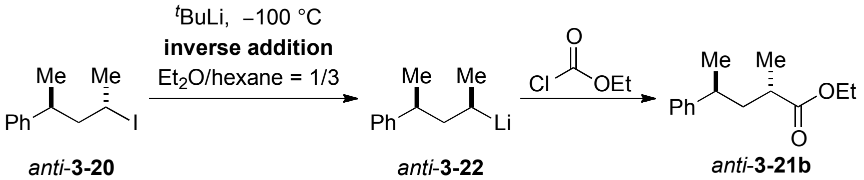
^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: 7.34-7.15 (m, 5H), 3.05 (hex, *J* = 7.2 Hz, 1H), 2.47 (dq, *J* = 7.1 and 6.6 Hz, 1H), 2.46 (t, *J* = 7.4 Hz, 1H), 1.74 (t, *J* = 7.3 Hz, 2H), 1.56-1.32 (m, 4H), 1.25 (dd, *J* = 7.0 and 0.8 Hz, 3H), 1.23 (dd, *J* = 7.0 and 0.8 Hz, 3H), 0.90 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 147.1, 128.5, 127.2, 126.2, 45.9, 38.2, 37.6, 32.1, 29.8, 22.7, 22.3, 13.8.

MS (70 eV, EI) *m/z* (%): 236 (18) $[M]^{+\bullet}$, 146 (32), 131 (100), 117 (4), 105 (23), 91 (11), 77 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3026 (w), 2954 (w), 2923 (w), 2869 (w), 1602 (w), 1493 (w), 1451 (w), 1374 (w), 1259 (w), 1118 (w), 1016 (w), 907 (w), 761 (m), 698 (vs).

HRMS (EI) *m/z*: calcd for $C_{15}H_{24}S^{+\bullet}$ $[M]^{+\bullet}$: 236.1599, found: 236.1598.



anti-**3-21b**

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (1.7 mL) and Et_2O (0.4 mL) and cooled to –100 °C. ^{t}BuLi (0.41 mL, 1.83 M in *n*-pentane, 0.75 mmol) was added to the reaction mixture. Then, a solution of *anti*-**3-20** (82 mg, 0.30 mmol, d.r. = 98:2) in *n*-hexane (0.4 mL) and Et_2O (0.3 mL) was added dropwise in 10 min. After stirring at –100 °C for 30 sec, $ClCO_2Et$ (57 µL, 0.60 mmol) was added and the mixture was stirred at –100 °C for 30 min. The reaction mixture was quenched with 7 drops of saturated NH_4Cl aqueous solution and after an addition of $MgSO_4$ this mixture was passed through a pad of silica gel with EtOAc. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/50 to afford *anti*-**3-21b** (31 mg, 47% yield, d.r. = 98:2) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*-**3-5d**, and by assuming the reaction sequence proceeds with retention of the configuration from *syn*-**3-5d** and other reaction with chloroformate.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.33-7.26 (m, 2H), 7.22-7.14 (m, 3H), 4.14 (dq, J = 10.8 and 7.4 Hz, 1H), 4.11(dq, J = 10.6 and 7.2 Hz, 1H), 2.72 (dqd, J = 9.4, 6.8 and 5.9 Hz, 1H), 2.27 (dqd, J = 9.3, 7.0 and 5.3 Hz, 1H), 1.98 (ddd, J = 13.9, 9.3 and 5.7 Hz, 1H), 1.61 (ddd, J = 14.0, 9.4 and 5.2 Hz, 1H), 1.26 (t, J = 7.1 Hz, 3H), 1.24 (d, J = 6.7 Hz, 3H), 1.09 (d, J = 7.0 Hz, 3H).

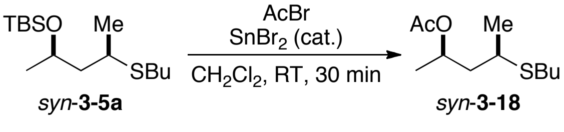
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 177.0, 146.8, 128.5, 127.2, 126.3, 60.3, 42.7, 38.1, 37.9, 22.7, 18.1, 14.4.

MS (70 eV, EI) *m/z* (%): 220 (9) $[M]^{+\bullet}$, 175 (24), 131 (8), 119 (66), 105 (100), 102 (98), 91 (30), 74 (41).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3025 (vw), 2961 (w), 2929 (w), 2872 (vw), 1730 (s), 1602 (w), 1494 (w), 1452 (m), 1375 (m), 1348 (w), 1251 (m), 1172 (s), 1136 (m), 1117 (m), 1094 (m), 1079 (m), 1053 (m), 1027 (m), 907 (vw), 853 (w), 761 (s), 699 (vs).

HRMS (EI) *m/z*: calcd for $C_{14}H_{20}O_2^{+\bullet}$ $[M]^{+\bullet}$: 220.1463, found: 220.1468.

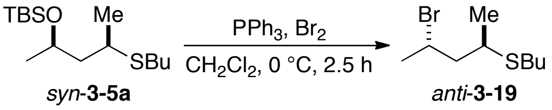
9.3.3 Transformation of the products



syn-**3-18**

A dry and N_2-flushed *Schlenk*-flask was charged with *syn*-**3-5a** (57 mg, 0.20 mmol, d.r. = 93:7) and $SnBr_2$ (3 mg, 0.01 mmol) in CH_2Cl_2 (1.0 mL). Acetyl bromide (39 mg, 0.30 mmol) was added and the reaction mixture was stirred at room temperature for 30 min. After quenching the reaction with sodium phosphate buffer (pH = 7), the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/20 to afford *syn*-**3-18** (39 mg, 91% yield, d.r. = 93:7) as colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 5.09 (dddd, J = 12.5, 8.7, 6.2 and 4.6 Hz, 1H), 2.73 (dq, J = 8.4 and 6.7 Hz, 1H), 2.47 (dqd, J = 12.1, 7.7 and 7.3 Hz, 1H), 2.0 (s, 3H), 1.78 (ddd, J = 14.4, 8.7 and 5.7 Hz, 1H), 1.60 (ddd, J = 14.4, 8.5 and 4.4 Hz, 1H), 1.56-1.46 (m, 2H), 1.43-1.31 (m, 2H), 1.28 (d, J = 6.8 Hz, 1H), 1.21 (d, J = 6.2 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 170.6, 69.4, 43.6, 36.8, 32.0, 30.1, 22.4, 22.2, 21.5, 20.4, 13.8.
MS (70 eV, EI) *m/z* (%): 218 (37) $[M]^{+\bullet}$, 158 (32), 143 (12), 129 (9), 115 (23), 101 (100), 87 (16), 69 (49), 61 (12).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2930 (w), 2873 (w), 1736 (s), 1452 (w), 1372 (w), 1238 (s), 1136 (w), 1063 (w), 1030 (w), 955 (w), 936 (w), 813 (w), 746 (w).
HRMS (EI) *m/z*: calcd for **$C_{11}H_{22}O_2S^{+\bullet}$** $[M]^{+\bullet}$: 218.1341, found: 218.1333.



anti-**3-19**

A dry and N_2-flushed *Schlenk*-flask was charged with triphenylphosphine (0.16 g, 0.60 mmol) in CH_2Cl_2 (2.5 mL) and was cooled down to 0 °C. Bromine (31 µL, 0.60 mmol) was added at 0 °C and the reaction mixture was stirred for 1 h. *syn*-**3-5a** (57 mg, 0.30 mmol, d.r. = 93:7) was added and the reaction mixture was stirred at 0 °C to room temperature for 2.5 h. Solvent mixture Et_2O/*i*-hexane = 1/4 was added to the reaction mixture and the precipitate was filtered off with the same solvent mixture. The filtrate was washed with saturated $Na_2S_2O_3$ aqueous solution and the organic phase was dried over $MgSO_4$. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/70 to afford *anti*-**3-19** (5 mg, 7% yield, d.r. = 99:1) as the first fraction and colorless oil, and *syn*-**3-19** (60 mg, 84% yield, d.r. = 99:1) as the second fraction and colorless oil

syn-**3-19**

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.24-4.17 (m, 1H), 2.94 (dqd, *J* = 8.6, 6.7 and 6.3 Hz, 1H), 2.58-2.48 (m, 2H), 2.17 (ddd, *J* = 14.8, 9.5 and 5.5 Hz, 1H), 1.77 (ddd, *J* = 14.3, 8.8 and 4.9 Hz, 1H), 1.72 (d, *J* = 6.6 Hz, 3H), 1.56 (tt, *J* = 7.6 and 7.4 Hz, 2H), 1.41 (tt, *J* = 7.4 and 7.3 Hz, 1H), 1.26 (d, *J* = 6.7 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 48.8, 48.4, 38.0, 32.0, 30.0, 26.6, 22.2, 20.5, 13.9.

MS (70 eV, EI) *m/z* (%): 238 (30) $[M]^{+\bullet}$, 159 (34), 117 (100), 75 (34), 69 (67), 61 (16).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (vs), 2923 (s), 2870 (m), 1455 (s), 1377 (s), 1259 (w), 1214 (s), 1182 (w), 1128 (w), 1044 (w), 1003 (w), 978 (w), 927 (w), 875 (w), 852 (w), 744 (w).

HRMS (EI) *m/z*: calcd for **$C_9H_{19}BrS^{+\bullet}$** $[M]^{+\bullet}$: 238.0391, found: 238.0379.

anti-**3-19**

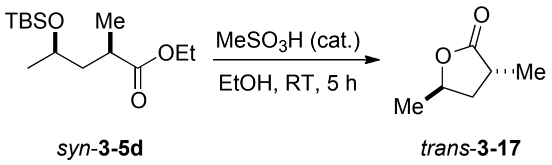
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.46 (dqd, *J* = 10.2, 6.6 and 3.2 Hz, 1H), 2.97 (dqd, *J* = 10.5, 6.8 and 4.0 Hz, 1H), 2.60-2.51 (m, 2H), 1.97 (ddd, *J* = 14.8, 10.4 and 3.8 Hz, 1H), 1.76 (ddd, *J* = 14.9, 10.5 and 3.3 Hz, 1H), 1.73 (d, *J* = 6.7 Hz, 3H), 1.61-1.54 (m, 2H), 1.48-1.36 (m, 1H), 1.33 (d, *J* = 6.8 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 50.1, 48.7, 39.4, 32.2, 30.3, 26.9, 23.0, 22.2, 13.8.

MS (70 eV, EI) *m/z* (%): 238 (32) $[M]^{+\bullet}$, 159 (32), 117 (100), 76 (33), 69 (58), 61 (17).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (vs), 2923 (s), 2870 (m), 1455 (s), 1377 (s), 1259 (w), 1214 (s), 1182 (w), 1128 (w), 1044 (w), 1003 (w), 978 (w), 927 (w), 875 (w), 852 (w), 744 (w).

HRMS (EI) *m/z*: calcd for **$C_9H_{19}BrS^{+\bullet}$** $[M]^{+\bullet}$: 238.0391, found: 238.0396.



trans-**3-17** (CAS: 24405-08-1)

A *Schlenk*-flask was charged with a solution of *syn*-**3-5d** (110 mg, 0.40 mmol, d.r. = 97:3) in EtOH (3.0 mL). Then MeSO$_3$H (16 mg, 0.16 mmol) was added and the mixture was stirred at room temperature for 5 h. The reaction mixture was poured into saturated NaHCO$_3$ aqueous solution and the mixture was extracted with Et$_2$O three times. The combined organic solution was dried over $MgSO_4$. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et_2O/*n*-pentane = 1/2 to afford *trans*-**3-17** (33 mg, 22% yield, d.r. = 97:3) as colorless oil. The relative configuration was determined by the comparison with the literature value.[124]

^{1}H-NMR (400 MHz, CDCl$_3$) δ: 4.66 (dqd, *J* = 7.0, 6.4 and 5.0 Hz, 1H), 2.71 (dqd, *J* = 8.5, 7.7 and 7.0 Hz, 1H), 2.07 (ddd, *J* = 12.0, 8.3 and 4.6 Hz, 1H), 2.02 (ddd, *J* = 12.8, 8.0 and 7.1 Hz, 1H), 1.35 (d, *J* = 6.4 Hz, 3H), 1.26 (d, *J* = 7.3 Hz, 3H).

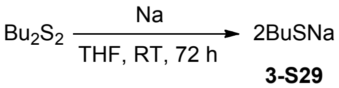
^{13}C-NMR (100 MHz, CDCl$_3$) δ: 180.1, 74.7, 37.1, 34.1, 21.2, 15.8.

MS (70 eV, EI) *m/z* (%): 114 (3) $[M]^{+\bullet}$, 99 (31), 70 (69), 55 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2974 (w), 2936 (w), 2878 (w), 1763 (vs), 1456 (w), 1384 (w), 1360 (w), 1347 (w), 1320 (w), 1178 (s), 1135 (w), 1121 (w), 1100 (m), 1054 (w), 1038 (w), 1028 (w), 1002 (w), 950 (s), 917 (w), 895 (w), 873 (w), 772 (w), 720 (w), 705 (w), 692 (w).

HRMS (EI) *m/z*: calcd for $C_5H_7O_2^{+\bullet}$ $[M\text{–}Me]^{+\bullet}$: 99.0448, found: 99.0443.

9.3.4 Conformation of the configuration

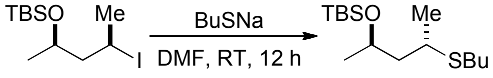


$$Bu_2S_2 \xrightarrow[\text{THF, RT, 72 h}]{\text{Na}} 2BuSNa$$

3-S29

3-S29[125]

A dry and Ar-flushed *Schlenk*-flask was charged with THF (35 mL). Bu_2S_2 (5.7 mL, 30.0 mmol) was added. Then, sodium (0.69 g, 30.0 mmol) was added and the mixture was stirred at room temperature for 72 h. The pale yellow precipitate was filtered off under N_2 and the precipitate was washed with THF one time and *n*-pentane two times. The solid was placed in a dry and Ar-flushed *Schlenk*-flask and it was dried under vacuum for 6 h to obtain **3-S29** (ca. 80% yield) as pale yellow solid.



syn-**3-3a** *anti*-**3-5a'**

anti-**3-5a'**

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[124] L. Coulombel, E. Duñach. *Synth. Commun.* **2005**, *35*, 153.

[125] T. A. Wark, D. W. Stephan. *Organometallics* **1989**, *8*, 2836.

A dry and Ar-flushed *Schlenk*-flask was charged with BuSNa (84 mg, 0.75 mmol). Then a solution of *anti*-**3-3a** (164 mg, 0.50 mmol, d.r. = 99:1) in DMF (1.5 mL) was added and the mixture was stirred at room temperature for 12 h. The reaction mixture was quenched with saturated NH_4Cl aqueous solution and it was extracted three times with a mixture of Et_2O:*i*-hexane = 1/4. The combined organic solution was dried over $MgSO_4$. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *anti*-**3-5a'** (33 mg, 22% yield, d.r. = 99:1) as colorless oil. (Elimination product is a major side product.)

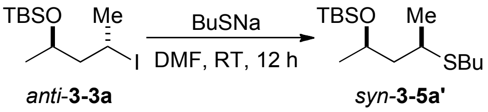
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 3.93 (dqd, *J* = 7.6, 6.0 and 4.8 Hz, 1H), 2.84 (dqd, *J* = 8.9, 6.7 and 5.1 Hz, 1H), 2.51 (td, *J* = 7.5 Hz, 2H), 1.79 (ddd, *J* = 13.6, 8.0 and 5.5 Hz, 1H), 1.63-1.49 (m, 2H), 1.48-1.33 (m, 3H), 1.25 (d, *J* = 6.7 Hz, 3H), 1.14 (d, *J* = 6.0 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 66.3, 47.5, 36.2, 32.1, 30.0, 26.0, 24.2, 22.3, 21.2, 18.2, 13.9, –4.0, –4.7.

MS (70 eV, EI) *m/z* (%): 275 (3) [M–Me]$^{+\bullet}$, 233 (100), 191 (14), 159 (5), 147 (55), 135 (4), 115 (5), 103 (5), 91 (7), 75 (16), 57 (4).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2927 (w), 2856 (w), 1472 (w), 1462 (w), 1373 (w), 1361 (w), 1255 (w), 1128 (w), 1103 (w), 1082 (w), 1051 (w), 1026 (w), 1005 (w), 989 (w), 968 (w), 885 (w), 854 (w), 834 (s), 824 (m), 806 (m), 772 (vs), 719 (w), 660 (w), 657 (w).

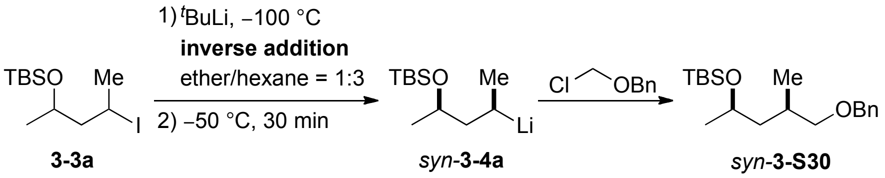
HRMS (EI) *m/z*: calcd for **$C_{15}H_{33}OSSi^{+\bullet}$** [M–H]$^{+\bullet}$: 289.2022, found: 289.2031.



anti-**3-5a'**

A dry and Ar-flushed *Schlenk*-flask was charged with BuSNa (84 mg, 0.75 mmol). Then a solution of *anti*-**3-3a** (164 mg, 0.50 mmol, d.r. = 99:1) in DMF (1.5 mL) was added and the mixture was stirred at room temperature for 12 h. The reaction mixture was quenched with saturated NH_4Cl aqueous solution and it was extracted three times with a mixture of Et_2O/*i*-hexane = 1/4. The combined organic solution was dried over $MgSO_4$. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *anti*-**3-5a'** (98 mg, 67% yield, d.r. = 99:1) as colorless oil. Experimental values were described in syn-**3-5a**.

The configuration of other thioether compounds was confirmed by GC analysis of the corresponding S$_N$2 reaction products.



***syn*-3-S30**

BnOCH$_2$Cl was distilled (5 mbar, 75 °C) before use.

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (1.7 mL) and Et$_2$O (0.4 mL) and cooled to –100 °C. ^{t}BuLi (0.50 mL, 1.51 M in *n*-pentane, 0.75 mmol) was added to the reaction mixture. Then, **3-3a** (99 mg, 5.0 mmol, d.r. = 50:50) in *n*-hexane (0.4 mL) and Et$_2$O (0.3 mL) was added dropwise in 30 min. After stirring at –100 °C for 10 min, the reaction mixture was warmed up to –50 °C and stirred for 30 min. BnOCH$_2$Cl (75 µL, 0.54 mmol) was added and the mixture was stirred at –50 °C for 1 h. The reaction was quenched with saturated NH$_4$Cl aqueous solution and the mixture was extracted with Et$_2$O three times. The combined organic solution was dried over MgSO$_4$. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/45 to afford *anti*-**3-S30** (40 mg, 41% yield, d.r. = 97:3) as colorless oil.

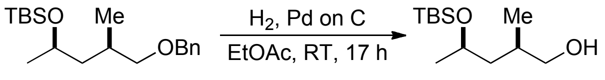
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.38-7.26 (m, 5H), 4.53 (d, *J* = 12.1 Hz, 1H), 4.48 (d, *J* = 12.1 Hz, 1H), 3.87 (ddq, *J* = 7.1, 6.3 and 6.0 Hz, 1H), 3.36 (dd, *J* = 9.0 and 5.3 Hz, 1H), 3.23 (d, *J* = 9.0 and 7.0 Hz, 1H), 1.87 (ddqdd, *J* = 7.1, 7.0, 6.7, 6.3 and 5.3 Hz, 1H), 1.47 (dt, *J* = 13.6 and 6.3 Hz, 1H), 1.32 (ddd, *J* = 13.8 and 7.1 Hz, 1H), 1.12 (d, *J* = 6.0 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 138.9, 128.4, 127.7, 127.6, 75.8, 73.1, 67.0, 44.0, 30.6, 26.1, 24.0, 18.3, 18.1, –4.2, –4.6.

MS (70 eV, EI) *m/z* (%): 321 (1) [M–H]$^{+\bullet}$, 265 (4), 173 (14), 159 (6), 91 (100), 75 (9).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2927 (w), 2854 (w), 1495 (w), 1472 (w), 1462 (w), 1453 (w), 1360 (w), 1254 (w), 1068 (s), 1029 (w), 1005 (w), 989 (w), 962 (w), 938 (w), 896 (w), 833 (s), 805 (m), 772 (vs), 732 (m), 695 (s), 677 (w), 662 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{25}O_2SSi^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 265.1624, found: 265,1608.



syn-**3-S30** *syn*-**3-S31**

syn-**3-S31**

A flask was charged with a solution of *syn*-**3-S30** (110 mg, 0.35 mmol, d.r. = 97:3) in EtOAc (2.5 mL). After an addition of Pd on C (74 mg, 0.04 mmol, 5% Pd) H_2 was bubbled into the mixture and it was stirred under H_2 atmosphere at room temperature for 17 h. Pd powder was filtered off and solvents were evaporated to afford *syn*-**3-S31** (72 mg, 88% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with those of *syn*-**3-S31**.

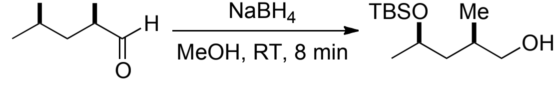
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 4.02 (qt, J = 6.4 and 4.8 Hz, 1H), 3.45 (dd, J = 11.0 and 4.7 Hz, 1H), 3.35 (dd, J = 10.9 and 7.4 Hz, 1H), 3.0 (s br, 1H), 1.88 (dqdd, J = 7.9, 7.2, 6.6 and 4.7 Hz, 1H), 1.49-1.43 (m, 2H), 1.17 (d, J = 6.3 Hz, 3H), 0.89 (s, 9H), 0.87 (d, J = 6.9 Hz, 3H), 0.07 (s, 6H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 68.7, 67.6, 44.6, 31.9, 25.9, 22.7, 18.4, 18.2, –4.5, –4.8.

MS (70 eV, EI) *m/z* (%): 175 (2) $[M–{}^{t}Bu]^{+\bullet}$, 159 (13), 129 (5), 119 (100), 103 (5), 83 (7), 75 (76), 55 (7).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3346 (w br), 2956 (w), 2929 (w), 2858 (w), 1472 (w), 1463 (w), 1378 (w), 1362 (w), 1254 (w), 1159 (w), 1132 (w), 1070 (w), 1038 (m), 1006 (w), 987 (w), 940 (w), 890 (w), 833 (s), 806 (m), 772 (vs), 720 (w), 677 (w), 662 (w).

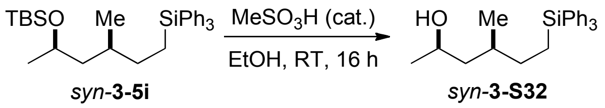
HRMS (EI) *m/z*: calcd for **$C_8H_{19}O_2SSi^{+\bullet}$** $[M–{}^{t}Bu]^{+\bullet}$: 175.1154, found: 175.1133.



syn-**3-5b** *syn*-**3-S31'**

syn-**3-S31′**

A flask was charged with a solution of *syn*-**3-5b** (27 mg, 0.12 mmol, d.r. = 91:9) in MeOH (3.0 mL). After cooling it down to 0 °C $NaBH_4$ (7 mg, 0.18 mmol) was added into the mixture and it was stirred at 0 °C for 8 min. The reaction mixture was quenched with saturated NH_4Cl aqueous solution and it was extracted with Et_2O three times. The combined organic solution was dried over $MgSO_4$. Solvents were evaporated to obtain *syn*-**3-S31′** (19 mg, 68 % yield, d.r. = 90:10) with a little impurity.



syn-**3-S32**

A flask was charged with a solution of *syn*-**3-5i** (1.3 g, 2.7 mmol, d.r. = 99:1) in EtOH (27 mL). $MeSO_3H$ (0.13 g, 1.5 mmol) was added into the mixture and it was stirred at 0 °C for 8 min. The reaction mixture was quenched with saturated $NaHCO_3$ aqueous solution and it was extracted with Et_2O three times. The combined organic solution was dried over $MgSO_4$. Solvents were evaporated and it was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/1 to afford *syn*-**3-S32** (1.0 g, 97% yield, d.r. = 99:1) as colorless oil.

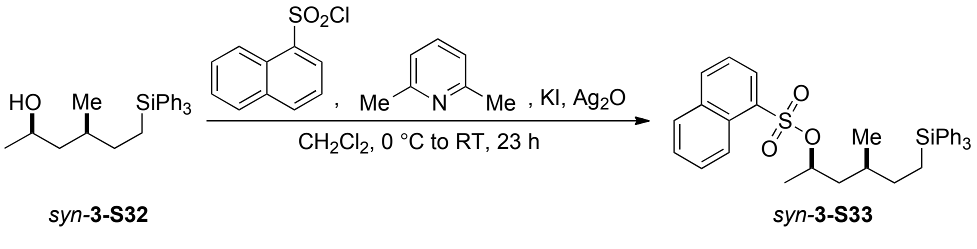
^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.58-7.53 (m 6H), 7.48-7.36 (m, 9H), 3.83 (tq, *J* = 6.8 and 6.1 Hz, 1H), 1.65-1.51 (m, 2H), 1.48-1.28 (m, 5H), 1.17 (d, *J* = 6.1 Hz, 3H), 0.96 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 135.8, 135.3, 129.5, 128.0, 66.4, 46.2, 32.8, 30.7, 23.8, 19.7, 9.9.

MS (70 eV, EI) *m/z* (%): 297 (11) $[M–Ph]^{+•}$, 279 (6), 259 (100), 199 (23), 181 (12), 122 (4), 105 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3369 (w br), 3068 (w), 2961 (w), 2919 (w), 1485 (w), 1427 (w), 1376 (w), 1259 (w), 1184 (w), 1109 (m), 1063 (w), 1015 (w), 997 (w), 905 (m), 867 (w), 820 (w), 728 (s), 712 (s), 697 (vs), 673 (w).

HRMS (EI) *m/z*: calcd for **$C_{19}H_{25}OSi^{+•}$** $[M–Ph]^{+•}$: 297.1675, found: 297.1668.



syn-**3-S33**

A flask was charged with a solution of *syn*-**3-S32** (112 mg, 0.30 mmol, d.r. = 99:1) in CH_2Cl_2 (1.5 mL). After cooling it to 0 °C 2,6-lutidine (84 µL, 0.75 mmol), KI (0,10 g, 0.60 mmol), Ag_2O (0,14 g, 0.60 mmol), 1-naphtylsulfonyl chloride (102 mg, 0.45 mmol) was added successively into the mixture and it was stirred at 0 °C to room temperature for 23 h. The reaction mixture was quenched with water and it was extracted with Et_2O three times. The combined organic solution was dried over $MgSO_4$. Solvents were evaporated and it was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/3, followed by the purification with preparative TLC (SiO_2) with Et_2O/*i*-hexane = 1/5 to afford *syn*-**3-S33** (90 mg, 53% yield, d.r. = 99:1) as white solid. The relative configuration was determined by X-ray crystallographic analysis of the single crystal recrystallized from dichloroethane and *n*-heptane.

m. p.: 134.1-135.4°C

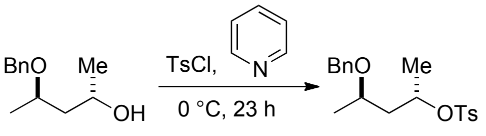
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.63 (d, *J* = 8.6 Hz, 1H), 8.21 (dd, *J* = 7.3 and 1.2 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.67 (ddd, *J* = 8.5, 6.9 and 1.4 Hz, 1H), 7.60 (ddd, *J* = 8.0, 7.0 and 1.1 Hz, 1H), 7.48-7.34 (m, 16H), 4.58 (hex, *J* = 6.4 Hz, 1H), 1.40 (t, *J* = 6.3 Hz, 2H), 1.33-1.20 (m, 2H), 1.16 (d, *J* = 6.2 Hz, 3H), 1.13-0.90 (m, 3H), 0.68 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 135.7, 135.1, 135.0, 134.2, 132.8, 129.9, 129.6, 128.8, 128.6, 128.5, 128.0, 127.3, 125.5, 124.1, 80.2, 43.2, 31.7, 30.3, 21.1, 19.0, 9.5.

MS (70 eV, EI) *m/z* (%): This compound is EI silence.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3369 (w), 3022 (w), 2958 (w), 2922 (w), 2882 (w), 2850 (w), 1587 (w), 1567 (w), 1506 (w), 1484 (w), 1455 (w), 1429 (w), 1426 (w), 1382 (w), 1357 (m), 1345 (w), 1267 (w), 1200 (w), 1173 (s), 1139 (w), 1126 (w), 1108 (m), 1070 (w), 1036 (w), 1029 (w), 997 (w), 911 (s), 900 (s), 864 (w), 828 (w), 809 (m), 742 (s), 712 (s), 702 (vs), 672 (s), 634 (w).

HRMS (ESI) *m/z*: calcd for $\mathbf{C_{35}H_{36}O_3NaSi^+}$ [M+Na]$^+$: 587.2052, found: 587.2054.



anti-**3-S8** *anti*-**3-S34**

anti-**3-S34**

An Ar-flushed *Schlenk*-flask was charged with a solution of *anti*-**3-S8** (1.2 g, 6.4 mmol, d.r. = 97:3) in pyridine (10 mL). After cooling it down to 0 ºC, TsCl (1.6 g, 8.3 mmol) was added and the mixture was stirred at 0 ºC for 23 h. 2 M HCl aqueous solution was added to the reaction mixture and it was extracted with Et_2O three times. The combined organic solution was dried over $MgSO_4$. Solvents were evaporated to obtain the crude product *anti*-**3-S34** (1.7 g, 77% yield, d.r. = 96:4) as yellow oil. It was used for the next step without further purification.

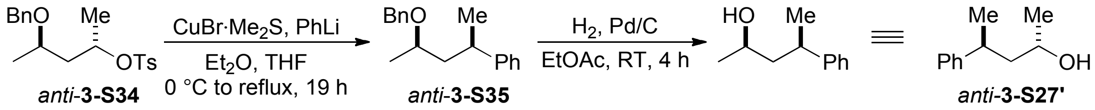
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.76 (d, J = 8.2 Hz, 2H), 7.38-7.24 (m, 7H), 4.75 (tq, J = 6.9 and 6.1 Hz, 1H), 4.51 (d, J = 11.8 Hz, 1H), 4.34 (d, J = 11.7 Hz, 1H), 3.50 (tq, J = 6.8 and 6.1 Hz, 1H), 2.43 (s, 3H), 2.01 (dt, J = 13.8 and 6.9 Hz, 1H), 1.58 (dt, J = 14.1 and 6.2 Hz, 1H), 1.25 (d, J = 6.3 Hz, 3H), 1.11 (d, J = 6.1 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 144.6, 138.7, 134.6, 129.9, 128.5, 127.9, 127.66, 127.71, 78.1, 71.2, 70.1, 43.6, 21.8, 21.0, 19.5.

MS (70 eV, EI) *m/z* (%): 177 (3) [M–OTs]$^+$, 159 (4), 135 (17), 91 (100), 65 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3031 (w), 2974 (w), 2929 (w), 2870 (w), 1597 (w), 1495 (w), 1453 (w), 1352 (m), 1306 (w), 1292 (w), 1210 (w), 1188 (m), 1174 (s), 1129 (s), 1091 (m), 1065 (w), 1028 (w), 1017 (w), 911 (s), 890 (vs), 862 (m), 815 (m), 780 (w), 735 (m), 697 (m), 689 (m), 662 (s).

HRMS (ESI) *m/z*: calcd for $C_{19}H_{24}O_4NaS^+$ [M+Na]$^+$: 371.1293, found: 371.1285.



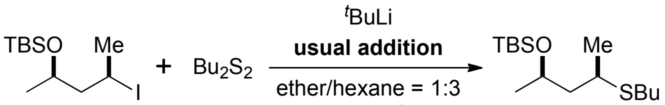
anti-**3-S27’**

A dry and Ar-flushed *Schlenk*-flask was charged with CuBr·Me$_2$S (1.2 g, 6.0 mmol) in Et$_2$O (15.0 mL) and cooled to 0 °C. PhLi (6.7 mL, 1.80 M in Bu$_2$O, 12.0 mmol) was added to the reaction mixture dropwise for 10 min. After stirring at 0 °C for 1 h, the reaction mixture was warmed up to room temperature. A solution of *anti*-**3-S34** (1.4 g, 3.0 mmol, d.r. = 96:4) in THF (30 mL) was added dropwise for 15 min and the reaction mixture was stirred at reflux for 19 h. The reaction was quenched with NH$_3$ aqueous solution and the mixture was extracted with Et$_2$O three times. The combined organic solution was dried over MgSO$_4$. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/30 to afford a mixture of *anti*-**3-S35** and other side products as colorless oil. This mixture was dissolved in EtOAc (5.0 mL) in a flask and Pd on C (0.25 g, 0.12 mmol, 10% Pd) was added to the reaction mixture. Then H$_2$ was bubbled into the mixture and it was stirred under H$_2$ atmosphere at room temperature for 4 h. Pd powder was filtered off and solvents were evaporated. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/2 to afford *anti*-**3-S27’** (141 mg, 29% yield over 2 steps, d.r. = 96:4) as colorless oil.

9.3.5 Kinetic measurement

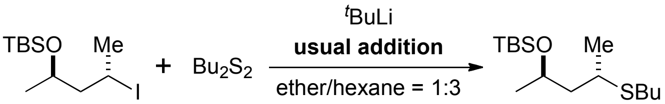
Kinetic measurements were carried out by using the general procedure of an I/Li exchange and the reaction mixture was stirred at different temperature for different times before quenching.

9.3.6 *In-situ* trapping reaction



syn-**3-3a** *syn*-**3-5a**

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (1.7 mL) and Et_2O (0.4 mL) and cooled to –100 °C. Bu_2S_2 (0.29 mL, 1.5 mmol) and *syn*-**3-3a** (99 mg, 0.30 mmol, d.r. = 98:2) in *n*-hexane (0.4 mL) and Et_2O (0.3 mL) was added. ^{t}BuLi (1.6 mL, 1.83 M in *n*-pentane, 2.7 mmol) was added dropwise and the reaction mixture was stirred for 30 min at –100 °C. The reaction was quenched with NH_4Cl aqueous solution and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$. Solvents were evaporated. The GC analysis revealed d.r. = 98:2 (74% conversion of *syn*-**3-5a**, 22% GC yield). The relative configuration was determined by S_N2 reactions of *syn*- and *anti*-**3-3a** with NaSBu.



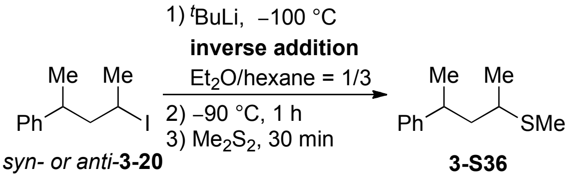
anti-**3-3a** *anti*-**3-5a**

A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (1.7 mL) and Et_2O (0.4 mL) and cooled to –100 °C. Bu_2S_2 (0.29 mL, 1.5 mmol) and *anti*-**3-3a** (99 mg, 0.30 mmol, d.r. = 98:2) in *n*-hexane (0.4 mL) and Et_2O (0.3 mL) was added. ^{t}BuLi (0.66 mL, 1.83 M in *n*-pentane, 1.2 mmol) was added dropwise and the reaction mixture was stirred for 30 min at –100 °C. The reaction was quenched with 7 drops of saturated NH_4Cl aqueous solution and after an addition of $MgSO_4$ this mixture was passed through a pad of silica gel with EtOAc. Solvents were evaporated. The GC analysis revealed d.r. = 95:5 (98% conversion of *syn*-**3-3a**). The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane =

1/100 to afford *syn*-**3-5a** (34 mg, 39% yield) as colorless oil. The relative configuration was determined by S_N2 reactions of *syn*- and *anti*-**3-3a** with NaSBu.

These experiments ensure I/Li exchange proceeds with retention of configuration.[36h] Also they ensure the trapping reaction with Bu_2S_2 is much faster than the epimerization. So this trapping reaction can be used for the epimerization kinetics.

9.3.7 Concentration effect on the epimerization



syn-**3-S36**

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.34-7.24 (m, 2H), 7.24-7.16 (m, 3H), 2.93 (dqd, *J* = 8.7, 6.7 and 6.5 Hz, 1H), 2.48 (dqd, *J* = 8.6, 6.5 and 6.0 Hz, 1H), 2.01 (s, 3H), 1.94 (ddd, *J* = 13.8, 8.7 and 6.1 Hz, 1H), 1.65 (ddd, *J* = 13.8, 8.5 and 6.5 Hz, 1H), 1.264 (d, *J* = 6.7 Hz, 3H), 1.260 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 146.9, 128.6, 127.1, 126.2, 45.1, 38.8, 37.6, 22.8, 20.6, 12.9.

MS (70 eV, EI) *m/z* (%): 194 (24) $[M]^{+\bullet}$, 146 (36), 131 (100), 115 (5), 105 (45), 91 (16), 77 (15), 61 (5), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3060 (w), 3025 (w), 2957 (w), 2917 (w), 2867 (w), 1602 (w), 1582 (w), 1492 (w), 1450 (w), 1375 (w), 1274 (w), 1186 (w), 1126 (w), 1061 (w), 1027 (w), 1010 (w), 953 (w), 907 (w), 761 (m), 698 (vs).

HRMS (ES) *m/z*: calcd for **$C_{12}H_{18}S^{+\bullet}$** $[M]^{+\bullet}$: 194.1129, found: 194.1137.

anti-**3-S36**

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.35-7.16 (m, 5H), 3.04 (dqd, *J* = 8.4, 7.0 and 6.3 Hz, 1H), 2.42 (dqd, *J* = 8.3, 6.5 and 6.3 Hz, 1H), 2.02 (s, 3H), 1.75 (dd, *J* = 8.1 and 6.4 Hz, 1H), 1.74 (dd, *J* = 8.5 and 6.4 Hz, 1H), 1.26 (d, *J* = 7.0 Hz, 3H), 1.23 (d, *J* = 6.7 Hz, 3H).

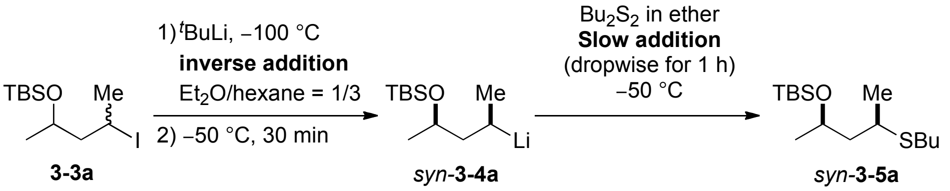
^{13}C-NMR (75 MHz, CDCl$_3$) δ: 147.1, 128.85, 127.2, 126.2, 45.3, 39.3, 37.5, 22.6, 21.7, 12.6.

MS (70 eV, EI) *m/z* (%): 194 (25) $[M]^{+\bullet}$, 146 (37), 131 (100), 105 (39), 91 (29), 77 (24).

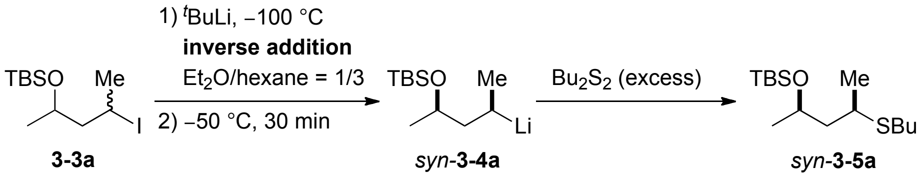
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3082 (w), 3026 (w), 2955 (w), 2916 (w), 2867 (w), 1602 (w), 1582 (w), 1493 (w), 1451 (w), 1373 (w), 1270 (w), 1259 (w), 1210 (w), 1046 (w), 1028 (w), 1016 (w), 954 (w), 907 (w), 761 (m), 698 (vs).

HRMS (ESI) *m/z*: calcd for $\mathbf{C_{12}H_{18}S^{+\bullet}}$ $[M]^{+\bullet}$: 194.1129, found: 194.1121.

9.3.8 Variation of the addition speed or the concentration of the electrophile



A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (1.7 mL) and Et$_2$O (0.4 mL) and cooled to –100 °C. ^{t}BuLi (0.36 mL, 2.10 M in *n*-pentane, 0.75 mmol) was added to the reaction mixture. Then, a solution of diastereomeric mixture of **3-3a** (99 mg, 0.30 mmol, d.r. = 50:50) in *n*-hexane (0.4 mL) and Et$_2$O (0.3 mL) was added dropwise in 10 min. After stirring at –100 °C for 10 min, the reaction mixture was warmed up to –50 °C and stirred for 30 min. Bu$_2$S$_2$ (114 µL, 0.60 mmol) in Et$_2$O (1.0 mL) was added dropwise for 1 h with a syringe pump to the reaction mixture and it was stirred at –50 °C for 30 min. The reaction mixture was quenched with 7 drops of saturated NH$_4$Cl aqueous solution and after an addition of MgSO$_4$ this mixture was passed through a pad of silica gel with EtOAc. Solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/100 to afford *syn*-**3-5a** (62 mg, 71% yield, d.r. = 86:14) as colorless oil. In the case of the addition at –100 °C, the reaction mixture was cooled down to –100 °C again after the 30 min stirring at –50 °C. Bu$_2$S$_2$ was added in one portion or its solution in Et$_2$O was added dropwise for 1 h with a syringe pump. After work-up, we have obtained the following results depending on the way of the addition: addition in one portion: 72% GC yield, d.r. = 90:10; slow addition: 73% GC yield, d.r. = 85:15.



A dry and Ar-flushed *Schlenk*-flask was charged with *n*-hexane (0.85 mL) and Et$_2$O (0.2 mL) and cooled to –100 °C. ^{t}BuLi (0.18 mL, 2.10 M in *n*-pentane, 0.38 mmol) was added to the reaction mixture. Then, a solution of diastereomeric mixture of **3-3a** (49 mg, 0.15 mmol, d.r. = 50:50) in *n*-hexane (0.2 mL) and Et$_2$O (0.15 mL) was dropwise added in 5 min. After stirring at –100 °C for 10 min, the reaction mixture was warmed up to –50 °C and stirred for

30 min. Bu_2S_2 (57 µL, 0.30 mmol or 284 µL, 1.5 mmol or 557 µL, 3.0 mmol) was added in one portion and the reaction mixture was stirred at –50 °C for 30 min. After work-up, we have obtained the following results depending on the electrophile amount: 2 equiv addition: 75% GC yield, d.r. = 93:7; 10 equiv addition: 73% yield, d.r. = 95:5; 20 equiv addition: 70% yield, d.r. = 95:5)

9.3.9 Theoretical calculation

Following earlier theoretical work on organolithium species[22, 126, 127, 128, 129] geometry optimizations have been performed at the B3LYP/6-31+G(d) level of theory. Thermal corrections to enthalpies (H_{298}) and free energies (G_{298}) at 298.15 K have been calculated at the same level using the rigid rotor/harmonic oscillator model. Single point energies have subsequently been calculated at the B3LYP/6-311+G(2d,p) and MP2(FC)/6-311+G(2d,p) level of theory and combined with thermal corrections obtained at B3LYP/6-31+G(d) level in order to calculate free energies at 298.15 K. Thermochemical corrections have also been calculated for –100 °C (= 173.15 K) in order to obtain free energies at this temperature (G_{173}). Solvation free energies have been calculated as the difference between the gas phase total energy and the free energy in solution as obtained from single point calculations with the SMD continuum solvation model at the B3LYP/6-31+G(d) level of theory.[130] Free energies in solution have been corrected to a reference state of 1 mol/l at 298.15 K through addition of RTln(24.46) = +7.925 kJ/mol to the gas phase (1 atm) free energies. At –100 °C (= 173.15 K) this correction amounts to +4.603 kJ/mol. All calculations have been performed with *Gaussian 09*.[131]

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Structure of all calculated species (most stable conformers each)

syn-**3-4a** (e,a)

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1\1\GINC-HP2\SP\RMP2-FC\6-311++G(2d,p)\C15H35Li1O2Si1\ZIPSE\19-Aug-201
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 =10GB\\aclieth_018, b3lyp/6-31+G(d) opt TBSO-ether + Et2O\\0,1\C,0,0.7
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 929,-1.9430627022,-1.910282895\H,0,1.5411419514,-1.4079290506,-0.35636
 08347\H,0,-0.2231301835,-1.4956216304,-0.5881836498\C,0,2.0430350791,0
 .579530342,-2.2971461918\H,0,1.8979674268,1.5971178359,-2.6988475192\H
 ,0,2.1051266147,-0.0737085558,-3.2005107313\C,0,3.2924661533,0.5607358
 749,-1.4034253908\O,0,0.5277364349,1.0914210092,-0.4339629545\Si,0,-0.
 9288925277,1.9041506106,-0.1154798172\C,0,-0.8524974895,2.30262783,1.7
 286400336\H,0,-1.7318580833,2.8733655493,2.0513760745\H,0,-0.833181670
 1,1.3746348663,2.3139018052\H,0,0.0389620268,2.8834320477,1.9919897195
 \C,0,-2.4013159343,0.7635583914,-0.4457113467\H,0,-3.3418457679,1.2710
 496525,-0.1962967317\H,0,-2.4710667293,0.4403253872,-1.4905034746\H,0,
 -2.3399194617,-0.1368391538,0.1777321318\C,0,-1.0543777965,3.511565052
 4,-1.1623711196\C,0,-2.3099887564,4.3073779654,-0.7358923166\H,0,-2.27
 19731332,4.6109439884,0.3177725811\H,0,-2.3946870919,5.2267054329,-1.3
 344550742\H,0,-3.2353334877,3.7373408028,-0.8894679451\C,0,-1.16421143
 43,3.1869092548,-2.6691854343\H,0,-1.247236243,4.1176343056,-3.2504560
 359\H,0,-0.2833295016,2.6510958139,-3.040850711\H,0,-2.0512094481,2.58
 29313459,-2.8983255309\C,0,0.195711263,4.3895729298,-0.9338291363\H,0,
 0.1205978457,5.317609871,-1.5203806153\H,0,0.3089577303,4.6803610569,0
 .1186100397\H,0,1.1146766309,3.8797328813,-1.2463866213\Li,0,2.3568802
 964,1.3541444348,0.2429184811\C,0,4.4737145884,1.1886915443,-2.1548124
 421\H,0,5.4059031136,1.1193139728,-1.5743521487\H,0,4.6876684226,0.727
 0578651,-3.1450379858\H,0,4.3113920555,2.2614168191,-2.3587110088\H,0,
 3.5590953339,-0.4985117087,-1.2237580319\O,0,2.837782246,2.0107660465,
 2.0401913785\C,0,4.0094226547,2.8437328279,2.139146333\H,0,3.972005587
 4,3.3735457727,3.1025305495\H,0,4.9085361857,2.2154887824,2.1225067008
 \C,0,2.6066260502,1.1644043005,3.1803901194\H,0,2.6128372491,1.7904781
 463,4.0848496668\H,0,1.589626408,0.7845114766,3.0453532832\C,0,3.59660
```

```
14075,0.0093194939,3.3052822014\H,0,4.6126775066,0.355349483,3.5215668
166\H,0,3.2870271844,-0.6458932537,4.1287944591\H,0,3.6236489513,-0.58
32400774,2.3841956096\C,0,4.0217590731,3.8198490049,0.9756255189\H,0,3
.1287130744,4.4546362216,0.9848613096\H,0,4.9037115298,4.4670283917,1.
0477862889\H,0,4.0731907038,3.2843052547,0.0204958887\\Version=AM64L-G
09RevC.01\State=1-A\HF=-1034.780601\MP2=-1037.7590254\RMSD=4.299e-09\P
G=C01 [X(C15H35Li1O2Si1)]\\@
```

syn-**3-4a** (a,e)

```
1\1\GINC-HP4\SP\RMP2-FC\6-311++G(2d,p)\C15H35Li1O2Si1\ZIPSE\13-Aug-201
4\0\\#P MP2(FC)/6-311++G(2d,p) scf=tight geom=check guess=read MaxDisk
=10GB\\aclieth_004, b3lyp/6-31+G(d) opt TBSO-ether + Et2O\\0,1\C,0,0.5
095722718,2.2428270639,-0.3592600969\H,0,1.1811153643,2.392992841,-1.2
121692459\C,0,0.9348795008,3.1414944212,0.7997319243\H,0,0.8044033208,
4.1931721642,0.5183790663\H,0,0.3133633497,2.9463005757,1.6822926645\H
,0,1.9845520464,2.9985977504,1.0816257759\C,0,-0.9335902608,2.52239529
76,-0.820392567\H,0,-0.8930586653,3.5669035261,-1.2142526595\H,0,-1.56
92704787,2.5812867699,0.0830587192\C,0,-1.5161538847,1.5089320198,-1.8
194468572\O,0,0.6396649088,0.8250845139,0.0382182849\Li,0,-1.118443286
,0.0806819935,-0.4296663364\Si,0,2.136640286,0.0165216887,0.1438986079
\C,0,2.6328040068,-0.0778120912,1.9667682033\H,0,3.5456405178,-0.67011
03443,2.1093198013\H,0,2.8251046849,0.9244037341,2.3684352284\H,0,1.84
28238922,-0.529111428,2.5785501876\C,0,3.4614755707,0.9582818848,-0.82
28276663\H,0,4.4261192292,0.4445197334,-0.7247879507\H,0,3.2314136877,
1.0274869956,-1.8923849702\H,0,3.6013934254,1.9776802016,-0.4459162365
\C,0,1.9133207837,-1.7482749294,-0.5912280365\C,0,3.2850203237,-2.4641
813004,-0.6014297719\H,0,3.713286311,-2.5588259846,0.4046557869\H,0,3.
1737330199,-3.4823866585,-1.0029570669\H,0,4.0169469781,-1.9465081228,
-1.2327434111\C,0,1.387239971,-1.6670775238,-2.0416936215\H,0,1.263455
3556,-2.6787817811,-2.4566994713\H,0,0.4178976784,-1.1580266759,-2.114
4988023\H,0,2.082263075,-1.1302585506,-2.6988313385\C,0,0.9370778987,-
2.5894265113,0.2593912086\H,0,0.8356425255,-3.5983216281,-0.1685477821
\H,0,1.2911079775,-2.7081374241,1.2913471308\H,0,-0.0698782564,-2.1582
398544,0.3021121606\O,0,-2.4259988243,-1.0159031177,0.5715644463\C,0,-
```

```
3.4316066148,-1.5483380387,-0.31949708\H,0,-2.9178846754,-1.6642487356
,-1.2776549654\H,0,-3.717233921,-2.5456358674,0.0472522184\C,0,-2.8217
781028,-0.9603100181,1.9505763723\H,0,-3.5950330101,-0.1919956068,2.08
04343209\H,0,-3.2578863035,-1.9319659581,2.2266646546\C,0,-1.612032659
,-0.6491714405,2.8154284502\H,0,-0.8557222379,-1.436375383,2.733338321
4\H,0,-1.1537451543,0.3037197527,2.529757935\H,0,-1.9203676296,-0.5762
653719,3.8649239115\C,0,-4.6474334851,-0.6456679933,-0.489225584\H,0,-
5.3111438952,-1.0784463189,-1.2478864388\H,0,-5.2265787141,-0.54276028
95,0.4350809595\H,0,-4.3353216195,0.3453484165,-0.8332691813\C,0,-0.85
50642784,1.6504643431,-3.194386541\H,0,-1.385900834,1.0578796332,-3.95
31048621\H,0,-0.8186815876,2.6975636886,-3.5760795237\H,0,0.1879087286
,1.2924109459,-3.208099671\H,0,-2.5828416414,1.7727926024,-1.932864224
3\\Version=AM64L-G09RevC.01\State=1-A\HF=-1034.7739027\MP2=-1037.75564
94\RMSD=5.315e-09\PG=C01 [X(C15H35Li1O2Si1)]\\@
```

anti-**3-4a** (a,a)

```
1\1\GINC-HP4\SP\RMP2-FC\6-311++G(2d,p)\C15H35Li1O2Si1\ZIPSE\19-Aug-201
 4\0\\#P MP2(FC)/6-311++G(2d,p) scf=tight geom=check guess=read MaxDisk
 =10GB\\aclieth_033, b3lyp/6-31+G(d) opt TBSO-ether + Et2O\\0,1\C,0,1.7
 162237005,0.7472565821,0.3441523402\H,0,1.4247858966,1.6951915785,0.81
 74989371\C,0,2.2310140076,1.0396560759,-1.061912514\H,0,3.1502359378,1
 .6352564582,-1.0067127098\H,0,2.4670463507,0.1086288658,-1.5876665537\
 H,0,1.4924597521,1.5968673848,-1.6502001995\C,0,2.7196738655,0.0122143
 641,1.2555194801\H,0,2.2607097424,-0.0084857767,2.2567805542\H,0,3.596
 1886048,0.6961968777,1.345435681\C,0,3.0933511577,-1.4201189726,0.8317
 480224\O,0,0.4960916821,-0.0805344533,0.2183731051\Si,0,-1.0834489482,
 0.4907144981,0.4637060267\C,0,-2.1794624593,-0.7574340382,-0.435355641
 1\H,0,-3.2425163551,-0.523478291,-0.2991356518\H,0,-1.9756515953,-0.73
 23947517,-1.513230232\H,0,-2.0164588464,-1.7845781192,-0.0888196727\C,
 0,-1.2966470412,2.1929616288,-0.3336221575\H,0,-2.3237308709,2.5553644
 244,-0.1984634078\H,0,-0.6245449109,2.9509628821,0.084294437\H,0,-1.10
 75988144,2.1410582594,-1.4129400131\C,0,-1.5065906961,0.5467388451,2.3
 384506222\C,0,-3.0013376436,0.8999460701,2.519434641\H,0,-3.6627112448
 ,0.15535424,2.0593961888\H,0,-3.2523476101,0.9387839846,3.5899184557\H
```

```
,0,-3.2509262328,1.8808934499,2.0947262917\C,0,-0.6573842053,1.6094382
811,3.0713452652\H,0,-0.9256799586,1.6364394554,4.138257818\H,0,0.4151
416055,1.3915609003,3.0136227501\H,0,-0.821346438,2.618084456,2.671347
6922\C,0,-1.2366760781,-0.8335199522,2.9770913348\H,0,-1.4801070058,-0
.8109199451,4.0500010779\H,0,-1.8483563349,-1.6239996059,2.5231908317\
H,0,-0.1836564249,-1.1248193519,2.8856329475\Li,0,1.2420766874,-1.8875
883587,0.0675523955\C,0,4.3827828406,-1.4751957927,-0.0040005303\H,0,5
.2227207861,-0.8849310211,0.4282080107\H,0,4.7444562609,-2.5101030319,
-0.0978244801\H,0,4.2622548878,-1.1024139389,-1.0336711916\H,0,3.30718
72613,-1.9678758264,1.7662286747\O,0,0.376806321,-3.448212225,-0.76311
43485\C,0,0.7097148505,-4.737615866,-0.2112969216\H,0,-0.0036596065,-5
.4742554063,-0.6091768826\H,0,1.7198189978,-5.0223715743,-0.5305524678
\C,0,0.6320507496,-4.6634243436,1.3039134059\H,0,0.8782746855,-5.64202
59674,1.7326679158\H,0,1.3519406919,-3.9337053928,1.6928087293\H,0,-0.
3755409175,-4.3873820252,1.6344107674\C,0,0.1723448229,-3.4412131418,-
2.1873258281\H,0,-0.5739011653,-4.2106455565,-2.4342880954\H,0,-0.2722
545125,-2.4646271439,-2.4010858611\C,0,1.4504737925,-3.6368082704,-2.9
98325043\H,0,1.8777309987,-4.6360460736,-2.863857776\H,0,1.225428754,-
3.5130734284,-4.0647825905\H,0,2.2098521945,-2.8983747996,-2.718704390
4\\Version=AM64L-G09RevC.01\State=1-A\HF=-1034.7782119\MP2=-1037.75706
18\RMSD=4.783e-09\PG=C01 [X(C15H35Li1O2Si1)]\\@
```

anti-**3-4a** (e,e)

```
1\1\GINC-HP1\SP\RMP2-FC\6-311++G(2d,p)\C15H35Li1O2Si1\ZIPSE\13-Aug-201
4\0\\#P MP2(FC)/6-311++G(2d,p) scf=tight geom=check guess=read MaxDisk
=10GB\\aclieth_005, b3lyp/6-31+G(d) opt TBSO-ether + Et2O\\0,1\C,0,1.6
537134136,0.9216588672,0.2221870226\H,0,1.3816599596,1.3517861689,1.19
41370969\C,0,1.9473918013,2.0366555043,-0.779592665\H,0,2.8408923564,2
.5894146169,-0.4665321968\H,0,2.1376885322,1.6146842565,-1.7736314049\
H,0,1.1233108328,2.7546831542,-0.8640167633\C,0,2.8503031691,-0.015471
3435,0.4341155349\H,0,3.6537069376,0.6348413517,0.8559360631\H,0,3.237
4306296,-0.3052438042,-0.5641486386\C,0,2.5526607417,-1.264857447,1.27
84571277\H,0,2.1677095566,-0.9146682391,2.255407362\C,0,3.8536617032,-
2.0302109428,1.5343948064\H,0,4.6710307966,-1.4178624716,1.9798796804\
```

```
H,0,3.6964607692,-2.8788118566,2.2171732626\H,0,4.2763627557,-2.451746
528,0.6051164398\O,0,0.4858151947,0.1394726692,-0.2353771728\Li,0,1.16
40300548,-1.7080611456,-0.1310599867\Si,0,-1.1160048313,0.7113903234,-
0.1488583663\C,0,-1.6235696025,1.3458729535,-1.8570895262\H,0,-2.67642
75095,1.6549565291,-1.8771095036\H,0,-1.0202841084,2.2157234571,-2.143
434883\H,0,-1.4856802439,0.5836150965,-2.6332212452\C,0,-1.2465339972,
2.11800133,1.10837012\H,0,-2.2772806206,2.4932867638,1.1383942442\H,0,
-0.9815250156,1.7981141252,2.1228633764\H,0,-0.6037154016,2.9669484232
,0.8491127141\C,0,-2.2268681113,-0.761510881,0.3910666404\C,0,-3.68606
18555,-0.2697217955,0.5421071619\H,0,-4.0946341777,0.1205618694,-0.398
797931\H,0,-4.3322211206,-1.1036652372,0.854240743\H,0,-3.7822261227,0
.5143543989,1.302733046\C,0,-1.7482699967,-1.3199086971,1.750740069\H,
0,-2.3737423808,-2.1745277268,2.0499931483\H,0,-0.7055464364,-1.661452
9036,1.7267056725\H,0,-1.8234086466,-0.5698048843,2.5476179374\C,0,-2.
2065657404,-1.8922204729,-0.6605007769\H,0,-2.8673491088,-2.7139617732
,-0.3452883027\H,0,-2.5603922512,-1.5492439255,-1.6410578663\H,0,-1.20
79902552,-2.3236990609,-0.7976064273\O,0,1.2482713911,-3.2644377843,-1
.321597245\C,0,1.7568732746,-4.4094943152,-0.5995178656\H,0,2.62844391
09,-4.7983310302,-1.145251206\H,0,2.1022875208,-3.9920474595,0.3506330
255\C,0,1.0099824412,-3.4830003088,-2.7189696595\H,0,1.8368064415,-4.0
849505743,-3.1230896862\H,0,0.0799297975,-4.0529480276,-2.8505718195\C
,0,0.9278852855,-2.1446053067,-3.4340328722\H,0,0.1177182669,-1.528105
3552,-3.0311046186\H,0,1.8668670643,-1.5894645162,-3.3353902048\H,0,0.
732492119,-2.306016761,-4.5006911499\C,0,0.7129592235,-5.4981288984,-0
.3809006401\H,0,1.1476587311,-6.2977849285,0.2311768577\H,0,-0.1586630
202,-5.1006327314,0.1510652695\H,0,0.3722454323,-5.9478708853,-1.32059
38381\\Version=AM64L-G09RevC.01\State=1-A\HF=-1034.7749314\MP2=-1037.7
550528\RMSD=1.467e-09\PG=C01 [X(C15H35Li1O2Si1)]\\@
```

anti-**3-22** (e,e)

```
1\1\GINC-T2\SP\RMP2-FC\6-311++G(2d,p)\C15H25Li1O1\ROOT\23-Aug-2014\0\\
 #P MP2(FC)/6-311++G(2d,p) scf=tight geom=check guess=read MaxDisk=10GB
 \\phlieth_017, b3lyp/6-31+G(d) opt TBSO-ether + Et2O\\0,1\C,0,0.576343
 0255,2.6775067335,-0.3687559629\H,0,1.0259683041,1.8849033469,-0.98530
```

```
72924\C,0,1.7057425321,3.6562101436,0.0203935325\H,0,2.1539480653,4.09
39125373,-0.8795549882\H,0,1.3191468428,4.4792671081,0.6353000746\H,0,
2.4995074274,3.1565852723,0.5900354112\C,0,-0.5090640016,3.3600032485,
-1.2324168571\H,0,0.024083023,3.8489592222,-2.078659418\H,0,-0.9355948
207,4.2029114082,-0.6577278939\C,0,-1.6271394656,2.4167281116,-1.69911
17129\Li,0,-2.432660448,1.4599411949,-0.0783761483\C,0,-2.5638595984,3
.1717165186,-2.6563247785\H,0,-2.0409390781,3.6715188934,-3.501881778\
H,0,-3.3167421204,2.5067821427,-3.1070723481\H,0,-3.1208310093,3.97380
50029,-2.1415063087\H,0,-1.1313799779,1.6256671873,-2.3021833271\O,0,-
3.9123622695,0.4000283313,0.5792971618\C,0,-3.7422484002,-0.9882518149
,0.9224456519\H,0,-2.7417237555,-1.0477997558,1.3605968652\H,0,-4.4685
58872,-1.2411625977,1.7082420721\C,0,-3.8674184758,-1.9330950692,-0.26
85950708\H,0,-3.6307377021,-2.9550477089,0.051751478\H,0,-4.8800305325
,-1.9432923969,-0.6856236026\H,0,-3.1678151756,-1.6531034276,-1.063987
0192\C,0,-5.2632982341,0.7895725309,0.2634547518\H,0,-5.5559275839,0.3
51028354,-0.6989430288\H,0,-5.9262442307,0.3878642764,1.0432826625\C,0
,-5.3420110756,2.305947029,0.2084473504\H,0,-4.6761530501,2.7099913069
,-0.5626990633\H,0,-6.3654552195,2.612016739,-0.0375945855\H,0,-5.0759
567775,2.7472598458,1.1755360663\C,0,0.0203216647,1.9984658108,0.87662
3898\C,0,0.3928426749,0.6843720659,1.2102176305\C,0,-0.828170832,2.677
6590929,1.7738766968\C,0,-0.050370249,0.0732857084,2.3893421757\H,0,1.
0476920114,0.1361150355,0.5357494156\C,0,-1.2784447236,2.0711933788,2.
950772634\H,0,-1.1295481146,3.698416845,1.5506199326\C,0,-0.8889317932
,0.7645602515,3.2677363429\H,0,0.2668875076,-0.9409568454,2.6223683039
\H,0,-1.9287021701,2.6232843147,3.6256801419\H,0,-1.2310116216,0.29657
85774,4.1874322442\\Version=AM64L-G09RevC.01\State=1-A\HF=-665.0469662
\MP2=-667.5948118\RMSD=2.306e-09\PG=C01 [X(C15H25Li1O1)]\\@
```

syn-**3-22** (a,e)

```
1\1\GINC-HP1\SP\RMP2-FC\6-311++G(2d,p)\C15H25Li1O1\ZIPSE\25-Aug-2014\0
\\#P MP2(FC)/6-311++G(2d,p) scf=tight geom=check guess=read MaxDisk=10
GB\\phlieth_026, b3lyp/6-31+G(d) opt TBSO-ether + Et2O\\0,1\C,0,0.7060
559912,1.8133507628,0.5342765075\H,0,0.7922286785,2.3516225423,-0.4200
442595\C,0,2.0775146578,1.9129556755,1.2386440275\H,0,2.3272552221,2.9
```

```
632551595,1.4312145351\H,0,2.0613685557,1.3905524182,2.2041833913\H,0,
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syn-**3-22** (2Eth)

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GB\\phli2eth_024, b3lyp/6-31+G(d) opt TBSO-ether + Et2O\\0,1\C,0,1.958
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anti-**3-22** (2Eth)

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1\H,0,3.8675027651,-2.9980358522,-1.7655567424\C,0,0.8394325084,-1.459
3388157,-0.7858212793\H,0,0.3042926392,-2.2736919962,-1.3075323025\H,0
,0.8875428232,-0.63201667,-1.5185502745\C,0,0.0360454694,-1.0602593496
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diethyl ether

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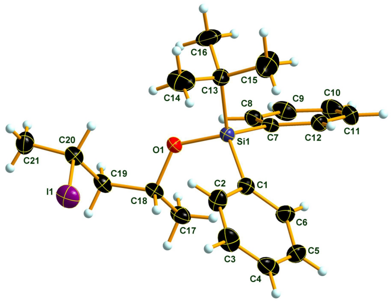
```

9.3.10 X-ray crystal information

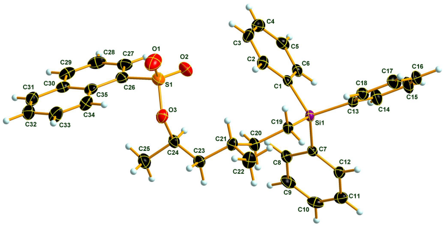
CCDC/1015348 (for *syn*-**3-3c**) and CCDC/1015349 (for *syn*-**3-S33**) contain supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



syn-**3-3c** (Thermal ellipsoids are drawn at 50 % probability level.)

net formula	$C_{21}H_{29}IOSi$
M/g mol^{-1}	452.43
crystal size/mm	0.20 × 0.15 × 0.10
T/K	173(2)
radiation	MoKα
diffractometer	‘Xcalibur, Sapphire3’
crystal system	monoclinic
space group	P 21/c
a/Å	13.2337(3)
b/Å	11.3563(2)
c/Å	14.4610(3)
α/°	90.00
β/°	90.819(2)
γ/°	90.00
V/Å^3	2173.06(8)
Z	4
calc. density/g cm^{-3}	1.383
μ/mm^{-1}	1.543
absorption correction	multi-scan
refls. measured	41138
R_{int}	0.0441
mean σ(*I*)/*I*	0.0281

θ range	4.50–29.49
observed refls	10437
x,y (weighting scheme)	0.0337, 0.5944
hydrogen refinement	mixed
refls in refinement	6322
parameters	240
restraints	0
$R(F_{\mathrm{obs}})$	0.0452
$R_{\mathrm{w}}(F^2)$	0.0750
S	1.020
shift/error$_{\mathrm{max}}$	0.001
max electron density/e Å^{-3}	0.572
min electron density/e Å^{-3}	–0.608



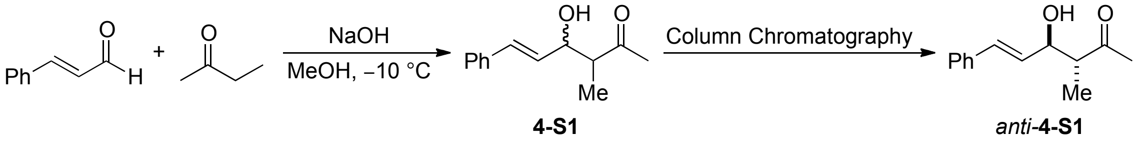
syn-**3-S33** (Thermal ellipsoids are drawn at 50 % probability level.)

net formula	$C_{35}H_{36}O_3SSi$
M/g mol^{-1}	564.79
crystal size/mm	0.224 × 0.155 × 0.092
T/K	173(2)
radiation	MoKα
diffractometer	'Xcalibur, Sapphire3'
crystal system	monoclinic
space group	P 21
a/Å	9.2179(4)
b/Å	15.1321(6)
c/Å	11.4528(7)
α/°	90.00
β/°	100.541(6)
γ/°	90.00

V/Å^3	1495.94(13)
Z	2
calc. density/g cm^{-3}	1.254
μ/mm^{-1}	0.182
absorption correction	multi-scan
refls. measured	15592
R_{int}	0.0374
mean $\sigma(I)/I$	0.0631
θ range	4.41–29.98
observed refls	4064
x,y (weighting scheme)	0.0374, 0.0641
hydrogen refinement	mixed
refls in refinement	8188
parameters	392
restraints	1
$R(F_{\mathrm{obs}})$	0.0631
$R_{\mathrm{w}}(F^2)$	0.0958
S	1.024
shift/error$_{\mathrm{max}}$	0.001
max electron density/e Å^{-3}	0.300
min electron density/e Å^{-3}	–0.271

9.4 Stereoretentive Preparation of Open-Chain Secondary Alkyllithiums Functionalized at 2-Position

9.4.1 Preparation of starting materials



anti-**4-S1** (CAS: 119752-16-8)

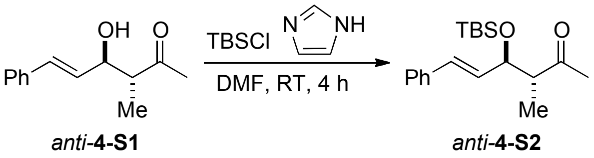
A 500 mL flask was charged with cinnam aldehyde (25.2 mL, 200 mmol) and methyl ethyl ketone (17.8 mL, 200 mmol) in MeOH (150 mL) and it was cooled down to −10 °C. NaOH aqueous solution was added to the reaction mixture at −10 °C and stirred for 2 h. The reaction was quenched by adding the reaction mixture into ice water containing AcOH (20 mL). It was extracted with the mixture of EtOAc/hexane = 2/1 three times. The combined organic phase was washed with saturated $NaHCO_3$ aqueous solution and dried over $MgSO_4$. Solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/4 to afford *anti*-**4-S1** (2.9 g, 7% yield, d.r. = 99:1) as yellow oil.

^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.35-7.15 (m, 5H), 6.54 (d, *J* = 15.9 Hz, 1H), 6.11 (dd, *J* = 15.9 and 7.3 Hz, 1H), 4.31 (t, *J* = 7.5 Hz, 1H), 2.70 (quint, *J* = 7.3 Hz, 1H), 2.17 (s, 3H), 1.07 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 213.3, 136.56, 132.4, 129.5, 128.7, 128.0, 126.7, 75.1, 52.4, 30.1, 14.0.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3407 (br, s), 2974 (w), 2934 (w), 2878 (w), 1703 (m), 1494 (w), 1451 (w), 1356 (w), 1240 (w), 1169 (w), 1105 (w), 1071 (w), 1038 (w), 1009 (w), 966 (s), 748 (s), 693 (vs).

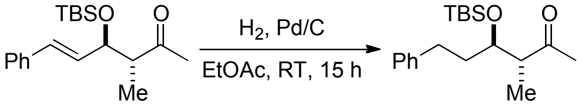
HRMS (ESI) *m/z*: calcd for **$C_{13}H_{15}O^{+\bullet}$** $[M–OH]^{+\bullet}$: 187.1123, found: 187.1117.



anti-**4-S2**

A 25 mL flask was charged with *anti*-**4-S1** (1.4 g, 7.0 mmol, d.r. = 99:1) and imidazole (1.2 g, 17.5 mmol) in DMF (15 mL) and it was cooled down to 0 °C. TBSCl (1.3 g, 8.4 mmol) was added to the reaction mixture at 0 °C and stirred for 2 h at room temperature. The reaction was quenched by saturated NH_4Cl aqueous solution. The reaction mixture was extracted with the mixture of Et_2O/*i*-hexane = 1/3 three times. The combined organic phase was dried over $MgSO_4$. Solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/5 to afford *anti*-**4-S2** (1.7 g, 78% yield, d.r. = 99:1) as yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: 7.35-7.18 (m, 5H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.01 (dd, *J* = 15.9 and 7.7 Hz, 1H), 4.32 (t, *J* = 8.1 Hz, 1H), 2.73 (quint, *J* = 7.1 Hz, 1H), 2.18 (s, 3H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.82 (s, 9H), 0.00 (s, 3H), –0.03 (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 212.1, 136.7, 131.9, 130.7, 128.8, 127.9, 126.6, 77.0, 53.3, 31.3, 26.0, 18.2, 13.4, –3.8, –4.9.
MS (70 eV, EI) *m/z* (%): 303 (1) $[M–Me]^{+\bullet}$, 261 (51), 247 (70), 189 (15), 157 (10), 143 (100), 129 (85), 115 (30), 91 (6), 75 (70).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2959 (w), 2930 (w), 2857 (w), 1716 (m), 1472 (w), 1462 (w), 1451 (w), 1359 (w), 1250 (w), 1166 (w), 1112 (w), 1055 (s), 1006 (w), 968 (m), 867 (m), 835 (vs), 813 (m), 776 (s), 741 (s), 692 (m), 668 (w).
HRMS (EI) *m/z*: calcd for $C_{18}H_{27}O_2Si^{+\bullet}$ $[M–Me]^{+\bullet}$: 303.1780, found: 303.1760.



anti-**4-S2** *anti*-**4-S3**

anti-**4-S3**

A 25 mL flask was charged with *anti*-**4-S2** (1.7 g, 5.3 mmol) and Pd on C (140 mg, Pd 5% wt) in EtOAc (10 mL). H_2 was bubbled to the reaction mixture at room temperature for 5 min and it was stirred for 15 h at room temperature. Pd on C was filtered off with Celite and EtOAc and solvents were evaporated to afford *anti*-**4-S3** (1.7 g, 99% yield, d.r. = 99:1) as yellow oil.

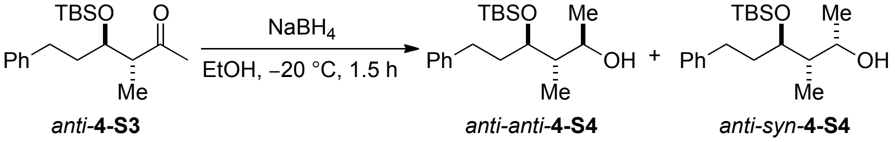
^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: 7.33-7.10 (m, 5H), 4.05-3.95 (m, 1H), 2.87-2.57 (m, 3H), 2.17 (s, 3H), 1.90-1.55 (m, 2H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.92 (s, 9H), 0.11 (s, 3H), 0.05 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 211.9, 142.4, 128.6, 126.0, 73.4, 51.8, 35.9, 30.6, 26.0, 18.2, 12.4, −4.2, −4.7.

MS (70 eV, EI) *m/z* (%): 305 (1) $[M{-}Me]^{+\bullet}$, 263 (70), 249 (4), 191 (11), 159 (21), 129 (66), 117 (54), 91 (56), 75 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2930 (w), 2857 (w), 1716 (m), 1496 (w), 1472 (w), 1462 (w), 1455 (w), 1357 (w), 1253 (w), 1173 (w), 1093 (w), 1053 (w), 1006 (w), 982 (m), 947 (w), 834 (vs), 814 (w), 774 (s), 746 (m), 698 (s), 666 (m).

HRMS (EI) *m/z*: calcd for **$C_{18}H_{29}O_2Si^{+\bullet}$** $[M{-}Me]^{+\bullet}$: 303.1937, found: 303.1929.



anti-syn-**4-S4** and *anti-anti*-**4-S4**

A 25 mL flask was charged with *anti*-**4-S3** (1.5 g, 4.8 mmol) in EtOH (10 mL) and it was cooled down to −20 °C. $NaBH_4$ (0.17 g, 4.5 mmol) was added portionwise to the reaction mixture and it was stirred for 2.5 h at room temperature. The reaction was quenched by saturated NH_4Cl aqueous solution. The reaction mixture was extracted with the mixture of Et_2O three times. The combined organic phase was dried over $MgSO_4$. Solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/5→1/4 to afford *anti-anti*-**4-S4** (0.42 g, 30% yield, d.r. = 99:1) as colorless oil and the first fraction, and *anti-syn*-**4-S4** (1.0 g, 67% yield, d.r. = 99:1) as white solid and the second fraction.

anti,syn-**4-S4**

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.33-7.25 (m, 2H), 7.22-7.14 (m, 3H), 3.83 (q, *J* = 5.0 Hz, 1H), 3.73 (dq, *J* = 7.9 and 6.3 Hz, 1H), 2.77-2.60 (m, 2H), 1.85-1.77 (m, 2H), 1.71 (h, *J* = 6.9 Hz, 1H), 1.17 (d, *J* = 6.2 Hz, 3H), 0.94 (s, 9H), 0.84 (d, *J* = 7.0 Hz, 1H), 0.12 (s, 3H), 0.11 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 142.8, 128.5, 128.5, 125.9, 75.9, 70.6, 44.9, 36.3, 30.9, 26.1, 21.2, 18.2, 12.8, −4.0, −4.5.

MS (70 eV, EI) *m/z* (%): 305 (1) $[M{-}Me]^{+\bullet}$, 263 (70), 249 (4), 191 (11), 159 (21), 129 (66), 117 (54), 91 (56), 75 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3426 (br, w), 2954 (w), 2929 (w), 2857 (w), 1496 (w), 1471 (w), 1462 (w), 1454 (w), 1379 (w), 1361 (w), 1253 (w), 1148 (w), 1058 (w), 1005 (w), 976 (w), 832 (vs), 813 (w), 773 (s), 747 (m), 697 (s), 665 (w).

HRMS (EI) *m/z*: calcd for **$C_{19}H_{35}O_2Si^{+\bullet}$** [M+H]$^{+\bullet}$: 323.2406, found: 323.2400.

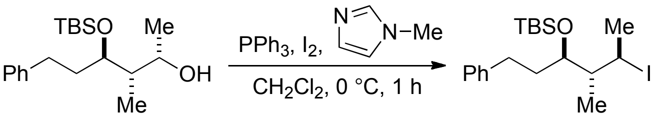
anti-anti-**4-S4**

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.33-7.25 (m, 2H), 7.23-7.14 (m, 3H), 4.29 (qd, *J* = 6.4 and 1.6 Hz, 1H), 3.78 (ddd, *J* = 8.0, 4.8 and 2.8 Hz, 1H), 2.64-2.49 (m, 2H), 2.10-1.98 (m, 1H), 1.95-1.81 (m, 1H), 1.60 (qt, *J* = 7.3 and 2.4 Hz, 1H), 1.14 (d, *J* = 6.4 Hz, 3H), 1.02 (d, *J* = 7.1 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 6H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 141.8, 128.6, 128.4, 126.1, 78.1, 66.3, 39.9, 36.8, 32.1, 26.0, 20.8, 18.1, 11.2, –4.1, –4.6.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3449 (br, w), 2954 (w), 2930 (w), 2857 (w), 1496 (w), 1471 (w), 1462 (w), 1454 (w), 1362 (w), 1253 (w), 1108 (w), 1057 (w), 1022 (m), 1002 (m), 978 (w), 960 (w), 938 (w), 919 (w), 833 (vs), 813 (w), 773 (s), 746 (m), 697 (s), 679 (m).

HRMS (ESI) *m/z*: calcd for **$C_{19}H_{35}O_2Si^{+\bullet}$** [M+H]$^{+\bullet}$: 323.2406, found: 323.2400.



anti-syn-**4-S4** *anti-anti*-**4-1a**

anti-anti-**4-1a**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.1 g, 4.2 mmol) in CH_2Cl_2 (20 mL) and cooled to 0 °C. PPh_3 (1.1 g, 4.2 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.33 mL, 4.2 mmol) was added. After 10 min of further stirring, *anti-syn*-**4-1a** (0.84 g, 2.6 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/3. The precipitation was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/400 to afford *anti-anti*-**4-1a** (0.13 g, 11% yield, d.r. = 99:1) as white solid.

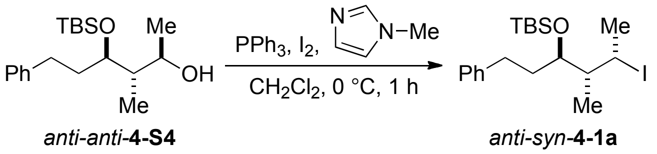
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.32-7.23 (m, 2H), 7.22-7.14 (m, 3H), 4.70 (qd, *J* = 7.1 and 2.4 Hz, 1H), 3.56 (dt, *J* = 7.7 and 3.5 Hz, 1H), 2.75 (td, *J* = 12.8 and 4.9 Hz, 1H), 2.58 (td, *J* = 12.9 and 5.3 Hz, 1H), 1.96 (d, *J* = 7.1 Hz, 1H), 1.94-1.72 (m, 2H), 0.95 (s, 9H), 0.91 (d, *J* = 6.4 Hz, 3H), 0.87-0.76 (m, 1H), 0.19 (s, 3H), 0.15 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 142.9, 128.6, 128.4, 125.9, 75.3, 44.9, 36.4, 35.6, 29.5, 27.5, 26.2, 18.4, 14.1, –3.8, –3.9.

MS (70 eV, EI) *m/z* (%): 375 (29) [M–^{t}Bu]$^{+•}$, 305 (6), 249 (26), 229 (13), 185 (24), 173 (59), 131 (34), 117 (56), 91 (100), 75 (79).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2953 (w), 2928 (w), 2856 (w), 1496 (w), 1471 (w), 1461 (w), 1454 (w), 1382 (w), 1361 (w), 1298 (w), 1252 (w), 1183 (w), 1121 (w), 1091 (m), 1057 (w), 1013 (w), 983 (w), 947 (w), 884 (w), 831 (vs), 812 (w), 772 (s), 744 (m), 697 (s), 666 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{24}O_2SiI^{+•}$** [M–^{t}Bu]$^{+•}$: 375.0641, found: 375.0634.



anti-anti-**4-S4** *anti-syn*-**4-1a**

anti-syn-**4-1a**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (0.58 g, 2.3 mmol) in CH_2Cl_2 (12 mL) and cooled to 0 °C. PPh_3 (0.60 g, 2.3 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.18 mL, 2.3 mmol) was added. After 10 min of further stirring, *anti-anti*-**4-S4** (0.46 g, 1.4 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/3. The precipitation was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/400 to afford *anti-syn*-**4-1a** (0.35 g, 25% yield, d.r. = 99:1) as colorless oil.

^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.33-7.24 (m, 2H), 7.22-7.15 (m, 3H), 4.40 (quint, *J* = 6.9 Hz, 1H), 3.87 (q, *J* = 5.6 Hz, 1H), 2.77-2.65 (m, 1H), 2.65-2.55 (m, 1H), 2.11 (h, *J* = 6.8

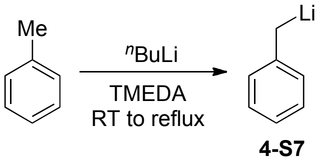
Hz, 1H), 1.87 (d, J = 6.9 Hz, 3H), 1.73-1.63 (m, 2H), 1.00 (d, J = 6.9 Hz, 3H), 0.93 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 142.7, 128.6, 128.5, 125.9, 75.2, 47.6, 34.7, 33.3, 31.4, 26.1, 25.2, 18.3, 11.9, −4.0, −4.3.

MS (70 eV, EI) *m/z* (%): 375 (18) [M–^{t}Bu]$^{+\bullet}$, 318 (7), 249 (34), 228 (13), 191 (43), 173 (39), 131 (19), 117 (53), 91 (100), 75 (97).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2953 (w), 2928 (w), 2856 (w), 1496 (w), 1471 (w), 1461 (w), 1454 (w), 1380 (w), 1360 (w), 1251 (w), 1070 (m), 1041 (w), 1005 (w), 967 (w), 832 (vs), 814 (w), 772 (s), 746 (m), 697 (s), 665 (w).

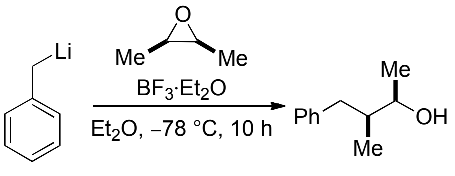
HRMS (EI) *m/z*: calcd for **$C_{15}H_{24}O_2SiI^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 375.0641, found: 375.0643.



4-S7

4-S7

A dry and N$_2$-flushed *Schlenk*-flask was charged with TMEDA (5.0 mL, 33.4 mmol) in toluene (80 mL). ^{n}BuLi (14.0 mL, 2.4 M in *n*-hexane, 33.4 mmol) was added dropwise at room temperature and the resulting solution was stirred for 2 h under reflux. The concentration was determined by titration to be 0.41 M (quant) and used without further manipulations.

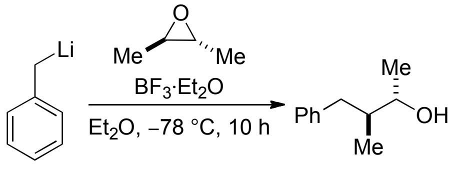


4-S7 *syn*-**4-S8**

syn-**4-S8 (**CAS: 1499-63-4)

A dry and N$_2$-flushed *Schlenk*-flask was charged with *cis*-1,2-dimethyl ethylene oxide (1.0 mL, 11.1 mmol) in Et$_2$O (40 mL) and cooled down to −60 °C. ^{n}BuLi complexed with TMEDA (40.0 mL, 0.41 M in toluene, 16.7 mmol) was added dropwise at −60 °C and then the mixture was cooled down further to −78 °C. BF$_3$·Et$_2$O (2.1 mL, 16.7 mmol) was added at −78 °C and the mixture was stirred at −78 °C for 20 min. After warmed up to room temperature, it was stirred for 10 h. After quenching the reaction with saturated NH$_4$Cl aqueous solution, saturated NaCl aqueous solution was added and the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/4 to afford *syn*-**4-S8** (1.3 g, 72% yield, d.r. = 99:1) as colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.32-7.23 (m, 2H), 7.23-7.14 (m, 3H), 3.70 (h, J = 6.2 Hz, 1H), 2.88 (dd, J = 13.4 and 4.9 Hz, 1H), 2.35 (dd, J = 13.4 and 9.3 Hz, 1H), 1.91-1.75 (m, 1H), 1.21 (d, J = 6.3 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 141.2, 129.3, 128.4, 125.9, 71.6, 42.4, 39.3, 19.9, 14.8.
MS (70 eV, EI) *m/z* (%): 164 (7) $[M]^{+\bullet}$, 146 (42), 131 (67), 91 (100), 77 (13).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3356 (br, s), 2969 (w), 2928 (w), 2878 (w), 1495 (w), 1453 (w), 1378 (w), 1124 (w), 1085 (w), 1056 (w), 1030 (w), 1000 (w), 932 (w), 911 (w), 892 (w), 739 (m), 689 (vs).
HRMS (EI) *m/z*: calcd for $C_{11}H_{16}O^{+\bullet}$ $[M]^{+\bullet}$: 164.1201, found: 164.1194.



4-S7 *anti*-**4-S8**

anti-**4-S8** (CAS:1499-64-5)

A dry and N_2-flushed *Schlenk*-flask was charged with *trans*-1,2-dimethyl ethylene oxide (1.0 mL, 11.1 mmol) in Et_2O (40 mL) and cooled down to −60 °C. ^{n}BuLi complexed with TMEDA (40.0 mL, 0.41 M in toluene, 16.7 mmol) was added dropwise at −60 °C and then the mixture was cooled down further to −78 °C. $BF_3\cdot Et_2O$ (2.1 mL, 16.7 mmol) was added at −78 °C and the mixture was stirred at −78 °C for 20 min. After warmed up to room temperature, it was stirred for 10 h. After quenching the reaction with saturated NH_4Cl aqueous solution, saturated NaCl aqueous solution was added and the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/4 to afford *anti*-**4-S8** (1.5 g, 72% yield, d.r. = 99:1) as colorless oil.

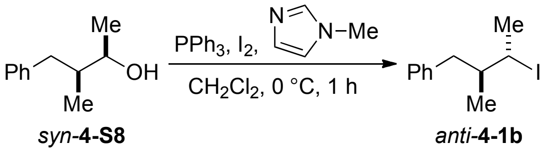
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.32-7.24 (m, 2H), 7.23-7.15 (m, 3H), 3.77 (qd, *J* = 6.4 and 3.8 Hz, 1H), 2.83 (dd, *J* = 13.3 and 5.9 Hz, 1H), 2.40 (dd, *J* = 13.3 and 9.0 Hz, 1H), 1.86-1.71 (m, 1H), 1.20 (d, *J* = 6.4 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 141.2, 129.3, 128.4, 125.9, 70.5, 41.9, 39.5, 20.7, 13.7.

MS (70 eV, EI) *m/z* (%): 164 (5) $[M]^{+\bullet}$, 146 (34), 114 (9), 91 (100), 77 (20).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3366 (br, s), 2969 (w), 2932 (w), 2878 (w), 1495 (w), 1453 (w), 1378 (w), 1144 (w), 1097 (w), 1078 (w), 1058 (w), 1030 (w), 993 (w), 928 (w), 913 (w), 893 (w), 736 (m), 698 (vs).

HRMS (EI) *m/z*: calcd for $C_{11}H_{16}O^{+\bullet}$ $[M]^{+\bullet}$: 164.1201, found: 164.1192.



anti-**4-1b**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.0 g, 4.0 mmol) in CH_2Cl_2 (16 mL) and cooled to 0 °C. PPh_3 (1.2 g, 4.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.32 mL, 4.0 mmol) was added. After 10 min of further stirring, *syn*-**4-S8** (0.41 g, 2.5 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/3. The precipitation was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with *i*-hexane to afford *anti*-**4-1b** (0.48 g, 69% yield, d.r. = 97:3) as pale pink oil.

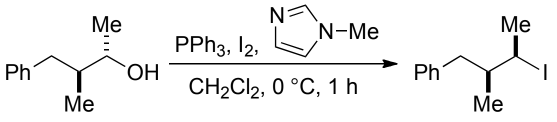
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.32-7.24 (m, 2H), 7.23-7.15 (m, 3H), 3.77 (qd, *J* = 6.4 and 3.8 Hz, 1H), 2.83 (dd, *J* = 13.3 and 5.9 Hz, 1H), 2.40 (dd, *J* = 13.3 and 9.0 Hz, 1H), 1.86-1.71 (m, 1H), 1.20 (d, *J* = 6.4 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 141.2, 129.3, 128.5, 126.3, 43.7, 43.2, 40.7, 26.9, 17.4.

MS (70 eV, EI) *m/z* (%): 274 (2) $[M]^{+\bullet}$, 147 (39), 115 (5), 91 (100), 65 (9).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3026 (w), 2965 (w), 2911 (w), 2853 (w), 1492 (w), 1452 (w), 1441 (w), 1378 (w), 1324 (w), 1265 (w), 1181 (w), 1103 (w), 1070 (w), 1030 (w), 1002 (w), 963 (w), 908 (w), 782 (w), 736 (s), 698 (vs).

HRMS (EI) *m/z*: calcd for **$C_{11}H_{15}O^{+\bullet}$** $[M]^{+\bullet}$: 274.0218, found: 274.0207.



anti-**4-S8** *syn*-**4-1b**

syn-**4-1b**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (0.76 g, 4.0 mmol) in CH_2Cl_2 (16 mL) and cooled to 0 °C. PPh_3 (0.79 g, 4.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.24 mL, 4.0 mmol) was added. After 10 min of further stirring, *anti*-**4-S8** (0.41 g, 2.5 mmol, d.r. = 99:1) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/3. The precipitation was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with *i*-hexane to afford *syn*-**4-1b** (0.29 g, 43% yield, d.r. = 98:2) as pale pink oil.

^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.33-7.25 (m, 2H), 7.23-7.13 (m, 3H), 7.34 (qd, *J* = 7.0 and 3.9 Hz, 1H), 2.86 (dd, *J* = 13.5 and 5.1 Hz, 1H), 2.39 (dd, *J* = 13.5 and 9.0 Hz, 1H), 1.94 (d, *J* = 7.0 Hz, 3H), 1.80-1.67 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 140.3, 129.2, 128.5, 126.2, 44.1, 41.0, 38.3, 25.0, 18.2.

MS (70 eV, EI) *m/z* (%): 274 (2) $[M]^{+\bullet}$, 147 (40), 115 (5), 91 (100), 65 (12).

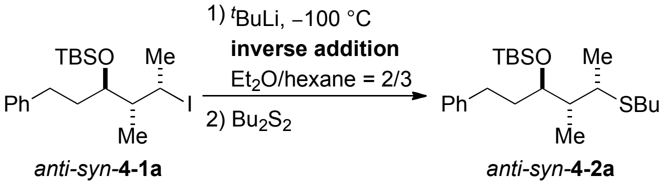
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3026 (w), 2964 (w), 2926 (w), 2857 (w), 1495 (w), 1453 (w), 1378 (w), 1270 (w), 1180 (w), 1166 (w), 1148 (w), 1097 (w), 1030 (w), 1006 (w), 961 (w), 908 (w), 801 (w), 783 (w), 737 (s), 698 (vs).

HRMS (EI) *m/z*: calcd for **$C_{11}H_{15}O^{+\bullet}$** $[M]^{+\bullet}$: 274.0218, found: 274.0209.

9.4.2 I/Li exchange and subsequent trapping reaction

[General procedure under kinetic control]

A dry and Ar-flushed *Schlenk*-tube was cooled down to –100 °C and charged with a solution of ^{t}BuLi (0.40 mL, 1.9 M in *n*-pentane, 0.75 mmol) in mixture of Et_2O (1.5 mL) and *n*-hexane (2.3 mL). A solution of alkyl iodide (0.30 mmol) in Et_2O (0.6 mL) was added dropwise for 5 min. After stirring for 10 sec, electrophile was added and the reaction mixture was stirred for 15 min at –100 °C. The reaction was quenched with 7 drops of saturated NH_4Cl aqueous solution and after an addition of $MgSO_4$ this mixture was passed through a pad of silica gel with EtOAc. Solvents were evaporated and the crude product was purified by column chromatography.



anti-syn-**4-2a**

According to general procedure, *anti-syn*-**4-1a** (100 mg, 0.18 mmol, d.r. = 99:1) as a starting material and Bu_2S_2 (0.09 mL, 0.53 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *anti-syn*-**4-2a** (37 mg, 53% yield, d.r. = 97:3) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *anti-anti*-**4-2b** and other trapping reactions with disulfide.

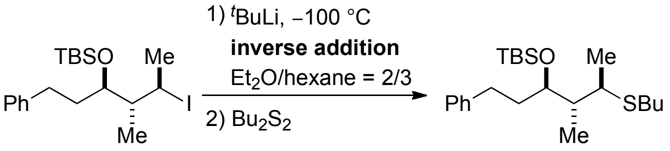
^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: 7.32-7.26 (m, 2H), 7.23-7.16 (m, 3H), 3.83 (dt, *J* = 6.8 and 4.7 Hz, 1H), 3.01 (quint, *J* = 6.8 Hz, 1H), 2.75-2.60 (m, 2H), 2.51 (t, *J* = 7.5 Hz, 1H), 1.88 (dq, *J* = 12.5 and 6.7 Hz, 1H), 1.80-1.72 (m, 2H), 1.58 (tt, *J* = 7.8 and 7.4 Hz, 2H), 1.42 (tq, *J* = 7.3 and 7.2 Hz, 2H), 1.18 (d, *J* = 6.9 Hz, 3H), 0.96-0.93 (m, 3H), 0.94 (s, 9H), 0.93 (t, *J* = 7.1 Hz, 2H), 0.11 (s, 3H), 0.07 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 143.1, 128.51, 128.47, 125.8, 73.3, 42.2, 40.9, 35.6, 32.2, 30.7, 30.6, 26.1, 22.3, 18.3, 16.9, 13.9, 10.8, –3.9, –4.5.

MS (70 eV, EI) *m/z* (%): 379 (1) $[M–Me]^{+\bullet}$, 247 (25), 191 (30), 171 (10), 147 (39), 117 (34), 91 (54), 75 (88), 57 (17).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2928 (w), 2857 (w), 1496 (w), 1471 (w), 1462 (w), 1379 (w), 1360 (w), 1252 (w), 1085 (m), 1055 (m), 1047 (w), 1005 (w), 969 (w), 940 (w), 832 (vs), 772 (s), 746 (m), 697 (s), 664 (w).

HRMS (EI) *m/z*: calcd for **$C_{22}H_{39}OSSi^{+\bullet}$** [M–Me]$^{+\bullet}$: 379.2491, found: 379.2488.



anti-anti-**4-1a** *anti-anti*-**4-2a**

anti-anti-**4-2a**

According to general procedure, *anti-anti*-**4-1a** (130 mg, 0.30 mmol, d.r. = 99:1) as a starting material and Bu$_2$S$_2$ (0.16 mL, 0.90 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/100 to afford *anti-anti*-**4-2a** (59 mg, 50% yield, d.r. = 97:3) as colorless oil. The relative configuration was determined by assuming the reaction sequence proceeds with retention of the configuration from *anti-anti*-**4-2b** and other trapping reactions with disulfide.

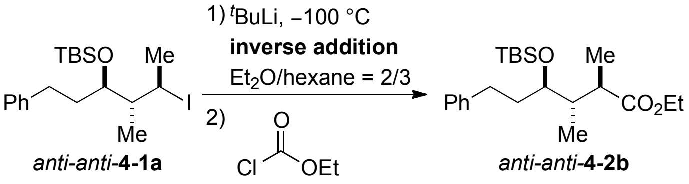
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.33-7.26 (m, 2H), 7.23-7.15 (m, 3H), 3.96-3.87 (m, 1H), 2.93 (dd, *J* = 6.6 and 6.1 Hz, 1H), 2.74-2.58 (m, 2H), 2.54 (dt, *J* = 11.8 and 7.5 Hz, 1H), 2.46 (dt, *J* = 11.8 and 7.3 Hz, 1H), 1.84-1.68 (m, 3H), 1.56 (tt, *J* = 7.4 and 7.0 Hz, 2H), 1.41 (tq, *J* = 7.3 and 7.2 Hz, 2H), 1.32 (d, *J* = 6.6 Hz, 3H), 0.96 (d, *J* = 7.4 Hz, 2H), 0.95 (s, 9H), 0.92 (d, *J* = 7.4 Hz, 3H), 0.13 (s, 3H), 0.11 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 143.1, 128.50, 128.48, 125.8, 72.9, 44.3, 43.1, 35.0, 32.2, 30.7, 30.6, 26.2, 22.4, 21.0, 18.4, 13.9, 11.4, –3.9, –4.4.

MS (70 eV, EI) *m/z* (%): 379 (1) [M-Me]$^{+\bullet}$, 247 (44), 191 (27), 171 (22), 147 (45), 117 (52), 91 (67), 75 (99), 57 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2928 (w), 2857 (w), 1496 (w), 1471 (w), 1461 (w), 1381 (w), 1360 (w), 1250 (w), 1086 (m), 1055 (m), 1005 (w), 987 (w), 947 (w), 832 (vs), 772 (s), 746 (m), 697 (m), 666 (w).

HRMS (EI) *m/z*: calcd for **$C_{22}H_{39}OSSi^{+\bullet}$** [M–Me]$^{+\bullet}$: 379.2491, found: 379.2489.



anti-anti-**4-2b**

According to general procedure, *anti-anti*-**4-1a** (130 mg, 0.30 mmol, d.r. = 99:1) as a starting material and $ClCO_2Et$ (0.07 mL, 0.75 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/20 to afford *anti-anti*-**4-2b** (65 mg, 57% yield, d.r. = 99:1) as colorless oil. The relative configuration was determined by further transformation to *trans-cis*-**4-4**.

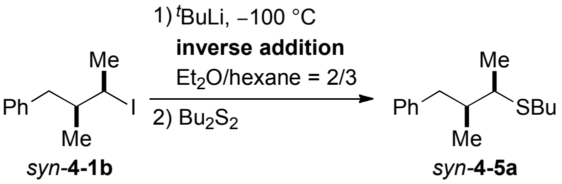
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.33-7.25 (m, 2H), 7.22-7.15 (m, 3H), 4.12 (q, *J* = 4.1 Hz, 2H), 3.84 (ddd, *J* = 7.9, 5.3 and 3.0 Hz, 1H), 2.77 (ddd, *J* = 13.4, 11.4 and 5.1 Hz, 1H), 2.54 (ddd, *J* = 13.5, 11.1 and 5.8 Hz, 1H), 2.43 (quint, *J* = 7.1 Hz, 1H), 1.83 (h, *J* = 7.0 Hz, 1H), 1.77-1.58 (m, 2H), 1.24 (d, *J* = 7.1 Hz, 3H), 1.10 (d, *J* = 7.0 Hz, 3H), 0.94 (s, 9H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.11 (s, 3H), 0.09 (s, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 176.2, 142.8, 128.50, 128.48, 125.9, 72.4, 60.2, 42.3, 41.8, 33.9, 31.9, 26.1, 18.3, 16.0, 14.4, 11.7, –4.2, –4.3.

MS (70 eV, EI) *m/z* (%): 363 (2) $[M\text{-}Me]^{+\bullet}$, 321 (100), 275 (32), 249 (27), 193 (7), 177 (6), 145 (34), 117 (30), 91 (78), 75 (100), 59 (13).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2930 (w), 2857 (w), 1732 (m), 1496 (w), 1471 (w), 1462 (w), 1454 (w), 1377 (w), 1252 (w), 1177 (w), 1161 (w), 1126 (w), 1088 (m), 1062 (s), 1005 (w), 976 (w), 958 (w), 832 (vs), 772 (s), 747 (m), 698 (m), 663 (w).

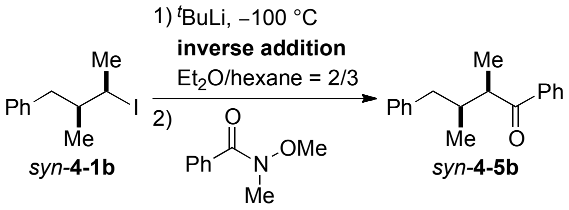
HRMS (EI) *m/z*: calcd for **$C_{21}H_{35}O_3Si^{+\bullet}$** $[M\text{–}Me]^{+\bullet}$: 363.2355, found: 363.2333.



syn-**4-5a**

According to general procedure, *syn*-**4-1b** (82 mg, 0.30 mmol, d.r. = 98:2) as a starting material and Bu_2S_2 (0.16 mL, 0.90 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/150 to afford *syn*-**4-5a** (43 mg, 61% yield, d.r. = 96:4) as colorless oil. The relative configuration was determined by the comparison with *syn*- and *anti*-**4-5b** and by assuming the reaction sequence proceeds with retention of the configuration from other trapping reactions with disulfide.

^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.31-7.25 (m, 2H), 7.22-7.14 (m, 3H), 2.80-2.69 (m, 2H), 2.53-2.43 (m, 3H), 2.02 (ddqd, *J* = 8.5, 6.9, 6.5 and 4.3 Hz, 1H), 1.53-1.44 (m, 2H), 1.42-1.31 (m, 2H), 1.24 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H) 0.89 (d, *J* = 7.3 Hz, 3H).
^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 141.2, 129.1, 128.4, 126.0, 44.2, 41.0, 39.8, 32.0, 31.0, 22.3, 16.5, 15.0, 13.9.
MS (70 eV, EI) *m/z* (%): 236 (32) $[M]^{+\bullet}$, 146 (94), 131 (100), 114 (38), 91 (83), 75 (30), 55 (14).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2959 (w), 2928 (w), 2872 (w), 1496 (w), 1454 (w), 1377 (w), 1222 (w), 1107 (w), 1030 (w), 909 (w), 740 (s), 698 (vs).
HRMS (EI) *m/z*: calcd for $C_{15}H_{24}S^{+\bullet}$ $[M]^{+\bullet}$: 236.1599, found: 236.1591.



syn-**4-5b** (CAS: 920985-27-9)
According to general procedure, *syn*-**4-1b** (82 mg, 0.30 mmol, d.r. = 98:2) as a starting material and *N*-Methoxy-*N*-methylbenzamide (0.09 mL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/60→1/50 to afford *syn*-**4-5b** (24 mg, 32% yield, d.r. = 69:31) as colorless oil. The relative configuration was determined by comparing with literature values.[132]

The peaks of major diastereomers are given.
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.62 (d, *J* = 7.3 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 2H), 7.18-7.13 (m, 1H), 7.11 (t, *J* = 7.1 Hz, 2H), 3.32 (qd, *J* = 6.8 and 4.9 Hz, 1H), 2.59 (dd, *J* = 13.3 and 7.6 Hz, 1H), 2.59 (dd, *J* = 13.4 and 7.2 Hz, 1H), 2.25-2.13 (m, 1H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.77 (d, *J* = 6.8 Hz, 3H).
^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 204.2, 140.8, 136.7, 132.8, 129.4, 128.6, 128.5, 128.4, 126.3, 43.4, 41.8, 37.4, 15.2, 10.9.

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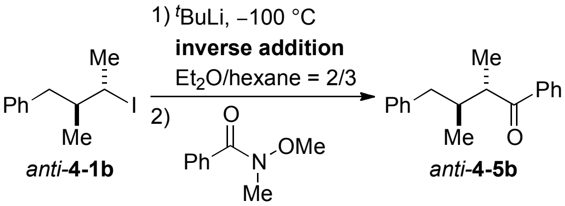
[132] J. N. Moorthy, A. L. Koner, S. Samanta, N. Singhal, W. M. Nau, R. G. Weiss, *Chem. Eur. J.* **2006**, *12*, 8744.

MS (70 eV, EI) *m/z* (%): 134 (100), 105 (68), 91 (25), 77 (30).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3026 (w), 2965 (w), 2931 (w), 2876 (w), 1678 (m), 1596, (w), 1581 (w), 1495 (w), 1448 (w), 1380 (w), 1364 (w), 1259 (w), 1220 (w), 1193 (w), 1180 (w), 1010 (w), 1002 (w), 968 (w), 957 (w), 738 (m), 694 (vs), 658 (w).

LRMS (EI) *m/z*: calcd for **$C_{11}H_{13}O^{+\bullet}$** $[M-Bn]^{+\bullet}$: 161.22, found: 161.16.



anti-**4-5b**

According to general procedure, *anti*-**4-1b** (82 mg, 0.30 mmol, d.r. = 98:2) as a starting material and *N*-Methoxy-*N*-methylbenzamide (0.09 mL, 0.60 mmol) were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/60→1/50 to afford *anti*-**4-1b** (43 mg, 57% yield, d.r. = 89:11) as colorless oil. The relative configuration was determined by comparing with literature values.[132]

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.85 (d, J = 7.3 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.39 (d, J = 7.6 Hz, 2H), 7.15 (t, J = 7.3 Hz, 2H), 7.13-7.06 (m, 1H), 6.97 (t, J = 7.3 Hz, 2H), 3.39 (quint, J = 6.8 Hz, 1H), 2.78 (q, J = 9.2 Hz, 1H), 2.20-2.09 (m, 2H), 1.19 (d, J = 6.3 Hz, 3H), 0.79 (d, J = 6.1 Hz, 3H).

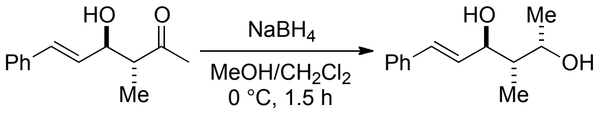
^{13}C-NMR (75 MHz, CDCl$_3$) δ: 204.7, 140.9, 137.4, 133.0, 129.3, 128.8, 128.33, 128.29, 125.9, 45.9, 39.2, 38.0, 17.8, 13.8.

MS (70 eV, EI) *m/z* (%): 134 (100), 105 (39), 91 (15), 77 (18).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3026 (w), 2966 (w), 2932 (w), 2874 (w), 1678 (m), 1596 (w), 1496 (w), 1448 (w), 1378 (w), 1259 (w), 1221 (w), 1182 (w), 1002 (w), 963 (w), 909 (w), 793 (w), 733 (m), 696 (vs).

LRMS (EI) *m/z*: calcd for **$C_{18}H_{21}O^{+\bullet}$** $[M+H]^{+\bullet}$: 253.37, found: 253.30

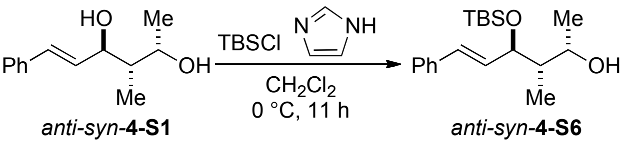
9.4.3 Conformation of the configuration



anti-**4-S1** *anti-syn*-**4-S5**

anti-syn-**4-S5** (CAS: 905588-19-4)

A 25 mL flask was charged with a solution of *anti*-**4-S1** (19.8 g, 96.9 mmol) in MeOH (22.0 mL) and CH_2Cl_2 (45 mL) and the reaction mixture was cooled down to 0 °C. $NaBH_4$ (3.8 g, 100 mmol) was added to the reaction mixture at 0 °C and it was stirred for 1.5 h. After quenched with saturated NH_4Cl aqueous solution, the reaction mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$. Solvents were evaporated. The crude product was purified by column chromatography on silica gel with Et_2O/CH_2Cl_2 = 1/4 to afford *anti-syn*-**4-S5** (0.38 g, 2% yield, d.r. = 99:1) as white solid. The relative configuration was determined by comparing with reported experimental values.[133]



anti-syn-**4-S1** *anti-syn*-**4-S6**

anti-syn-**4-S6**

A 25 mL flask was charged with a solution of *anti-syn*-**4-S1** (0.21 g, 1.0 mmol) and imidazole (0.82 g, 1.2 mmol) in CH_2Cl_2 (2 mL) and the reaction mixture was cooled down to 0 °C. TBSCl (0.12 g, 0.8 mmol) in CH_2Cl_2 (5 mL) was added to the reaction mixture at 0 °C and it was stirred at 0 °C for 11.5 h. After quenched with H_2O, the reaction mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$. Solvents were evaporated. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/3 to afford *anti-syn*-**4-S6** (0.10 g, 30% yield, d.r. = 99:1) as white solid.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.40-7.20 (m, 5H), 6.47 (d, J = 15.9 Hz, 1H), 6.13 (d, J = 16.0 and 7.8 Hz, 1H), 4.24 (t, J = 7.7 Hz, 1H), 3.81 (dq, J = 8.1 and 6.1 Hz, 1H), 1.67 (tq, J = 7.3 and 7.0 Hz, 1H), 1.19 (d, J = 6.3 Hz, 3H), 0.92 (s, 9H), 0.81 (d, J = 7.0 Hz, 3H), 0.12 (s, 3H), 0.06 (s, 3H).

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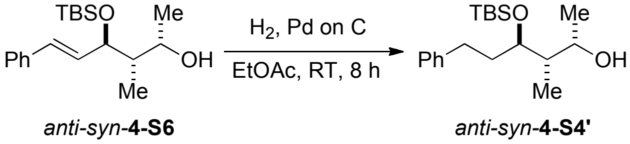
[133] A. Abate, E. Brenna, A. Aostantini, C. Fuganti, F. G. Gatti, L. Malpezzi, S. Serra, *J. Org. Chem.* **2006**, *71*, 5228.

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 136.8, 131.5, 128.8, 127.87, 126.6, 79.7, 71.1, 46.6, 26.0, 25.8, 21.2, 18.2, 18.1, 12.7, –3.5, –4.6.

MS (70 eV, EI) *m/z* (%): 263 (5) [M–^{t}Bu]$^{+\bullet}$, 247 (100), 207 (36), 189 (7), 144 (14), 129 (45), 113 (25), 91 (12), 75 (85).

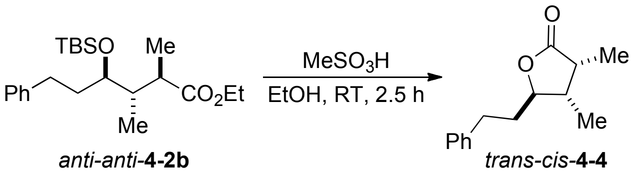
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3407 (br w), 2956 (w), 2929 (w), 2886 (w), 2856 (w), 1495 (w), 1471 (w), 1462 (w), 1449 (w), 1377 (w), 1361 (w), 1251 (w), 1054 (m), 1004 (w), 968 (w), 936 (w), 868 (w), 833 (vs), 812 (w), 773 (s), 744 (s), 691 (s), 668 (w).

HRMS (EI) *m/z*: calcd for **$C_{19}H_{30}OSi^{+\bullet}$** [M–$H_2O$]$^{+\bullet}$: 302.2066, found: 302.2064.



anti-syn-**4-S4'**

A 25 mL flask was charged with *anti-syn*-**4-S6** (0.06 g, 0.20 mmol) and Pd on C (30 mg, Pd 5% wt) in EtOAc (5 mL). H_2 was bubbled to the reaction mixture at room temperature for 5 min and it was stirred for 8 h at room temperature. Pd on C was filtered off with Celite and EtOAc and solvents were evaporated to afford *anti-syn*-**4-S4'** (0.06 g, 97% yield, d.r. = 99:1) as colorless oil.



trans-cis-**4-4**

A 25 mL flask was charged with a solution of *anti-anti*-**4-2b** (0.05 g, 0.13 mmol) in EtOH (3.0 mL). 3 drops of methane sulfonic acid was added to the reaction mixture and it was stirred at room temperature for 2.5 h. After quenched with saturated $NaHCO_3$ aqueous solution, the reaction mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$. Solvents were evaporated. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/1 to afford *trans-cis*-**4-5** (26 mg, 90% yield, d.r. = 99:1) as colorless oil. The relative configuration was determined by comparing with literature values.[134]

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[134] R. Bénéteau, J. Lebreton, F. Dénès, *Chem. Asian J.* **2012**, *7*, 1516.

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.33-7.27 (m, 2H), 7.24-7.17 (m, 3H), 4.05 (dt, J = 8.1 and 5.4 Hz, 1H), 2.88 (ddd, J = 14.5, 8.6 and 6.3 Hz, 1H), 2.80-2.66 (m, 2H), 2.29 (dq, J = 14.3 and 7.1 Hz, 1H), 1.98-1.89 (m, 2H), 1.16 (d, J = 7.6 Hz, 3H), 1.00 (d, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 180.0, 141.1, 128.7, 128.6, 126.3, 84.5, 38.7, 38.3, 35.9, 32.2, 13.3, 10.4.

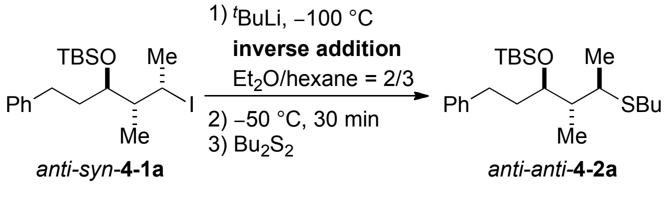
MS (70 eV, EI) *m/z* (%): 218 (39) [M]$^{+\bullet}$, 144 (100), 117 (40), 104 (62), 91 (76), 56 (15).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2930 (w), 1766 (vs), 1496 (w), 1454 (w), 1386 (w), 1361 (w), 1246 (w), 1204 (m), 1167 (m), 1115 (w), 1050 (w), 1030 (w), 1006 (m), 952 (w), 910 (m), 835 (w), 729 (s), 699 (s).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{18}O_2^{+\bullet}$** [M]$^{+\bullet}$: 218.1307, found: 218.1301.

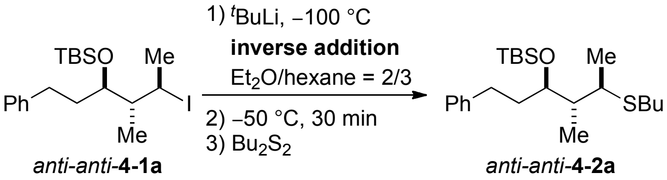
[General procedure under thermodynamic control]

A dry and Ar-flushed *Schlenk*-tube was cooled down to −100 °C and charged with a solution of ^{t}BuLi (0.40 mL, 1.9 M in *n*-pentane, 0.75 mmol) in mixture of Et$_2$O (1.5 mL) and *n*-hexane (2.3 mL). A solution of alkyl iodide (0.30 mmol) in Et$_2$O (0.6 mL) was added dropwise for 5 min. After stirring for 10 sec, the reaction mixture was warmed up to −50 °C and stirred for 30 min at −50 °C. electrophile was added and the reaction mixture was stirred for 15 min at −50 °C. The reaction was quenched with 7 drops of saturated NH$_4$Cl aqueous solution and after an addition of MgSO$_4$ this mixture was passed through a pad of silica gel with EtOAc. Solvents were evaporated and the crude product was purified by column chromatography.



anti-anti-**4-2a**

According to general procedure, *anti-syn*-**4-1a** (130 mg, 0.30 mmol, d.r. = 98:2) as a starting material and Bu$_2$S$_2$ (0.16 mL, 0.90 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/100 to afford *anti-anti*-**4-2a** (17 mg, 24% yield, d.r. = 82:18) as colorless oil. The relative configuration was determined by comparing NMR spectra with those in kinetic control.

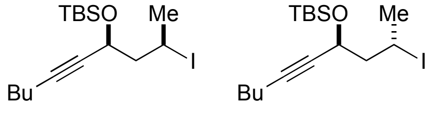


anti-anti-**4-2a**

According to general procedure, *anti-anti*-**4-1a** (130 mg, 0.30 mmol, d.r. = 98:2) as a starting material and Bu_2S_2 (0.16 mL, 0.90 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford *anti-anti*-**4-2a** (59 mg, 50% yield, d.r. = 82:18) as colorless oil. The relative configuration was determined by comparing NMR spectra with those in kinetic control.

9.5 Intramolecular Carbolithiation of Secondary Alkyllihtiums Prepared by Stereoselective I/Li exchange

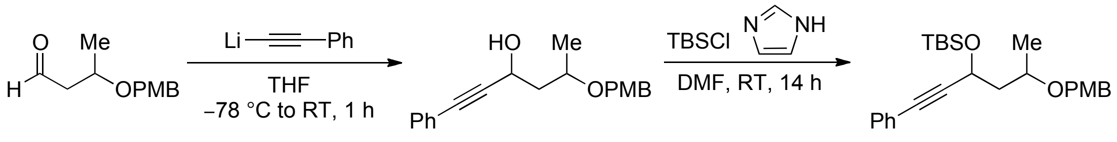
9.5.1 Preparation of starting materials



syn-**5-1a** *anti*-**5-1a**

syn-**5-1a** and *anti*-**5-1a**

They were synthesized in the same way as *syn*-**3-3j** and *anti*-**3-3j**.



5-S1 **5-S2** **5-S3**

5-S3

A dry and N_2-flushed *Schlenk*-flask was charged with trimethylsilyl acetylene (1.6 mL, 14.4 mmol) in THF (30 mL) and cooled down to −78 °C. ^{n}BuLi (6.0 mL, 2.4 M in hexane, 14.4 mmol) was added dropwise at −78 °C and the reaction mixture was stirred at −78 °C for 1 h. **5-S1**[119] (2.5 g, 12.0 mmol, CAS: 186743-05-5) in THF (10 mL) was added at −78 °C and the mixture was stirred at −78 °C for 20 min. After warmed up to room temperature, it was stirred for 1 h. After quenching the reaction with saturated NH_4Cl aqueous solution, the reaction mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated to obtain the crude **5-S2**. A 250 mL flask was charged with the crude **5-S2** (3.7 g) and imidazole (2.0 g, 30.0 mmol) in DMF (30 mL), and the reaction mixture was cooled down to 0 °C. TBSCl (2.2 g, 14.4 mmol) was added at 0 °C and the reaction mixture was stirred for 14 h at 0 °C to room temperature. After quenching the reaction with saturated NH_4Cl aqueous solution, the reaction mixture was extracted with a mixture of Et_2O/*i*-hexane = 1/3 three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/20 to afford **5-S3** (4.5 g, 88% yield in 2 steps, d.r. = 65:35) as colorless oil.

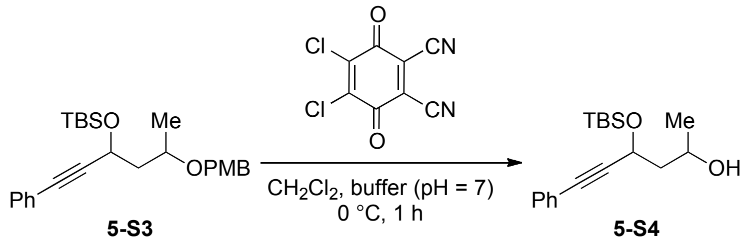
^{1}H-NMR (400 MHz, CDCl$_3$) δ: <u>Major:</u> 7.42-7.34 (m, 2H), 7.33-7.25 (m, 5H), 6.84 (d, J = 8.7 Hz, 2H), 4.79 (dd, J = 8.3 and 6.2 Hz, 1H), 4.54 (d, J = 11.3 Hz, 1H), 4.41 (d, J = 11.3 Hz, 1H), 3.86-3.77 (m, 1H), 3.76 (s, 3H), 2.10 (ddd, J = 13.5, 8.2 and 6.1 Hz, 1H), 1.82 (ddd, J = 13.5, 8.2 and 4.8 Hz, 1H), 1.25 (d, J = 6.1 Hz, 3H), 0.92 (s, 9H), 0.18 (s, 3H), 0.15 (s, 3H). **<u>Minor:</u>** 7.42-7.34 (m, 2H), 7.33-7.25 (m, 5H), 6.87 (d, J = 8.7 Hz, 2H), 4.82 (dd, J = 9.4 and 3.7 Hz, 1H), 4.55 (d, J = 10.9 Hz, 1H), 4.36 (d, J = 10.9 Hz, 1H), 3.86-3.77 (m, 1H), 3.80 (s, 3H), 2.02 (ddd, J = 14.0, 8.9 and 3.7 Hz, 1H), 1.90 (ddd, J = 14.0, 8.9 and 3.7 Hz, 1H), 1.25 (d, J = 6.1 Hz, 3H), 0.93 (s, 9H), 0.20 (s, 3H), 0.16 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: <u>Major</u>: 159.2, 131.6, 131.1, 129.4, 128.4, 128.2, 123.2, 113.9, 30.9, 84.7, 71.9, 70.4, 61.4, 55.4, 46.0, 26.0, 19.9, 18.4, −4.2, −4.8. **<u>Minor</u>**: 159.2, 131.6, 131.2, 129.3, 128.4, 128.2, 123.3, 113.9, 91.4, 84.2, 71.3, 70.3, 60.2, 55.4, 46.6, 26.0, 20.0, 18.4, −4.1, −4.7

MS (70 eV, EI) *m/z* (%): 424 (1) $[M]^{+\bullet}$, 325 (3), 292 (6), 156 (7), 121 (100), 73 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2928 (w), 2856 (w), 1613 (w), 1513 (m), 1490 (w), 1463 (w), 1442 (w), 1372 (w), 1361 (w), 1343 (w), 1301 (w), 1246 (s), 1172 (w), 1139 (w), 1100 (m), 1067 (s), 1035 (s), 1006 (m), 954 (w), 938 (w), 902 (w), 834 (s), 776 (s), 755 (vs), 690 (s), 667 (w).

HRMS (EI) *m/z*: calcd for **$C_{26}H_{39}O_3Si^{+\bullet}$** $[M]^{+\bullet}$: 424.2434, found: 424.2419.



5-S4

A 250 mL flask was charged with **5-S3** (4.4 g, 10.4 mmol, d.r. = 65:35) in CH$_2$Cl$_2$ (50 mL) and phosphate buffer solution (pH = 7; 25 mL) and the reaction mixture was cooled down to 0 °C. DDQ (4.7 g, 20.8 mmol) was added at 0 °C and the reaction mixture was stirred for 30 min at 0 °C to room temperature. After quenching the reaction saturated NaHCO$_3$ aqueous solution, the reaction mixture was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/10 to afford **5-S4** (1.6 g, 51% yield, d.r. = 72:38) as colorless oil.

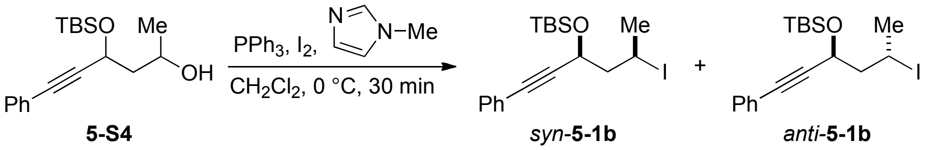
^{1}H-NMR (400 MHz, $CDCl_3$) δ: **Major:** 7.43-7.37 (m, 2H), 7.34-7.29 (m, 3H), 4.83 (dd, J = 8.7 and 4.8 Hz, 1H), 4.10 (dqd, J = 8.7, 6.2 and 2.4 Hz, 1H), 3.1 (br s, 1H), 2.05-1.80 (m, 2H), 1.29 (d, J = 6.1 Hz, 3H), 0.94 (s, 9H), 0.24 (s, 3H), 0.21 (s, 3H). **Minor:** 7.43-7.37 (m, 2H), 7.34-7.29 (m, 3H), 4.93 (t, J = 4.7 Hz, 1H), 4.38 (dqd, J = 8.8, 6.3 and 2.5 Hz, 1H), 3.1 (br s, 1H), 1.29 (d, J = 6.1 Hz, 3H), 0.94 (s, 9H), 0.22 (s, 3H), 0.19 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: Major: 131.6, 128.6, 128.5, 122.7, 90.1, 85.2, 67.2, 63.7, 46.7, 25.9, 23.6, 18.2, –4.0, –4.8. Minor: 131.7, 128.6, 128.50, 128.45, 122.8, 89.7, 85.4, 65.5, 62.9, 45.5, 25.9, 23.5, 18.2 –4.4, –5.1.

MS (70 eV, EI) *m/z* (%): 304 (1) $[M]^{+\bullet}$, 247 (5), 205 (100), 145 (27), 128 (13), 75 (66).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3363 (br s), 2955 (w), 2929 (w), 2857 (w), 1490 (w), 1471 (w), 1463 (w), 1443 (w), 1407 (w), 1372 (w), 1361 (w), 1342 (w), 1301 (w), 1251 (m), 1131 (w), 1100 (m), 1070 (m), 1029 (w), 1006 (w), 996 (w), 938 (w), 910 (w), 872 (w), 833 (s), 810 (m), 776 (s), 754 (vs), 689 (s), 667 (w).

HRMS (EI) *m/z*: calcd for $C_{14}H_{19}O_2Si^{+\bullet}$ $[M]^{+\bullet}$: 247.1154, found: 247.1162.



syn-**5-1b** and *anti*-**5-1b**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (50 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 4.3 mmol) was added. After 10 min of further stirring, **5-S4** (1.5 g, 5.0 mmol) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/4. The precipitation was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/800→1/300 to afford *syn*-**5-1b** (1.1 g, 52% yield, d.r = 99:1) as the first fraction and colorless oil, and *anti*-**5-1b** (0.74 g, 36% yield, d.r. = 99:1) as the second fraction and colorless oil. The relative configuration was determined by the comparison of NMR spectra with other alkyl iodide with OTBS group at 3-position.

syn-**5-1b**

^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.44-7.39 (m, 2H), 7.34-7.28 (m, 3H), 4.72 (dd, *J* = 9.9 and 2.9 Hz, 1H), 4.34 (dqd, *J* = 10.2, 6.9 and 3.2 Hz, 1H), 2.20 (ddd, *J* = 14.2, 10.9 and 3.0 Hz, 1H), 2.01 (d, *J* = 7.0 Hz, 3H), 1.96 (ddd, *J* = 14.6, 11.2 and 3.2 Hz, 1H), 0.95 (s, 9H), 0.24 (s, 3H), 0.23 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 131.6, 128.4, 122.9, 90.2, 84.8, 63.7, 51.1, 29.3, 26.6, 26.0, 18.3, −4.0, −4.6.

MS (70 eV, EI) *m/z* (%): 357 (8) [M–^{t}Bu]$^{+\bullet}$, 315 (100), 245 (5), 229 (9), 185 (23), 159 (47), 129 (14), 102 (5), 73 (23).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2928 (w), 2856 (w), 1489 (w), 1471 (w), 1462 (w), 1443 (w), 1360 (w), 1340 (w), 1251 (w), 1235 (w), 1158 (w), 1125 (w), 1103 (s), 1060 (m), 1032 (w), 1004 (w), 989 (w), 951 (w), 913 (m), 900 (w), 835 (s), 824 (s), 808 (m), 777 (s), 753 (vs), 688 (s), 664 (w).

HRMS (ESI) *m/z*: calcd for **$C_{14}H_{18}OISi^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 357.0172, found: 357.0168.

anti-**5-1b**

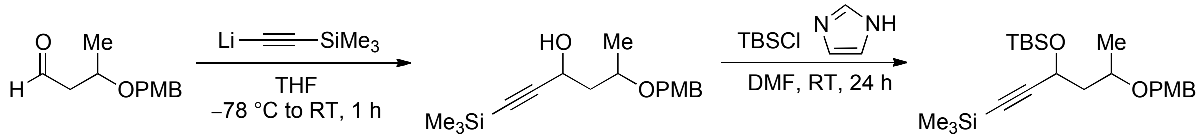
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.46-7.38 (m, 2H), 7.38-7.27 (m, 3H), 4.76 (dd, *J* = 7.8 and 6.2 Hz, 1H), 4.35 (dq, *J* = 8.9 and 6.8 Hz, 1H), 2.05 (ddd, *J* = 13.7, 7.7 and 5.5 Hz, 1H), 2.37 (ddd, *J* = 14.8, 9.1 and 6.2 Hz, 1H), 2.00 (d, *J* = 6.8 Hz, 3H), 0.94 (s, 9H), 0.21 (s, 3H), 0.19 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 131.7, 128.5, 128.4, 122.8, 89.4, 85.4, 64.4, 51.1, 28.9, 26.0, 24.1, 18.4, −4.2, −4.8.

MS (70 eV, EI) *m/z* (%): 357 (5) [M–^{t}Bu]$^{+\bullet}$, 315 (100), 245 (5), 229 (6), 185 (11), 159 (32), 115 (9), 73 (25).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2928 (w), 2856 (w), 1489 (w), 1471 (w), 1462 (w), 1443 (w), 1360 (w), 1336 (w), 1251 (w), 1226 (w), 1145 (w), 1120 (w), 1075 (s), 1039 (w), 1005 (w), 953 (w), 939 (w), 908 (w), 866 (w), 834 (vs), 809 (w), 776 (s), 753 (s), 689 (s), 668 (w).

HRMS (ESI) *m/z*: calcd for **$C_{14}H_{18}OISi^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 357.0172, found: 357.0164.



5-S1 **5-S5** **5-S6**

5-S6

A dry and N_2-flushed *Schlenk*-flask was charged with trimethylsilyl acetylene (1.7 mL, 13.2 mmol) in THF (25 mL) and cooled down to −78 °C. ^{n}BuLi (4.6 mL, 2.6 M in *n*-hexane, 12.7 mmol) was added dropwise at −78 °C and the reaction mixture was stirred at −78 °C for 1 h. **5-S1** (2.3 g, 11.0 mmol) in THF (10 mL) was added at −78 °C and the mixture was stirred at −78 °C for 20 min. After warmed up to room temperature, it was stirred for 1 h. After quenching the reaction with saturated NH_4Cl aqueous solution, the reaction mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated to obtain the crude **5-S5**. A 250 mL flask was charged with the crude **5-S5** (5.2 g) and imidazole (1.9 g, 27.5 mmol) in DMF (25 mL), and the reaction mixture was cooled down to 0 °C. TBSCl (2.0 g, 13.2 mmol) was added at 0 °C and the reaction mixture was stirred for 24 h at 0 °C to room temperature. After quenching the reaction with saturated NH_4Cl aqueous solution, the reaction mixture was extracted with a mixture of Et_2O/*i*-hexane = 1/4 three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/30 to afford **5-S6** (3.9 g, 84% yield in 2 steps, d.r. = 72:38) as colorless oil.

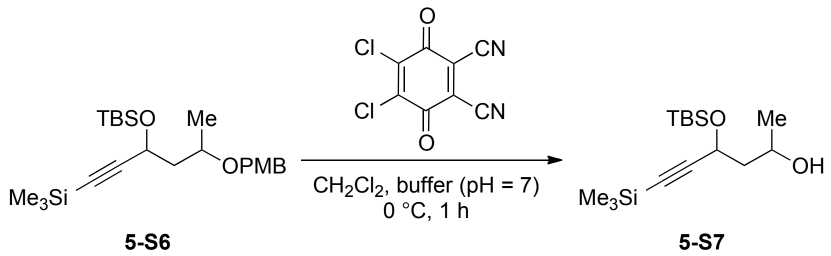
^{1}H-NMR (600 MHz, $CDCl_3$) δ: **Major:** 7.29-7.23 (m, 2H), 6.86 (d, J = 8.2 Hz, 2H), 4.57-4.50 (m, 1H), 4.49 (d, J = 11.7 Hz, 1H), 4.38 (d, J = 11.0 Hz, 1H), 3.80 (s, 3H), 3.78-3.69 (m, 1H), 2.06-1.96 (m, 1H), 1.74-1.67 (m, 1H), 1.21 (d, J = 6.0 Hz, 3H), 0.88 (s, 9H), 0.15 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H). **Minor:** 7.29-7.23 (m, 2H), 6.86 (d, J = 8.2 Hz, 1H), 4.59 (d, J = 9.5 Hz, 1H), 4.57-4.50 (m, 1H), 4.32 (d, J = 10.9 Hz, 1H), 3.80 (s, 3H), 3.78-3.69 (m, 1H), 1.94-1.87 (m, 1H), 1.83-1.75 (m, 1H), 1.21 (d, J = 6.0 Hz, 3H), 0.90 (s, 9H), 0.15 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$) δ: **Major**: 159.2, 131.2, 129.4, 113.9, 107.6, 89.2, 72.2, 70.6, 61.3, 55.4, 45.7, 26.0, 20.0, 18.4, 0.00, –4.3, –4.8. **Minor**: 159.2, 131.2, 129.2, 113.9, 108.2, 88.6, 71.2, 70.2, 60.1, 55.4, 46.6, 26.0, 20.0, 18.4, –0.1, –4.1, –4.7

MS (70 eV, EI) *m/z* (%): 420 (1) $[M]^{+\bullet}$, 137 (5), 121 (100), 73 (7).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2928 (w), 2856 (w), 1613 (w), 1513 (w), 1471 (w), 1463 (w), 1429 (w), 1372 (w), 1362 (w), 1342 (w), 1302 (w), 1247 (m), 1172 (w), 1141 (w), 1099 (w), 1075 (m), 1036 (m), 966 (w), 834 (vs), 776 (s), 759 (m).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{23}H_{40}O_3Si_2}^{+\bullet}$ $[M]^{+\bullet}$: 420.2516, found: 420.2524.



5-S7

A 250 mL flask was charged with **5-S6** (6.6 g, 15.6 mmol) in CH_2Cl_2 (60 mL) and phosphate buffer solution (pH = 7, 30 mL) and the reaction mixture was cooled down to 0 °C. DDQ (7.1 g, 31.2 mmol) was added at 0 °C and the reaction mixture was stirred for 30 min at 0 °C to room temperature. After quenching the reaction saturated $NaHCO_3$ aqueous solution, the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/10 to afford **5-S7** (4.6 g, 97% yield, d.r. = 72:38) as colorless oil.

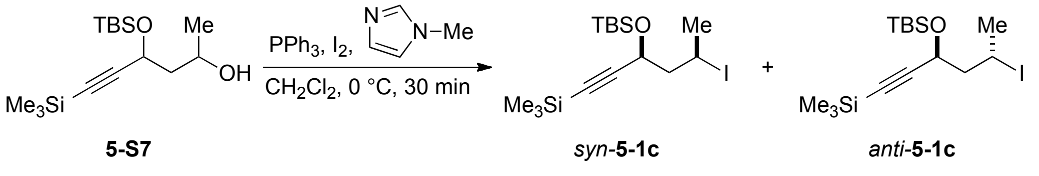
^{1}H-NMR (600 MHz, CDCl$_3$) δ: Major: 4.60-4.55 (m, 1H), 4.07-4.00 (m, 1H), 3.1 (br s, 1H), 1.92-1.70 (m, 2H), 1.22-1.17 (m, 3H), 0.91 (s, 9H), 0.18 (s, 3H), 0.18-0.14 (s, 12H). **Minor:** 4.70-4.64 (m, 1H), 4.29-4.23 (m, 1H), 3.1 (br s, 1H), 1.92-1.72 (m, 2H), 1.22-1.17 (m, 3H), 0.91 (s, 9H), 0.18-0.14 (m, 12H), 0.14 (s, 3H).

^{13}C-NMR (150 MHz, CDCl$_3$) δ: **Major**: 106.8, 90.1, 673.0, 63.5, 46.6, 25.9, 23.5, 18.2, −0.2, −4.1, −4.8. **Minor**: 106.5, 90.2, 65.3, 62.8, 45.5, 25.9, 23.5, 18.2, −0.1, −4.5, −5.1.

MS (70 eV, EI) *m/z* (%): 299 (1) $[M-H]^{+\bullet}$, 241 (5), 201 (100), 185 (5), 171 (5), 157 (9), 147 (14), 133 (24), 119 (4), 109 (5), 75 (23).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3430 (br w), 2957 (w), 2928 (w), 2857 (w), 1472 (w), 1463 (w), 1361 (w), 1337 (w), 1249 (w), 1132 (w), 1074 (w), 1004 (w), 966 (w), 938 (w), 909 (w), 833 (vs), 777 (s), 759 (m), 699 (w), 669 (w).

HRMS (EI) *m/z*: calcd for $C_{15}H_{32}O_2Si_2^+$ $[M]^+$: 300.1941, found: 300.1908.



syn-**5-1c** and *anti*-**5-1c**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.1 g, 4.3 mmol) in CH_2Cl_2 (35 mL) and cooled to 0 °C. PPh_3 (1.1 g, 4.3 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.34 mL, 4.3 mmol) was added. After 10 min of further stirring, **5-S7** (1.0 g, 3.6 mmol) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/4. The precipitation was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/600 to afford *syn*-**5-1c** (0.68 g, 49% yield, d.r = 99:1) as the first fraction and colorless oil, and *anti*-**5-1c** (0.28 g, 20% yield, d.r. = 99:1) as the second fraction and colorless oil. The relative configuration was determined by the comparison of NMR spectra with other alkyl iodide with OTBS group at 3-position.

syn-**5-1c**

^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 4.47 (dd, *J* = 10.0 and 2.9 Hz, 1H), 4.26 (dqd, *J* = 11.0, 7.9 and 3.1 Hz, 1H), 2.08 (ddd, *J* = 14.0, 11.0 and 2.9 Hz, 1H), 1.96 (d, *J* = 6.9 Hz, 3H), 1.83 (ddd, *J* = 14.8, 10.0 and 3.1 Hz, 1H), 0.91 (s, 9H), 0.184 (s, 3H), 0.178 (s, 3H), 0.15 (s, 9H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 106.9, 89.4, 63.7, 50.9, 29.3, 26.6, 26.0, 18.3, –0.1, –4.1, –4.7.

MS (70 eV, EI) *m/z* (%): 353 (10) $[M-{}^tBu]^{+\bullet}$, 311 (100), 283 (14), 259 (6), 241 (7), 185 (10), 155 (9), 97 (4), 73 (18).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2928 (w), 2857 (w), 1471 (w), 1463 (w), 1360 (w), 1338 (w), 1249 (w), 1236 (w), 1160 (w), 1127 (w), 1104 (m), 1064 (w), 1040 (w), 1005 (w), 957 (w), 915 (w), 900 (w), 835 (vs), 808 (m), 777 (s), 759 (m), 698 (w), 661 (w).

HRMS (ESI) *m/z*: calcd for **$C_{11}H_{22}OISi_2^+$** $[M]^+$: 353.0254, found: 353.0234.

anti-**5-1c**

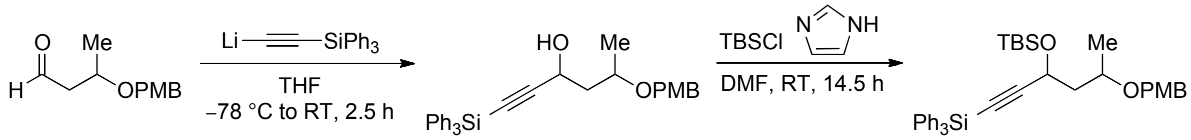
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 4.49 (dd, *J* = 7.4 and 6.5 Hz, 1H), 4.26 (ddq, *J* = 12.8, 8.7 and 7.0 Hz, 1H), 2.28 (ddd, *J* = 14.1, 8.6 and 6.6 Hz, 1H), 1.99-1.91 (m, 1H), 1.95 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.16 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 106.0, 90.1, 64.1, 51.0, 28.7, 25.9, 23.9, 18.4, −0.1, −4.3, −4.8.

MS (70 eV, EI) *m/z* (%): 353 (6) [M−^{t}Bu]$^{+\bullet}$, 311 (100), 283 (14), 259 (5), 241 (7), 185 (7), 155 (8), 73 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2927 (w), 2857 (w), 1472 (w), 1463 (w), 1360 (w), 1331 (w), 1249 (w), 1146 (w), 1123 (m), 1081 (m), 1043 (w), 1009 (w), 988 (w), 938 (w), 907 (w), 876 (w), 834 (vs), 777 (m), 759 (m), 698 (w), 670 (w).

HRMS (EI) *m/z*: calcd for **$C_{11}H_{22}OISi_2^+$** [M]$^+$: 353.0254, found: 353.0234.



5-S1 **5-S8** **5-S9**

5-S9

A dry and N$_2$-flushed *Schlenk*-flask was charged with triphenylsilyl acetylene (4.1 g, 14.4 mmol) in THF (30 mL) and cooled down to −78 °C. ^{n}BuLi (6.0 mL, 2.4 M in *n*-hexane, 14.4 mmol) was added dropwise at −78 °C and the reaction mixture was stirred at −78 °C for 1 h. **5-S1** (2.5 g, 12.0 mmol) in THF (10 mL) was added at −78 °C and the mixture was stirred at −78 °C for 20 min. After warmed up to room temperature, it was stirred for 5 h. After quenching the reaction with saturated NH$_4$Cl aqueous solution, the reaction mixture was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and solvents were evaporated to obtain the crude **5-S8**. A 250 mL flask was charged with the crude 5-**S8** (5.2 g) and imidazole (2.0 g, 30.0 mmol) in DMF (30 mL), and the reaction mixture was cooled down to 0 °C. TBSCl (2.2 g, 14.4 mmol) was added at 0 °C and the reaction mixture was stirred for 14.5 h at 0 °C to room temperature. After quenching the reaction saturated NH$_4$Cl aqueous solution, the reaction mixture was extracted with a mixture of Et$_2$O/*i*-hexane = 1/3 three times. The combined organic phase was dried over MgSO$_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/15 to afford a diastereomeric mixture of **5-S9** (6.2 g, 85% yield in 2 steps, d.r. = 70:30) as colorless oil.

^{1}H-NMR (300 MHz, CDCl$_3$) δ: **Major:** 7.66-7.62 (m, 6H), 7.44-7.39 (m, 3H), 7.38-7.33 (m, 6H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.71 (dd, *J* = 7.9 and 6.4 Hz, 1H), 4.45

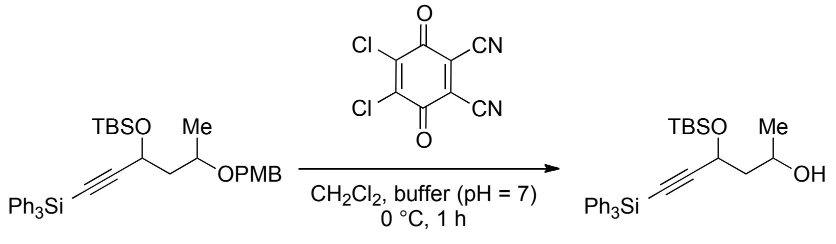
(d, *J* = 11.2 Hz, 1H), 4.31 (d, *J* = 11.2 Hz, 1H), 3.85-3.76 (m, 1H), 3.74 (s, 3H), 2.10 (ddd, *J* = 13.9, 8.0 and 6.4 Hz, 1H), 1.85 (ddd, *J* = 13.2, 8.1 and 5.0 Hz, 1H), 1.22 (d, *J* = 6.2 Hz, 3H), 0.88 (s, 9H), 0.10 (s, 6H). **Minor:** 7.66-7.62 (m, 6H), 7.44-7.39 (m, 3H), 7.38-7.33 (m, 6H), 7.25 (d, *J* = 8.9 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.75 (dd, *J* = 9.5 and 3.5 Hz, 1H), 4.52 (d, *J* = 10.9 Hz, 1H), 4.33 (d, *J* = 11.1 Hz, 1H), 3.85-3.76 (m, 1H), 3.79 (s, 3H), 2.04 (ddd, *J* = 13.9, 8.9 and 3.5 Hz, 1H), 1.92 (ddd, *J* = 13.6, 9.6 and 3.6 Hz, 1H), 1.25 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.10 (s, 6H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: **Major**: 159.1, 135.7, 133.6, 131.1, 130.0, 129.3, 128.0, 113.9, 112.5, 84.3, 72.4, 70.7, 61.6, 55.4, 45.9, 25.9, 20.0, 18.3, –4.3, –4.8. **Minor**: 159.1, 135.7, 133.6, 131.1, 130.0, 129.3, 128.0, 112.5, 84.3, 71.2, 70.3, 60.3, 55.4, 46.6, 25.9, 20.0, 18.3, –4.2, –4.8

MS (70 eV, EI) *m/z* (%): 474 (1) [M–TBSOH]$^{+\bullet}$, 296 (3), 259 (12), 181 (5), 121 (100), 73 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2928 (w), 2856 (w), 1613 (w), 1513 (w), 1463 (w), 1429 (w), 1372 (w), 1361 (w), 1340 (w), 1301 (w), 1247 (m), 1172 (w), 1141 (w), 1112 (m), 1074 (m), 1035 (m), 967 (w), 902 (w), 834 (w), 777 (m), 741 (w), 708 (s), 697 (vs).

HRMS (EI) *m/z*: calcd for **$C_{32}H_{30}O_2Si^{+\bullet}$** [M–TBSOH]$^{+\bullet}$: 474.2015, found: 474.1940.



5-S9 **5-S10**

5-S10

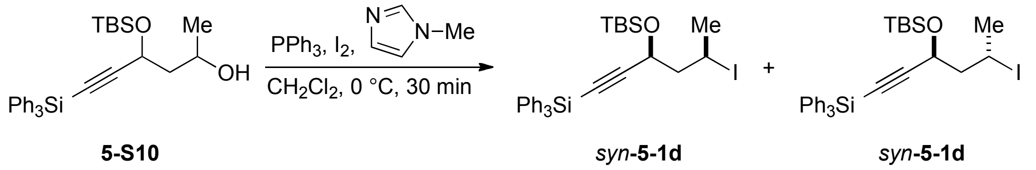
A 250 mL flask was charged with **5-S9** (6.0 g, 10.0 mmol) in CH$_2$Cl$_2$ (50 mL) and phosphate buffer solution (pH = 7, 25 mL) and the reaction mixture was cooled down to 0 °C. DDQ (4.5 g, 20.3 mmol) was added at 0 °C and the reaction mixture was stirred for 30 min at 0 °C to room temperature. After quenching the reaction with saturated NaHCO$_3$ aqueous solution, the reaction mixture was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/10 to afford a diastereomeric mixture of **5-S10** with 4-methoxybnezaldehyde. A 100 mL flask was charged with the obtained mixture in THF (30 mL) and tosyl hydrazine (2.1 g, 11.0 mmol) was added. The reaction mixture was stirred for 70 h at room temperature. The solvents were evaporated and the crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/3.5 to afford a diastereomeric mixture of **5-S10** (4.4 g, 91% yield, d.r. = 70:30) as colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: **Major:** 7.68-7.62 (m, 6H), 7.48-7.35 (m, 9H), 4.75 (dd, J = 8.6 and 5.0 Hz, 1H), 4.09 (dqd, J = 9.1, 6.2 and 2.9 Hz, 1H), 2.10-1.86 (m, 2H), 1.23 (d, J = 6.3 Hz, 3H), 0.91 (s, 9H), 0.17 (s, 3H), 0.14 (s, 3H). **Minor:** 7.68-7.62 (m, 6H), 7.48-7.35 (m, 3H), 4.85 (t, J = 4.9 Hz, 1H), 4.45-4.32 (m, 1H), 2.10-1.86 (m, 2H), 1.23 (d, J = 6.3 Hz, 1H), 0.93 (s, 9H), 0.16 (s, 3H), 0.17 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: **Major**: 135.7, 133.4, 133.3, 128.1, 111.1, 85.1, 67.0, 63.7, 46.7, 25.8, 23.6, 18.2, –4.2, –5.0. **Minor**: 135.6, 133.4, 133.3, 128.1, 111.2, 85.1, 65.3, 62.8, 45.7, 25.8, 23.6, 18.2, –4.5, –5.1.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3443 (br w), 2956 (w), 2928 (w), 2857 (w), 1471 (w), 1462 (w), 1429 (w), 1252 (w), 1187 (w), 1112 (m), 1074 (m), 1023 (w), 966 (w), 909 (w), 834 (m), 809 (w), 778 (m), 740 (w), 708 (s), 696 (vs).

HRMS (ESI) *m/z*: calcd for $C_{30}H_{42}O_2NSi^+$ $[M+NH_4]^+$: 504.2754, found: 504.2751.



syn-**5-1d** and *anti*-**5-1d**

A dry and Ar-flushed *Schlenk*-flask was charged with a solution of I_2 (1.5 g, 6.0 mmol) in CH_2Cl_2 (50 mL) and cooled to 0 °C. PPh_3 (1.6 g, 6.0 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1 h at 0 °C. Then *N*-methylimidazole (0.47 mL, 6.0 mmol) was added. After 10 min of further stirring, **5-S10** (2.4 g, 5.0 mmol) dissolved in CH_2Cl_2 (5 mL) was added and the reaction mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated ($NaHSO_3$+$Na_2S_2O_5$) aqueous solution[106] and was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated at 30 °C.[107] The residue was triturated three times with a mixture of Et_2O/*i*-hexane = 1/3. The precipitation was filtered off and all organic phase was combined. Solvents were evaporated at 30 °C.[108] The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/400→1/150 to afford *syn*-**5-1d** (1.5 g, 50% yield, d.r = 99:1) as the first fraction and white solid, and *anti*-**5-1d** (0.74 g, 25% yield, d.r. = 99:1) as the second fraction and white solid. The relative configuration was determined by the comparison of NMR spectra with other alkyl iodide with OTBS group at 3-position.

syn-5-1d

^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.63 (d, J = 7.2 Hz, 6H), 7.47-7.33 (m, 9H), 4.63 (dd, J = 10.0 and 2.7 Hz, 1H), 4.30 (dqd, J = 10.0, 6.9 and 3.1 Hz, 1H), 2.21 (ddd, J = 14.1, 11.0 and 2.8 Hz, 1H), 2.07-1.93 (m, 1H), 2.00 (d, J = 7.0 Hz, 3H), 0.89 (s, 9H), 0.19 (s, 3H), 0.14 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 135.7, 133.3, 130.1, 128.1, 111.4, 84.4, 63.9, 51.0, 29.3, 26.4, 26.0, 18.3, −4.1, −4.6.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2952 (w), 2928 (w), 2856 (w), 1470 (w), 1427 (w), 1361 (w), 1252 (w), 1156 (w), 1113 (m), 1098 (m), 1062 (w), 1039 (w), 1003 (w), 958 (w), 915 (w), 900 (w), 837 (w), 806 (w), 777 (m), 743 (w), 710 (s), 695 (vs).

HRMS (ESI) *m/z*: calcd for **$C_{30}H_{41}O_2NISi^+$** [M+NH$_4$]$^+$: 614.1771, found: 614.1773.

anti-5-1d

^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.63 (d, J = 7.2 Hz, 6H), 7.47-7.34 (m, 9H), 4.67 (t, J = 7.0 Hz, 1H), 4.31 (dqd, J = 8.8, 6.7 and 6.0 Hz, 1H), 2.35 (ddd, J = 14.8, 8.9 and 6.4 Hz, 1H), 2.05 (ddd, J = 13.7, 7.4 and 5.8 Hz, 1H), 1.95 (d, J = 6.8 Hz, 3H), 0.89 (s, 9H), 0.124 (s, 3H), 0.119 (s, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 135.7, 133.3, 130.1, 128.1, 111.7, 85.2, 64.6, 50.9, 28.9, 25.9, 23.7, 18.3, −4.4, −4.8.

MS (70 eV, EI) *m/z* (%): 539 (1) [M–^{t}Bu]$^{+\bullet}$, 497 (93), 418 (16), 411 (22), 369 (100), 341 (28), 305 (55), 291 (78), 259 (100), 197 (20), 191 (27), 181 (37), 135 (26), 105 (42), 73 (100).

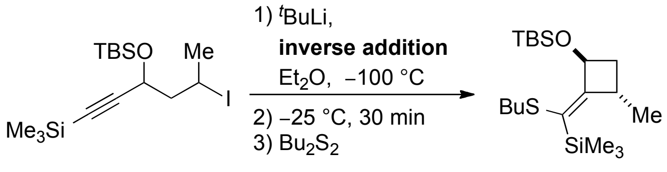
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2928 (w), 2857 (w), 1471 (w), 1429 (w), 1360 (w), 1331 (w), 1252 (w), 1227 (w), 1146 (w), 1112 (m), 1080 (m), 1043 (w), 1007 (w), 962 (w), 907 (w), 834 (m), 778 (m), 740 (w), 708 (s), 695 (vs).

HRMS (EI) *m/z*: calcd for **$C_{26}H_{28}OISi_2^+$** [M–^{t}Bu]$^{+\bullet}$: 539.0723, found: 539.0707.

9.5.2 I/Li exchange followed by subsequent carbolithiation and trappin reaction

[General procedure for thermodynamic control]

A dry and Ar-flushed *Schlenk*-tube was cooled down to −100 °C and charged with a solution of ^{t}BuLi (0.36 mL, 2.1 M in *n*-pentane, 0.75 mmol) in Et_2O (3.3 mL). A solution of alkyl iodide (0.30 mmol) in Et_2O (0.7 mL) was added dropwise for 5 min. After stirring for 10 sec, the reaction mixture was warmed up to −25 °C and stirred for 30 min at −25 °C. Electrophile was added and the reaction mixture was stirred for 15 min at −25 °C to room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution and the reaction mixture was extracted with Et_2O three times. It was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by column chromatography.



5-1c *trans*-**5-3a**

trans-**5-3a**

According to general procedure, diastereomeric mixture **5-1c** (123 mg, 0.30 mmol, d.r. = 70:30) as a starting material and Bu_2S_2 (0.11 mL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on Florisil® with *i*-hexane to afford *trans*-**5-3a** (67 mg, 60% yield) as a colorless oil. The original diastereoselectivity and the combined yield were calculated to be d.r = 86:14 and 70% yield from gas chromatography analysis. The relative configuration was determined by the comparison of NMR spectra with **5-4**.

The peaks of the major diastereomer are given.

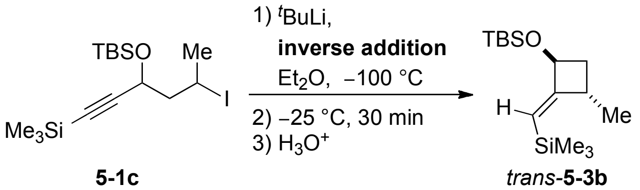
^{1}H-NMR (400 MHz, C_6D_6) δ: 5.07 (ddd, J = 8.0, 6.5 and 3.6 Hz, 1H), 2.97 (dqt, J = 9.8, 7.3 and 3.8 Hz, 1H), 2.76 (dt, J = 12.2 and 7.4 Hz, 1H), 2.64 (dt, J = 12.2 and 7.4 Hz, 1H), 2.14 (ddd, J = 11.3, 10.1 and 6.4 Hz, 1H), 1.79 (ddd, J = 11.6, 8.0 and 3.8 Hz, 1H), 1.63-1.54 (m, 3H), 1.44-1.33 (m, 2H), 1.07 (d, J = 7.2 Hz, 3H), 1.05 (s, 9H), 0.86 (t, J = 7.3 Hz, 2H), 0.25 (s, 9H), 0.23 (s, 3H), 0.18 (s, 3H).

^{13}C-NMR (100 MHz, C_6D_6) δ: 166.2, 128.4, 72.3, 37.6, 34.8, 32.3, 26.4, 22.8, 22.7, 18.7, 14.3, 0.5, −3.8, −4.2.

MS (70 eV, EI) *m/z* (%): 372 (1) $[M]^{+\bullet}$, 315 (100), 209 (9), 147 (16), 91 (10), 73 (80).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 2928 (w), 2857 (w), 1363 (w), 1361 (w), 1249 (w), 1123 (w), 1072 (w), 998 (w), 939 (w), 890 (w), 833 (vs), 776 (m) 758 (w), 686 (w).

HRMS (EI) *m/z*: calcd for **$C_{19}H_{40}OSSi_2$**$^{+\bullet}$ $[M]^{+\bullet}$: 272.2338, found: 272.2329.



trans-**5-3b**

According to general procedure, diastereomeric mixture **5-1c** (123 mg, 0.30 mmol, d.r. = 70:30) as a starting material and saturated NH_4Cl aqueous solution (1 mL) as an electrophile were used. The crude product was purified by column chromatography on Florisil® with Et_2O/*i*-hexane = 1/1000 to afford *trans*-**5-3b** (39 mg, 41% yield, d.r. = 86:14) with impurity (elimination: 5% yield) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with **5-4**.

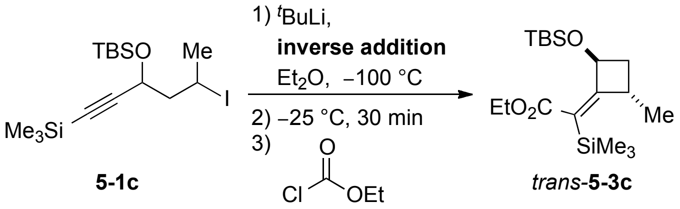
^{1}H-NMR (400 MHz, C_6D_6) δ: ***anti*-5-3b**: 5.64-5.60 (m, 1H), 4.75 (tt, J = 7.9 and 2.1 Hz, 1H), 2.77-2.64 (m, 1H), 1.96 (td, J = 10.1 and 7.7 Hz, 1H), 1.68 (ddd, J = 10.8, 8.4 and 2.8 Hz, 1H), 1.00 (d, J = 7.3 Hz, 3H), 0.85 (s, 9H), 0.00 (s, 9H), −0.03 (s, 3H), −0.07 (s, 3H). ***syn*-5-3b:** 5.67-5.64 (m, 1H), 4.31 (td, J = 7.7 and 1.3 Hz, 1H), 2.43-2.33 (m, 1H), 2.16 (dt, J = 10.3 and 8.2 Hz, 1H), 1.38 (dt, J = 10.3 and 8.1 Hz, 1H), 1.05 (d, J = 6.8 Hz, 3H), 0.84 (s, 9H), 0.00 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H).

^{13}C-NMR (100 MHz, C_6D_6) δ: ***anti*-5-3b**: 167.4, 116.8, 72.8, 37.3, 33.9, 26.1, 21.4, 18.4, 0.1, −4.3, −4.4. ***syn*-5-3b:** 168.8, 117.2, 70.5, 38.4, 33.5, 26.1, 20.9, 18.5, −0.1, −4.36, −4.39.

MS (70 eV, EI) *m/z* (%): 284 (32) $[M]^{+\bullet}$, 269 (4), 227 (28), 211 (19), 185 (3), 157 (13), 147 (100), 126 (24), 101 (18), 73 (56), 59 (4).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2930 (w), 2858 (w), 1655 (w), 1463 (w), 1390 (w), 1362 (w), 1248 (m), 1220 (w), 1189 (w), 1146 (w), 1086 (w), 1046 (w), 1006 (w), 968 (w), 944 (w), 862 (m), 833 (vs), 774 (m), 689 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{32}OSi_2$**$^{+\bullet}$ $[M]^{+\bullet}$: 284.1992, found: 284.1983.



trans-**5-3c**

According to general procedure, diastereomeric mixture **5-1c** (123 mg, 0.30 mmol, d.r. = 70:30) as a starting material and $ClCO_2Et$ (0.11 mL, 0.60 mmol) as an electrophile were used. The crude product was purified by column chromatography on Florisil® with Et_2O/*i*-hexane = 0/1→1/30 to afford *trans*-**5-3c** (39 mg, 36% yield, d.r. = 82:18) as colorless oil. The relative configuration was determined by the comparison of NMR spectra with **5-4**.

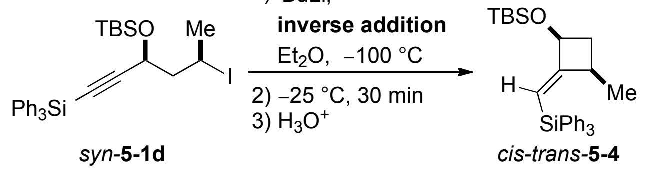
^{1}H-NMR (400 MHz, C_6D_6) δ: ***anti*-5-3c:** 5.18 (td, J = 7.9 and 3.4 Hz, 1H), 4.24-4.08 (m, 2H), 2.72 (dqd, J = 13.8, 7.2 and 3.7 Hz, 1H), 2.02 (td, J = 10.0 and 7.7 Hz, 1H), 1.75 (ddd, J = 10.8, 8.2 and 2.8 Hz, 1H), 1.09 (t, J = 7.1 Hz, 3H), 1.04 (d, J = 7.3 Hz, 3H), 0.97 (s, 9H), 0.21 (s, 9H), 0.16 (s, 3H), 0.13 (s, 3H). ***syn*-5-3c:** 4.92 (td, J = 7.0 and 1.2 Hz, 1H), 4.24-4.08 (m, 2H), 2.56 (tqd, J = 7.4, 7.0 and 1.1 Hz, 1H), 2.28 (dt, J = 11.4 and 8.3 Hz, 1H), 1.49 (dt, J = 11.3 and 6.5 Hz, 1H), 1.17 (d, J = 7.0 Hz, 3H), 1.08 (t, J = 7.1 Hz, 3H), 0.97 (s, 9H), 0.22 (s, 9H), 0.17 (s, 3H), 0.14 (s, 3H).

^{13}C-NMR (100 MHz, C_6D_6) δ: ***anti*-5-3c:** 169.8, 169.1, 127.5, 72.5, 59.9, 37.3, 33.2, 26.1, 21.5, 18.4, 14.5, 0.0, −4.7, −4.8. ***syn*-5-3c:** 169.9, 169.6, 127.5, 69.9, 59.9, 38.4, 33.9, 26.1, 21.7, 18.3, 14.5, −0.1, −4.7, −4.8.

MS (70 eV, EI) *m/z* (%): 356 (19) $[M]^{+\bullet}$, 299 (100), 255 (34), 147 (15), 101 (14), 73 (57).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 2931 (w), 2857 (w), 1713 (w), 1649 (w), 1472 (w), 1362 (w), 1248 (w), 1208 (m) 1191 (m), 1040 (w), 1004 (w), 938 (w), 834 (vs), 775 (m), 673 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{18}H_{36}O_3Si_2}^{+\bullet}$ $[M]^{+\bullet}$: 356.2203, found: 356.2195.



cis-trans-**5-4**

According to general procedure, *syn*-**5-1d** (179 mg, 0.30 mmol, d.r. = 99:1) as a starting material and saturated NH_4Cl aqueous solution (1 mL) as an electrophile were used. The crude product was purified by column chromatography on Florisil® with Et_2O/*i*-hexane = 1/300 to afford *cis-trans*-**5-4** (70 mg, 50% yield, d.r. = 98:2, *cis*:*trans* = 1:99) as colorless oil. The relative configuration was determined by NOE-NMR experiment.

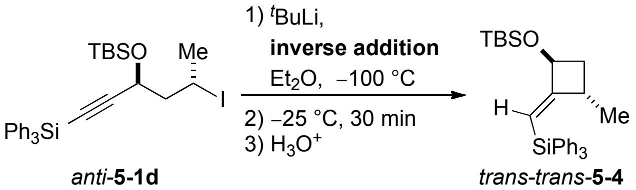
^{1}H-NMR (400 MHz, C_6D_6) *δ*: 7.67-7.60 (m, 2H), 7.10-7.00 (m, 3H), 6.25 (t, *J* = 1.9 Hz, 1H), 4.44 (td, *J* = 7.7 and 1.4 Hz, 1H), 2.32-2.20 (m, 1H), 2.15 (dt, *J* = 10.2 and 8.4 Hz, 1H), 1.45 (dt, *J* = 10.2 and 8.4 Hz, 1H), 0.87 (s, 9H), 0.62 (d, *J* = 6.8 Hz, 3H), 0.00 (s, 3H), −0.03 (s, 3H).

^{13}C-NMR (100 MHz, C_6D_6) *δ*:173.4, 136.3, 136.2, 129.7, 128.2, 111.4, 70.8, 38.3, 34.5, 26.2, 20.3, 18.5, −4.27, −4.29.

MS (70 eV, EI) *m/z* (%): 470 (7) $[M]^{+\bullet}$, 413 (3), 333 (14), 293 (5), 259 (100), 181 (13), 135 (4), 105 (9), 73 (30).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2928 (w), 2856 (w), 1645 (w), 1471 (w), 1462 (w), 1428 (w), 1361 (w), 1251 (w), 1220 (w), 1198 (w), 1151 (w), 1108 (m), 997 (w), 944 (w), 867 (m), 834 (m), 806 (w), 776 (m), 740 (m), 698 (s), 670 (w).

HRMS (EI) *m/z*: calcd for **$C_{30}H_{38}OSi_2^{+\bullet}$** $[M]^{+\bullet}$: 470.2461, found: 470.2447.



trans-trans-**5-4**

According to general procedure, *anti*-**5-1d** (179 mg, 0.30 mmol, d.r. = 99:1) as a starting material and saturated NH_4Cl aqueous solution (1 mL) as an electrophile were used. The crude product was purified by column chromatography on Florisil® with Et_2O/*i*-hexane = 1/2000 to afford *trans-trans*-**5-4** (90 mg, 64% yield, d.r. = 95:5, *cis*:*trans* = 1:99) as colorless oil. The relative configuration was determined by NOE-NMR experiment.

^{1}H-NMR (400 MHz, C_6D_6) *δ*: 7.65-7.59 (m, 2H), 7.10-7.00 (m, 3H), 6.31-6.28 (m, 1H), 4.86 (tt, *J* = 8.0 and 2.3 Hz, 1H), 2.40-2.28 (m, 1H), 1.93 (td, *J* = 10.1 and 7.4 Hz, 1H), 1.62 (ddd, *J* = 10.9, 8.6 and 2.8 Hz, 1H), 0.88 (s, 9H), 0.60 (d, *J* = 7.3 Hz, 3H), 0.00 (s, 3H), −0.03 (s, 3H).

^{13}C-NMR (100 MHz, C_6D_6) *δ*: 172.8, 136.4, 135.9, 129.7, 128.2, 110.9, 73.3, 37.1, 34.3, 26.1, 20.5, 18.4, –4.30, –4.34.

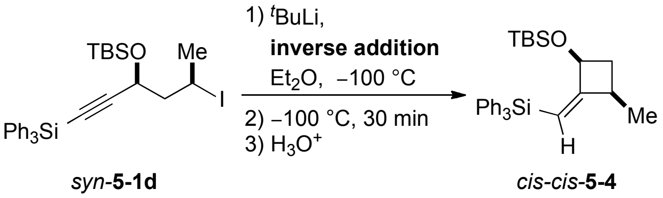
MS (70 eV, EI) *m/z* (%): 470 (6) $[M]^{+\bullet}$, 413 (3), 333 (3), 271 (3), 259 (100), 209 (5), 181 (13), 155 (3), 105 (9), 73 (35).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2928 (w), 2856 (w), 1649 (w), 1472 (w), 1462 (w), 1428 (w), 1361 (w), 1252 (w), 1222 (w), 1188 (w), 1145 (w), 1109 (m), 1046 (w), 998 (w), 942 (w), 865 (w), 835 (m), 808 (w), 775 (m), 740 (w), 697 (vs), 675 (w), 658 (w).

HRMS (EI) *m/z*: calcd for **$C_{30}H_{38}OSi_2^{+\bullet}$** $[M]^{+\bullet}$: 470.2461, found: 470.2454.

[General procedure for kinetic control]

A dry and Ar-flushed *Schlenk*-tube was cooled down to –100 °C and charged with a solution of ^{t}BuLi (0.36 mL, 2.1 M in *n*-pentane, 0.75 mmol) in Et_2O (3.3 mL). A solution of alkyl iodide (0.30 mmol) in Et_2O (0.7 mL) was added dropwise for 5 min. After stirring for 20 min, electrophile was added and the reaction mixture was stirred for 15 min at –100 °C to room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution and the reaction mixture was extracted with Et_2O three times. It was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by column chromatography.



cis-cis-**5-4**

According to general procedure, *syn*-**5-1d** (179 mg, 0.30 mmol, d.r. = 99:1) as a starting material and saturated NH_4Cl aqueous solution (1 mL) as an electrophile were used. The crude product was purified by column chromatography on Florisil® with Et_2O/*i*-hexane = 1/900 to afford *cis-cis*-**5-4** (84 mg, 60% yield, d.r. = 98:2, *cis*:*trans* = 99:1) as colorless oil. The original stereoselectivity was determined by the crude NMR to be d.r. = 99:1 and *cis*:*trans* = 86:14 The relative configuration was determined by the X-ray crystallography of the single crystal recrystallized from *n*-heptane.

^{1}H-NMR (400 MHz, C_6D_6) *δ*: 7.80-7.73 (m, 2H), 7.25-7.17 (m, 3H), 5.79 (t, *J* = 2.0 Hz, 1H), 4.51 (td, *J* = 7.6 and 1.9 Hz, 1H), 2.41-2.30 (m, 1H), 2.27 (td, *J* = 9.2 and 8.0 Hz, 1H), 1.50

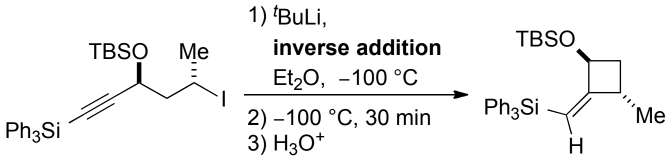
(td, *J* = 9.0 and 8.2 Hz, 1H), 1.10 (d, *J* = 6.5 Hz, 3H), 0.71 (s, 9H), −0.30 (s, 3H), −0.54 (s, 3H).

^{13}C-NMR (100 MHz, C_6D_6) δ: 172.3, 136.6, 136.5, 129.4, 128.1, 109.9, 71.7, 39.2, 33.6, 26.1, 18.1, 17.9, −5.0, −5.2.

MS (70 eV, EI) *m/z* (%): 470 (6) $[M]^{+\bullet}$, 333 (13), 293 (6), 259 (100), 211 (8), 181 (14), 135 (4), 105 (10), 73 (36).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2951 (w), 2927 (w), 2854 (w), 1648 (w), 1470 (w), 1428 (w), 1358 (w), 1250 (w), 1194 (w), 1149 (w), 1110 (m), 1096 (w), 971 (w), 937 (w), 869 (w), 829 (m), 808 (w), 785 (w), 742 (w), 724 (w), 696 (vs), 668 (w).

HRMS (EI) *m/z*: calcd for **$C_{30}H_{38}OSi_2^{+\bullet}$** $[M]^{+\bullet}$: 470.2461, found: 470.2449.



anti-**5-1d** *trans-cis*-**5-4**

trans-cis-**5-4**

According to general procedure, *anti*-**5-1d** (179 mg, 0.30 mmol, d.r. = 99:1) as a starting material and saturated NH_4Cl aqueous solution (1 mL) as an electrophile were used. The crude product was purified by column chromatography on Florisil® with Et_2O/*i*-hexane = 1/900 to afford *trans-cis*-**5-4** (58 mg, 38% yield, d.r. = 97:3, *cis*:*trans* = 99:1) as colorless oil. The original stereoselectivity was determined by the crude NMR to be d.r. = 99:1 and *cis*:*trans* = 66:34. The relative configuration was determined by NOE-NMR experiment.

^{1}H-NMR (400 MHz, C_6D_6) δ: 7.79-7.73 (m, 2H), 7.24-7.18 (m, 3H), 5.92 (t, *J* = 1.7 Hz, 1H), 4.72 (ddt, *J* = 7.2, 5.2 and 2.5 Hz, 1H), 3.05-2.93 (m, 1H), 2.09 (td, *J* = 10.6 and 5.5 Hz, 1H), 1.71 (ddd, *J* = 11.9, 7.4 and 5.5 Hz, 1H), 1.06 (d, *J* = 6.5 Hz, 3H), 0.81 (s, 9H), −0.23 (s, 3H), −0.45 (s, 3H).

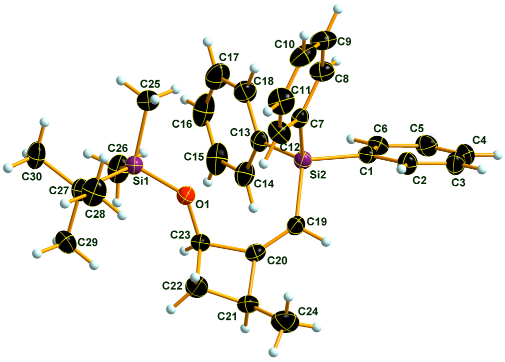
^{13}C-NMR (100 MHz, C_6D_6) δ: 172.0, 136.6, 136.1, 129.6, 128.1, 114.5, 72.3, 37.6, 37.3, 26.2, 20.5, 18.1, −4.6, −5.0.

MS (70 eV, EI) *m/z* (%): 470 (4) $[M]^{+\bullet}$, 312 (7), 259 (100), 234 (4), 181 (12), 105 (8), 73 (22).

IR (ATR) $\widetilde{\nu}$ (cm^{-1}): 2928 (w), 2853 (w), 1648 (w), 1471 (w), 1427 (w), 1360 (w), 1345 (w), 1251 (w), 1186 (w), 1124 (m), 1109 (m), 1044 (w), 958 (w), 932 (m), 868 (m), 854 (m), 835 (m), 807 (m), 774 (m), 740 (w), 730 (m), 697 (vs), 677 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{30}H_{38}OSi_2}^{+\bullet}$ [M]$^{+\bullet}$: 470.2461, found: 470.2455.

9.5.3 X-ray crystal information



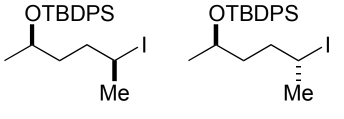
cis-cis-**5-4** (Thermal ellipsoids are drawn at 50 % probability level.)

net formula	$C_{30}H_{38}OSi_2$
M/g mol^{-1}	470.78
crystal size/mm	0.40 × 0.17 × 0.06
T/K	173(2)
radiation	MoKα
diffractometer	‘Oxford Xcalibur 3’
crystal system	monoclinic
space group	*P*21/*n*
a/Å	16.9553(10)
b/Å	10.2132(4)
c/Å	17.6883(10)
α/°	90.00
β/°	114.304(6)
γ/°	90.00
V/Å^3	2791.6(3)
Z	4
calc. density/g cm^{-3}	1.120
μ/mm^{-1}	0.146
absorption correction	multi-scan

refls. measured	21824
R_{int}	0.0545
mean $\sigma(I)/I$	0.0470
θ range	4.14–26.37
observed refls	4058
hydrogen refinement	constr
refls in refinement	5696
restraints	0
$R(F_{\mathrm{obs}})$	0.0470
$R_{\mathrm{w}}(F^2)$	0.0753
S	1.032
shift/error$_{\mathrm{max}}$	0.001
max electron density/e Å^{-3}	0.324
min electron density/e Å^{-3}	–0.218

9.6 Stereoselective Retentive Domino-Transmetalations of Secondary Alkyllithiums to Functionalized Secondary Alkylcopper Reagents

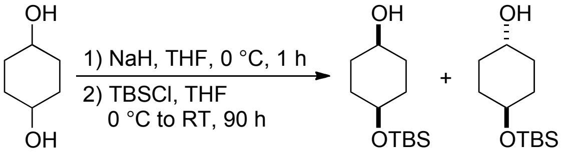
9.6.1 Preparation of starting materials



syn-**6-2a** *anti*-**6-2b**

syn-**6-2a** and *anti*-**6-2a**

They were synthesized in the same way as *syn*-**2-1b** and *anti*-**2-1b**.



6-S1 *cis*-**6-S2** *trans*-**6-S2**

cis-**6-S2** and *trans*-**6-S2**

A N_2-flushed 250 mL *Schlenk*-flask was charged with a suspension of NaH (2.4 g, 60 wt% in mineral oil, 60.0 mmol) in THF (30 mL) and cooled to 0 °C. The diastereomeric mixture of **6-S1** (7.0 g, 60.0 mmol) in THF (30 mL) was added and the resulting solution was stirred for 1 h at 0 °C to room temperature. Then a solution of TBSCl (9.0 g, 60.0 mmol) in THF (10 mL) was added dropwise and the mixture was stirred for 90 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and the mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography two times on silica gel with EtOAc/*i*-hexane = 1/4 to afford **6-S2** (7.6 g, 55% yield) as white solid. The relative configuration was determined by comparison with the reported values.[135]

cis-**6-S2** (CAS: 103202-62-6)

m.p.: 47.6-49.4 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.80 (tt, J = 5.4 and 2.9 Hz, 1H), 3.66 (tt, J = 8.3 and 3.8 Hz, 1H), 1.79-1.57 (m, 6H), 1.55-1.40 (m, 2H), 0.88 (s, 9H), 0.03 (s, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 69.1, 67.0, 31.5, 30.4, 26.0, 18.2, –4.7.

MS (70 eV, EI) *m/z* (%): 230 (2) $[M]^{+\bullet}$, 173 (50), 115 (4), 97 (100), 81 (20), 75 (49), 59 (6).

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[135] Y. Mizuno, K. Nomiyama, K. Takayanagi, *Jpn. Kokai Tokkyo Koho*. JP 2008189592, August 21, 2008.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3282 (br w), 2928 (w), 2856 (w), 1471 (w), 1461 (w), 1376 (w), 1360 (w), 1250 (m), 1096 (m), 1046 (m), 1022 (m), 1004 (w), 964 (m), 880 (w), 857 (s), 832 (vs), 771 (s), 668 (m).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{26}O_2Si^{+\bullet}$** [M]$^{+\bullet}$: 230.1702, found: 230.1678.

trans-**6-S2** (CAS: 103202-63-7)

m.p.: 74.1-76.4 °C.

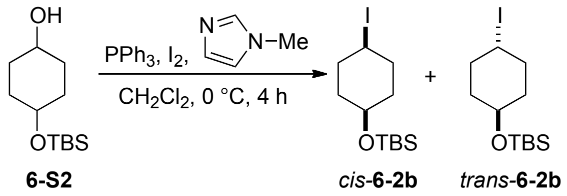
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 3.72-3.56 (m, 2H), 2.00-1.77 (m, 4H), 1.43-1.23 (m, 4H), 0.87 (s, 9H), 0.04 (s, 6H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 70.2, 69.6, 32.9, 32.8, 26.0, 18.3, –4.6.

MS (70 eV, EI) *m/z* (%): 229 (1) [M–H]$^{+\bullet}$, 173 (3), 155 (11), 131 (11), 115 (4), 101 (5), 93 (14), 81 (100), 75 (57), 59 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3329 (br w), 2932 (w), 2855 (w), 1472 (w), 1444 (w), 1372 (w), 1252 (m), 1121 (w), 1095 (w), 1048 (s), 1016 (m), 1005 (m), 966 (w), 905 (w), 876 (m), 834 (s), 807 (m), 771 (vs), 733 (s), 676 (w).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{25}O_2Si^{+\bullet}$** [M–H]$^{+\bullet}$: 229.1624, found: 229.1624.



cis-**6-2b and** *trans*-**6-2b**

A dry and N$_2$-flushed *Schlenk*-flask was charged with a solution of I$_2$ (7.6 g, 30.0 mmol) in CH$_2$Cl$_2$ (60 mL) and cooled to 0 °C. PPh$_3$ (7.2 g, 27.5 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (2.5 mL, 31.7 mmol) was added. After 10 min of further stirring, **6-S2** (6.7 g, 29.0 mmol) was added and the reaction mixture was stirred for 4 h at 0 °C. The reaction was quenched with saturated NH$_4$Cl aqueous solution and the mixture was extracted with CH$_2$Cl$_2$ three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/200→1/150 to afford *cis*-**6-2b** (3.4 g, 34% yield, d.r. = 99:1) as the first eluent and pale yellow oil, and *trans*-**6-2b** (1.4 g, 14% yield, d.r. = 99:1) as the second eluent and colorless oil. In addition to the interpretation of NMR data, the relative configuration was also confirmed by analogy with ((4-iodocyclohexyl)oxy)triisopropylsilane.[22]

cis-**6-2b** (CAS: 1537869-40-1)

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.37 (tt, J = 8.8 and 3.9 Hz, 1H), 3.90 (tt, J = 6.5 and 3.5 Hz, 1 H), 2.30 (dtd, J = 13.4, 9.0 and 4.2 Hz, 2 H), 1.99-1.85 (m, 2 H), 1.75-1.51 (m, 4H), 0.90 (s, 9 H), 0.04 (s, 6 H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 67.0, 34.9, 34.7, 31.6, 26.0, 18.3, –4.6.

MS (70 eV, EI) *m/z* (%): 339 (1) [M]$^{+\bullet}$, 283 (49), 241 (12), 215 (5), 185 (20), 155 (16), 133 (5), 101 (5), 81 (100), 75 (21), 59 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2948 (w), 2928 (w), 2884 (w), 2855 (w), 1471 (w), 1462 (w), 1440 (w), 1368 (w), 1251 (w), 1231 (w), 1156 (w), 1091 (m), 1041 (m), 1011 (w), 992 (m), 880 (w), 828 (vs), 771 (s), 675 (w), 655 (w).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{25}IO_2Si^{+\bullet}$** [M]$^{+\bullet}$: 340.0719, found: 340.0715.

trans-**6-2b** (CAS: 1537869-39-8)

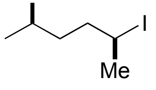
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.34 (tt, J = 7.8 and 3.5 Hz, 1H), 3.74 (tt, J = 7.8 and 3.5 Hz, 1H), 2.22 (ddt, J = 13.1, 6.5 and 3.4 Hz, 2H), 1.90 (ddt, J = 13.9, 9.7 and 4.4 Hz, 2H), 1.84-1.73 (m, 4H), 1.42 (dddd, J = 13.3, 9.3, 8.1 and 3.9 Hz, 2H), 0.87 (s, 9H), 0.04 (s, 6H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 68.4, 36.0, 35.4, 31.7, 26.0, 18.2, –4.6.

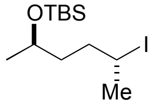
MS (70 eV, EI) *m/z* (%): 340 (1) [M]$^{+\bullet}$, 325 (3), 283 (100), 213 (7), 185 (3), 155 (3), 133 (4), 101 (4), 84 (29), 75 (43), 59 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2927 (w), 2855 (w), 1471 (w), 1462 (w), 1451 (w), 1436 (w), 1373 (w), 1360 (w), 1331 (w), 1250 (m), 1221 (m), 1167 (w), 1094 (m), 1039 (m), 1010 (m), 1005 (m), 855 (m), 832 (vs), 771 (s), 678 (m).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{25}IO_2Si^{+\bullet}$** [M]$^{+\bullet}$: 340.0719, found: 340.0703.



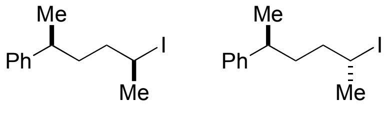
syn-**6-2c**



anti-**6-2c**

syn-**6-2c** (CAS: 1597405-80-5) and *anti*-**6-2c** (CAS: 1597405-79-2)

They were synthesized in the same way as *syn*-**2-1a** and *anti*-**2-1a**.



syn-**6-2d** *anti*-**6-2d**

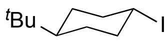
syn-**6-2d** (CAS: 1597406-23-9) and *anti*-**6-2d** (CAS: 1597406-22-8)

They were synthesized in the same way as *syn*-**2-1f** and *anti*-**2-1f**.

syn-**6-2e** *anti*-**6-2e**

syn-**6-2e** and *anti*-**6-2e**

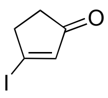
They were synthesized in the same way as *syn*-**3-20** and *anti*-**3-20**.



trans-**6-2f**

trans-**6-2f** (CAS: 16133-42-9)

These compounds were prepared according to the previous literature.[22]



6-7c

6-7c (CAS: 61765-46-6)

It was prepared according to the previous literature.[136]

$Me_3SiCH_2ZnBr·LiBr$ (CAS: 122652-84-0; without LiBr)

A dry *Schlenk*-tube was charged with $ZnBr_2$ (6.3 g, 28.0 mmol) and it was heated at 300 °C under vacuum for 5 min, followed by drying at 140 °C under vacuum overnight. After the addition of THF (30 mL) under Ar atmosphere, it was cooled down to 0 °C. Me_3SiCH_2Li (28.0 mL, 1.0 M in *n*-pentane, 28.0 mmol, Aldrich) was added dropwise to the reaction mixture and it was stirred at room temperature for 1 h. Solvents were evaporated under Ar atmosphere at 0 °C and Et_2O (3 mL) was added. Then solvents were evaporated again. This process was repeated three times and finally the residue was dissolved in Et_2O (20 mL) to obtain the desired ether solution (0.73 M in Et_2O, 66% yield). The concentration was determined by titration of a small aliquot with I_2.[103]

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[136] M. Chebib, G. A. R. Johnston, J. Hanrahan, *PTC Int. Appl.* W0 2003045897 A1, Jun 05 2003.

$CuBr\cdot 2LiCl\cdot Me_2S$

A dry and Ar-flushed *Schlenk*-tube was charged with LiCl (2.4 g, 56.0 mmol) and it was dried by heating 300 °C under vacuum. Then $CuBr\cdot Me_2S$ (5.8 g, 28.0 mmol), which was freshly recrystallized from Me_2S and *n*-hexane, was added and the mixture was dissolved in THF (37.0 mL) under Ar atmosphere.

$Me_3SiCH_2ZnCl\cdot LiCl$ (CAS: 61765-46-6; without LiCl)

A dry *Schlenk*-tube was charged with $ZnCl_2$ (0.41 g, 3.0 mmol) and was heated at 300 °C under vacuum for 5 min. After the addition of THF (3 mL) under Ar atmosphere, it was cooled to 0 °C. Me_3SiCH_2Li (3.0 mL, 1.0 M in *n*-pentane, 3.0 mmol, Aldrich) was added dropwise to the reaction mixture and it was stirred at room temperature for 1 h. Solvents were evaporated under Ar atmosphere at 0 °C and Et_2O (3 mL) was added. Then solvents were evaporated again. This process was repeated three times and finally the residue was dissolved in Et_2O (3 mL) to obtain the desired ether solution (0.66 M in Et_2O, 77% yield). The concentration was determined by titration of a small aliquot with I_2.[103]

Me_3SiCH_2ZnI (CAS: 151450-00-9)

A dry *Schlenk*-tube was charged with Zn dust (3.9 g, 60.0 mmol) and was dried by heating at 300 °C under vacuum for 5 min. After the addition of THF (35 mL) under Ar atmosphere, Me_3SiCH_2I (4.3 g, 20.0 mmol, CAS: 4206-67-1) in THF (5 mL) was added dropwise for 5 min. The reaction mixture was stirred at room temperature for 5 h. Unreacted Zn dust was filtered off with membrane filter. Solvents were evaporated under Ar atmosphere at −25 °C and Et_2O (10 mL) was added. Then solvents were evaporated again at −25 °C. This process was repeated three times and finally the residue was dissolved in Et_2O (20 mL) to obtain the desired ether solution (0.81 M in Et_2O, 81% yield). The concentration was determined by titration of a small aliquot with I_2.[103]

$CuCl\cdot Me_2S$ (CAS: 54678-22-7) and **$CuI\cdot Me_2S$** (CAS: 54678-24-9)

These compounds were prepared according to literature.[137] Their solutions containing LiCl were prepared in the same way as $CuBr\cdot 2LiCl\cdot Me_2S$.

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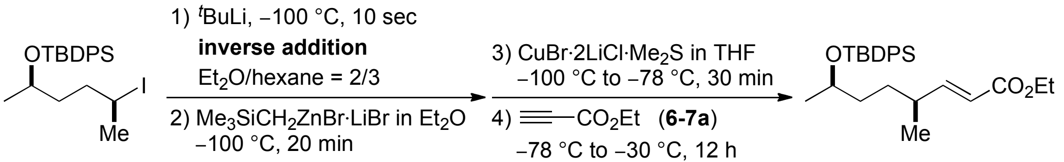
[137] J. S. Filippo, Jr., L. E. Zyontz, J. Potenza, *Inorg. Chem.* **1975**, *14*, 1667.

9.6.2 Domino-transmetalations and trapping reaction sequence

[General procedure]

A dry and Ar-flushed *Schlenk*-tube was cooled to –100 °C and charged with a solution of ^{t}BuLi (0.38 mL, 2.0 M in *n*-pentane, 0.75 mmol) in mixture of Et_2O (1.3 mL) and *n*-hexane (2.0 mL). A solution of alkyl iodide (0.30 mmol) in Et_2O (0.6 mL) was added dropwise for 1 min. After stirring for 10 sec, an ether solution of $Me_3SiCH_2ZnBr\cdot LiBr$ (1.0 mL, 0.73 M in Et_2O, 0.75 mmol) was added and the reaction mixture was stirred for 20 min at –100 °C. Next, a THF solution of $CuBr\cdot 2LiCl\cdot Me_2S$ (1.0 mL, 0.75 M in THF, 0.75 mmol) was added and the reaction mixture was stirred for 30 min at –78 °C. Then electrophile (1.5 mmol) was added and the reaction mixture was stirred for 6–48 h at –30 °C. After quenching the reaction with an aqueous NH_3 solution, the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The obtained crude product was purified by column chromatography. The relative configuration was determined by comparing NMR spectrum with those of already assigned compounds.[138]



syn-**6-2a** *syn*-**6-6a**

syn-**6-6a**

According to general procedure, *syn*-**6-2a** (140 mg, 0.30 mmol, d.r. = 97:3) as a starting material and ethyl propiolate (**6-7a**; 0.15 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with THF/*i*-hexane = 1/60 to afford *syn*-**6-6a** (63 mg, 48% yield, d.r. = 91:9) as colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.

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[138] The configuration of *syn*- and *anti*-**6-6b** and *syn*- and *anti*-**2-4a** was determined by comparing them with literature values. We have observed consistent chemical shift difference in ^{13}C-NMR for a carbon connected with the OTBDPS group for the *syn*- and *anti*-stereoisomers. Thus, the chemical shift in the *anti*-stereoisomers occurred at higher ppm value than that in the *syn*-stereoisomer. We assigned the relative configurations by using this observation for the products **6-6a** and **6-6c–f** resulting from trapping reactions of the alkylcopper reagent **6-5a** with ethyl propiolate, 3-iodocyclopentenone, ethylene oxide, 2,2-dimethoxypropane and ethyl (bromomethyl)acrylate.

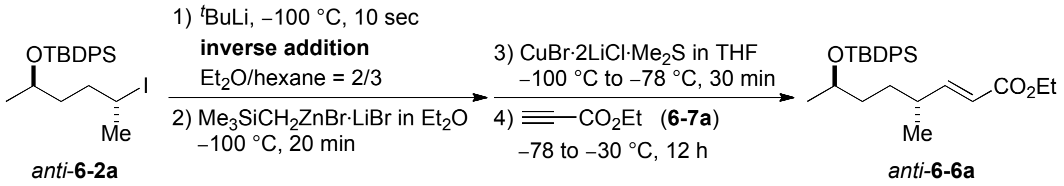
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.70-7.62 (m, 4H), 7.45-7.33 (m, 6H), 6.56 (dd, *J* = 15.7 and 7.9 Hz, 1H), 5.71 (dd, *J* = 15.7 and 1.1 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.86-3.75 (m, 1H), 2.23-2.10 (m, 1H), 1.48-1.26 (m, 4H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.044 (d, *J* = 6.0 Hz, 3H), 1.043 (s, 9H), 0.97 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 167.0, 154.6, 136.01, 135.99, 134.9, 134.5, 129.64, 129.56, 127.6, 127.5, 119.8, 69.6, 60.3, 37.0, 36.7, 31.6, 27.2, 23.3, 19.5, 19.4, 14.4.

MS (70 eV, EI) *m/z* (%): 381 (91) $[\mathrm{M}-{}^t\mathrm{Bu}]^{+\bullet}$, 335 (7), 227 (41), 199 (100), 183 (31), 135 (22), 109 (41), 95 (47), 67 (19).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2962 (w), 2931 (w), 2857 (w), 1717 (m), 1651 (w), 1472 (w), 1462 (w), 1427 (w), 1367 (w), 1303 (w), 1264 (w), 1211 (w), 1177 (w), 1133 (w), 1109 (m), 1042 (m), 984 (w), 939 (w), 861 (w), 821 (w), 739 (w), 700 (vs), 686 (m), 611 (m).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{27}H_{37}O_3Si^{+\bullet}}$ $[\mathrm{M}-\mathrm{H}]^{+\bullet}$: 437.2512, found: 437.2515.



anti-**6-6a**

According to general procedure, *anti*-**6-2a** (140 mg, 0.30 mmol, d.r. = 99:1) as a starting material and ethyl propiolate (**6-7a**; 0.15 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with THF/*i*-hexane = 1/60 to afford *anti*-**6-6a** (68 mg, 52% yield, d.r. = 94:6) as colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.[138]

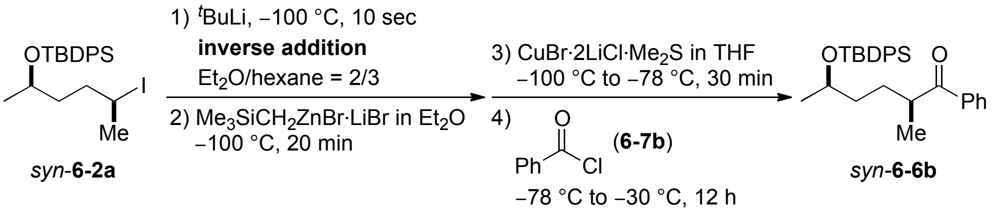
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.72-7.63 (m, 4H), 7.45-7.34 (m, 6H), 6.79 (dd, *J* = 15.7 and 7.9 Hz, 1H), 5.69 (dd, *J* = 15.7 and 1.2 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.81 (qt, *J* = 6.0 and 5.4 Hz, 1H), 2.15 (dtq, *J* = 7.6, 6.7 and 6.3 Hz, 1H), 1.50-1.30 (m, 4H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.052 (d, *J* = 6.0 Hz, 3H), 1.049 (s, 9H), 0.97 (d, *J* = 6.3 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 167.0, 154.6, 136.01, 135.99, 134.9, 134.5, 129.7, 129.6, 127.6, 127.5, 119.8, 69.4, 60.3, 36.9, 36.6, 31.4, 27.2, 23.4, 19.5, 19.4, 14.4.

MS (70 eV, EI) *m/z* (%): 381 (91) $[\mathrm{M}-{}^t\mathrm{Bu}]^{+\bullet}$, 335 (7), 227 (42), 199 (100), 183 (30), 135 (18), 109 (32), 95 (38), 67 (16).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2962 (w), 2931 (w), 2857 (w), 1717 (m), 1651 (w), 1472 (w), 1462 (w), 1427 (w), 1367 (w), 1302 (w), 1264 (w), 1208 (w), 1177 (w), 1133 (w), 1109 (m), 1040 (m), 983 (w), 939 (w), 863 (w), 821 (w), 739 (w), 700 (vs), 686 (m), 611 (m).

HRMS (EI) *m/z*: calcd for $C_{26}H_{35}O_3Si^{+\bullet}$ [M–Me]$^{+\bullet}$: 423.2355, found: 423.2336.



syn-**6-6b**

According to general procedure, *syn*-**6-2a** (140 mg, 0.30 mmol, d.r. = 97:3) as a starting material and benzoyl chloride (**6-7b**; 0.17 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/30 to afford *syn*-**6-6b** (87 mg, 65% yield, d.r. = 94:6) as colorless oil. The relative configuration was determined by comparing with TBS protected derivative in the previous literature.[30]

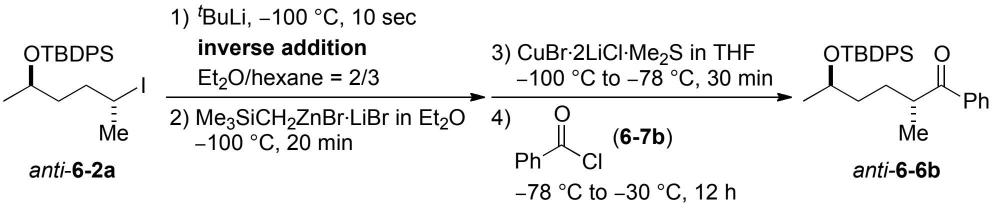
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.96-7.90 (m, 2H), 7.70-7.63 (m, 4H), 7.59-7.53 (m, 1H), 7.49-7.32 (m, 8H), 3.84 (qt, *J* = 6.1 and 5.7 Hz, 1H), 3.37 (tq, *J* = 6.8 and 6.6 Hz, 1H), 1.85-1.70 (m, 1H), 1.54-1.35 (m, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.2 Hz, 3H), 1.03 (s, 9H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 204.4, 136.8, 135.97, 135.96, 134.9, 134.5, 132.9, 129.6, 129.5, 128.7, 128.4, 127.6, 127.5, 69.7, 40.8, 37.1, 29.4, 27.1, 23.3, 19.4, 17.3.

MS (70 eV, EI) *m/z* (%): 387 (23) [M–^{t}Bu]$^{+\bullet}$, 345 (3), 269 (14), 199 (100), 181 (7), 139 (23), 131 (10), 105 (20), 91 (5), 77 (15).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2964 (w), 2931 (w), 2857 (w), 1681 (w), 1472 (w), 1461 (w), 1447 (w), 1427 (w), 1376 (w), 1229 (w), 1194 (w), 1130 (w), 1105 (w), 1056 (m), 998 (w), 970 (w), 908 (w), 821 (w), 731 (m), 699 (vs), 686 (m), 648 (w), 611 (m).

HRMS (EI) *m/z*: calcd for $C_{29}H_{35}O_2Si^{+\bullet}$ [M–H]$^{+\bullet}$: 443.2406, found: 443.2388.



anti-**6-6b**

According to general procedure, *anti*-**6-2a** (140 mg, 0.30 mmol, d.r. = 99:1) as a starting material and benzoyl chloride (**6-7b**: 0.17 mL, 1.50 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/30 to afford *anti*-**6-6b** (83 mg, 62% yield, d.r. = 94:6) as colorless oil. The relative configuration was determined by comparing with TBS protected derivative in the previous literature.[30]

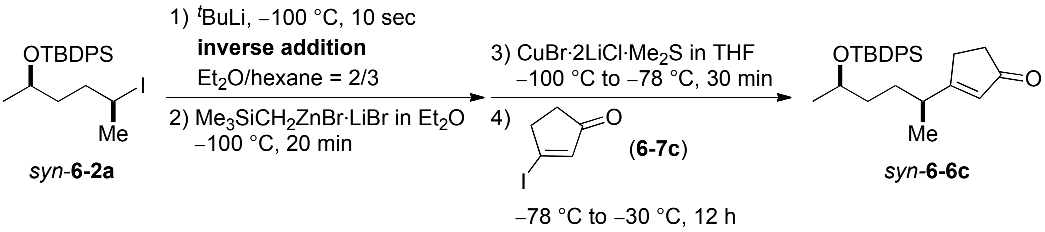
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.90-7.84 (m, 2H), 7.71-7.63 (m, 4H), 7.58-7.52 (m, 1H), 7.48-7.32 (m, 8H), 3.83 (qt, J = 6.0 and 5.7 Hz, 1H), 3.31 (tq, J = 6.7 and 6.5 Hz, 1H), 1.90-1.75 (m, 1H), 1.55-1.36 (m, 3H), 1.14 (d, J = 6.8 Hz, 3H), 1.06 (d, J = 6.1 Hz, 3H), 1.04 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 204.4, 136.7, 135.99, 135.98, 134.8, 134.5, 132.9, 129.6, 129.5, 128.7, 128.3, 127.6, 127.5, 69.3, 40.5, 37.0, 29.1, 27.1, 23.3, 19.4, 17.2.

MS (70 eV, EI) *m/z* (%): 387 (14) $[M–{}^tBu]^{+\bullet}$, 345 (4), 269 (21), 199 (100), 181 (7), 139 (23), 131 (8), 105 (17), 91 (4), 77 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2960 (w), 2930 (w), 2857 (w), 1716 (m), 1472 (w), 1462 (w), 1427 (w), 1377 (w), 1191 (w), 1155 (w), 1132 (w), 1109 (m), 1065 (w), 1027 (w), 966 (w), 983 (w), 940 (w), 821 (w), 736 (w), 700 (vs), 686 (m), 611 (m).

HRMS (EI) *m/z*: calcd for **$C_{29}H_{35}O_2Si^{+\bullet}$** $[M–H]^{+\bullet}$: 443.2406, found: 443.2370.



syn-**6-6c**

According to general procedure, *syn*-**6-2a** (140 mg, 0.30 mmol, d.r. = 97:3) as a starting material and a solution of 3-iodo-cyclopentenone (**6-7c**: 0.31 g, 1.5 mmol) in Et_2O (1.0 mL) as an electrophile were used. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/8 to afford *syn*-**6-6c** (74 mg, 59% yield, d.r. = 93:7) as colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.[138]

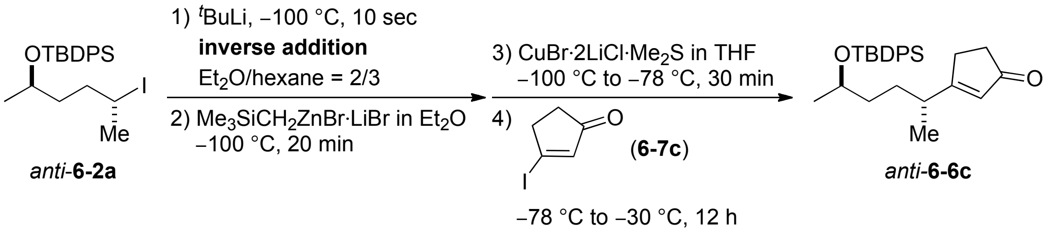
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.68-7.64 (m, 4H), 7.46-7.33 (m, 6H), 5.87 (s, 1H), 3.84 (qt, *J* = 6.0 and 5.7 Hz, 1H), 2.52-2.32 (m, 5H), 1.60-1.24 (m, 4H), 1.075 (d, *J* = 7.0 Hz, 3H), 1.073 (d, *J* = 6.0 Hz, 3H), 1.05 (s, 9H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 210.4, 187.7, 136.0, 135.9, 134.7, 134.5, 129.7, 129.6, 129.0, 127.7, 127.6, 69.4, 37.5, 36.8, 35.3, 30.5, 29.0, 27.2, 23.3, 19.4, 18.9.

MS (70 eV, EI) *m/z* (%): 363 (100) $[M-{}^tBu]^{+\bullet}$, 308 (6), 229 (6), 199 (86), 181 (11), 147 (9), 105 (9), 77 (9).

IR (ATR) $\widetilde{\nu}$ (cm^{-1}): 2963 (w), 2930 (w), 2857 (w), 1709 (m), 1610 (w), 1472 (w), 1461 (w), 1427 (w), 1377 (w), 1263 (w), 1184 (w), 1132 (w), 1104 (m), 1049 (w), 996 (w), 860 (w), 821 (w), 740 (m), 700 (vs), 686 (m), 611 (m).

HRMS (EI) *m/z*: calcd for **$C_{29}H_{35}O_2Si^{+\bullet}$** $[M-Me]^{+\bullet}$: 405.2250, found: 405.2248.



anti-**6-6c**

According to general procedure, *anti*-**6-2a** (140 mg, 0.30 mmol, d.r. = 99:1) as a starting material and a solution of 3-iodo-cyclopentenone (**6-7c**: 0.31 g, 1.5 mmol) in Et$_2$O (1.0 mL) as an electrophile were used. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/8 to afford *anti*-**6-6c** (80 mg, 63% yield, d.r. = 94:6) as colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.[138]

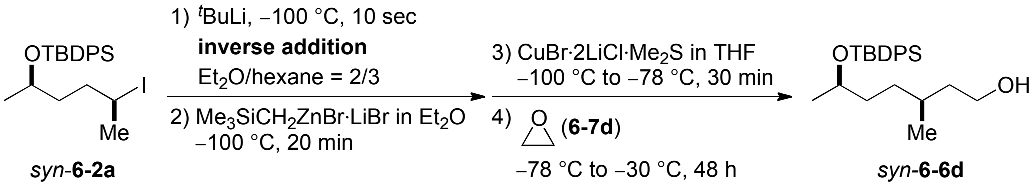
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.70-7.62 (m, 4H), 7.46-7.32 (m, 6H), 5.84 (s, 1H), 3.83 (qt, *J* = 6.0 and 5.8 Hz, 1H), 2.52-2.36 (m, 3H), 2.35 (t, *J* = 4.6 Hz, 2H), 1.62-1.29 (m, 4H), 1.08 (d, *J* = 6.3 Hz, 3H), 1.06 (d, *J* = 6.0 Hz, 3H), 1.05 (s, 9H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 210.4, 187.6, 136.0, 135.9, 134.7, 134.4, 129.7, 129.6, 129.0, 127.6, 127.5, 69.3, 37.4, 36.9, 35.2, 30.6, 29.0, 27.1, 23.4, 19.4, 19.0.

MS (70 eV, EI) *m/z* (%): 363 (100) [M–^{t}Bu]$^{+\bullet}$, 308 (6), 229 (6), 199 (86), 181 (11), 147 (9), 105 (9), 77 (9).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2962 (w), 2930 (w), 2857 (w), 1709 (m), 1610 (w), 1472 (w), 1461 (w), 1427 (w), 1377 (w), 1263 (w), 1184 (w), 1132 (w), 1104 (m), 1050 (w), 996 (w), 860 (w), 821 (w), 740 (w), 700 (vs), 686 (m), 611 (m).

HRMS (EI) *m/z*: calcd for **$C_{29}H_{35}O_2Si^{+\bullet}$** [M–Me]$^{+\bullet}$: 405.2250, found: 405.2230.



syn-**6-6d**

According to general procedure, *syn*-**6-2a** (140 mg, 0.30 mmol, d.r. = 97:3) as a starting material and a THF solution of ethylene oxide (**6-7d**: 1.5 mL, 2.5-3.3 M in THF, >4.0 mmol, Aldrich) as an electrophile were used. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/3.5 to afford *syn*-**6-6d** (42 mg, 37% yield, d.r. = 91:9) as colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.[138]

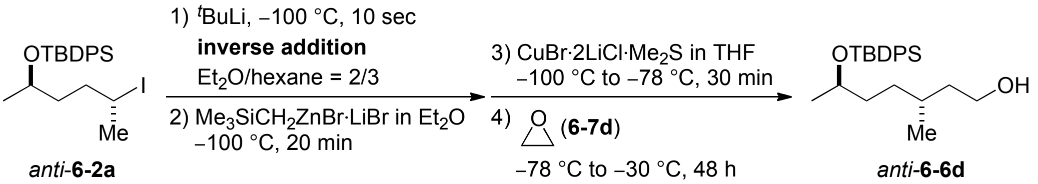
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.74-7.63 (m, 4H), 7.45-7.32 (m, 6H), 3.82 (h, J = 6.0 Hz, 1H), 3.67-3.55 (m, 2H), 1.55-1.20 (m, 7H), 1.07 (d, J = 6.2 Hz, 3H), 1.06 (s, 9H), 0.81 (d, J = 6.6 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 136.0, 135.0, 134.7, 129.6, 129.5, 127.6, 127.5, 69.9, 61.3, 39.9, 36.7, 32.5, 29.6, 27.2, 23.4, 19.7, 19.4.

MS (70 eV, EI) *m/z* (%): 327 (5) [M–^{t}Bu]$^{+\bullet}$, 217 (4), 199 (100), 181 (10), 139 (21), 111 (41), 69 (63).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3338 (br w), 2954 (w), 2930 (w), 2858 (w), 1472 (w), 1461 (w), 1427 (w), 1378 (w), 1248 (w), 1110 (m), 1053 (m), 1005 (w), 997 (w), 858 (w), 836 (w), 822 (m), 739 (w), 700 (vs), 688 (m).

HRMS (EI) *m/z*: calcd for **$C_{24}H_{35}O_2Si^{+\bullet}$** [M–H]$^{+\bullet}$: 383.2406, found: 383.2394.



anti-**6-6d**

According to general procedure, *anti*-**6-2a** (140 mg, 0.30 mmol, d.r. = 99:1) as a starting material and a THF solution of ethylene oxide (**6-7d**: 1.5 mL, 2.5-3.3 M in THF, >4.0 mmol, Aldrich) as an electrophile were used. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/3.5 to afford *anti*-**6-6d** (42 mg, 37% yield, d.r. = 93:7) as colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.[138]

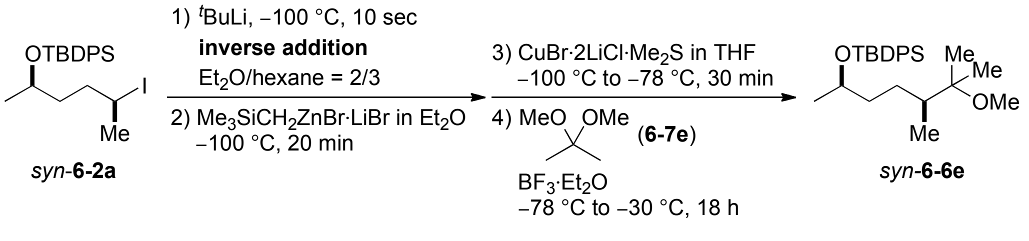
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.72-7.65 (m, 4H), 7.45-7.34 (m, 6H), 3.81 (h, J = 6.0 Hz, 1H), 3.67-3.55 (m, 2H), 1.56-1.23 (m, 7H), 1.07 (d, J = 6.1 Hz, 3H), 1.06 (s, 9H), 0.81 (d, J = 6.5 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 136.0, 135.0, 134.7, 129.6, 129.5, 127.6, 127.5, 69.9, 61.3, 40.0, 36.8, 32.6, 29.6, 27.2, 23.4, 19.7, 19.4.

MS (70 eV, EI) *m/z* (%): 327 (5) $[M-{}^tBu]^{+\bullet}$, 217 (4), 199 (100), 181 (10), 139 (21), 111 (41), 69 (63).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3336 (br w), 2960 (w), 2930 (w), 2857 (w), 1472 (w), 1461 (w), 1427 (w), 1377 (w), 1110 (m), 1058 (m), 997 (w), 822 (w), 739 (w), 701 (vs), 686 (w).

HRMS (EI) *m/z*: calcd for **$C_{24}H_{35}O_2Si^{+\bullet}$** $[M-{}^tBu]^{+\bullet}$: 327.1780, found: 327.1780.



syn-**6-6e**

According to general procedure, *syn*-**6-2a** (140 mg, 0.30 mmol, d.r. = 97:3) as a starting material and 2,2-dimethoxy propane (**6-7e**: 0.19 mL, 1.5 mmol) together with $BF_3 \cdot Et_2O$ (0.19 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/20 to afford *syn*-**6-6e** (55 mg, 44% yield, d.r. = 91:9) as a colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.[138]

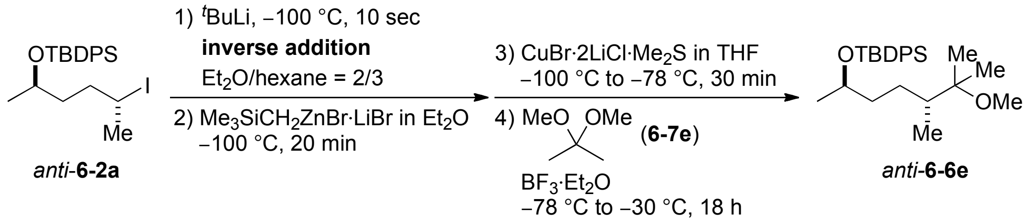
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.73-7.65 (m, 4H), 7.45-7.34 (m, 6H), 3.84 (qt, *J* = 6.0 and 5.7 Hz, 1H), 3.13 (s, 3H), 1.65-1.40 (m, 3H), 1.30-1.20 (m, 1H), 1.09 (d, *J* = 6.1 Hz, 3H), 1.06 (s, 9H), 1.03 (s, 3H), 1.02 (s, 3H), 0.97-0.84 (m, 1H), 0.76 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 136.0, 135.0, 134.7, 129.6, 129.5, 127.6, 127.5, 77.5, 70.2, 48.7, 40.5, 38.5, 27.2, 23.5, 22.3, 22.3, 19.4, 14.3.

MS (70 eV, EI) *m/z* (%): 397 (1) [M–Me]$^{+\bullet}$, 355 (2), 283 (3), 231 (12), 213 (32), 199 (38), 135 (16), 125 (46), 83 (54), 73 (78), 69 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2966 (w), 2930 (w), 2857 (w), 1472 (w), 1462 (w), 1427 (w), 1375 (w), 1363 (w), 1129 (w), 1105 (m), 1075 (m), 1050 (m), 996 (w), 821 (w), 738 (w), 699 (vs), 687 (m).

HRMS (EI) *m/z*: calcd for **$C_{25}H_{37}O_2Si^{+\bullet}$** [M–H]$^{+\bullet}$: 397.2563, found: 397.2555.



anti-**6-6e**

According to general procedure, *anti*-**6-2a** (140 mg, 0.30 mmol, d.r. = 99:1) as a starting material and 2,2-dimethoxy propane (**6-7e**: 0.19 mL, 1.5 mmol) together with BF$_3$·Et$_2$O (0.19 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/20 to afford *anti*-**6-6e** (53 mg, 43% yield, d.r. = 91:9) as colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.[138]

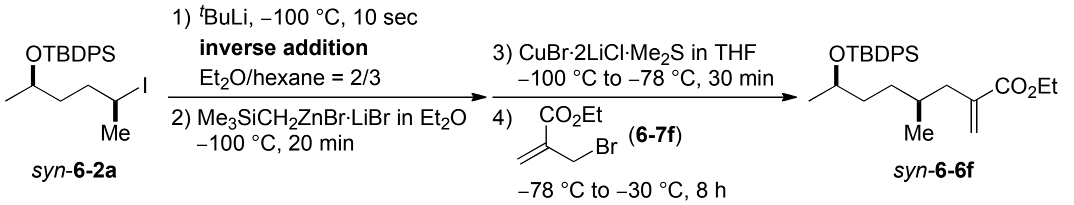
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.72-7.64 (m, 4H), 7.45-7.33 (m, 6H), 3.82 (qt, *J* = 6.0 and 5.7 Hz, 1H), 3.09 (s, 3H), 1.60-1.20 (m, 4H), 1.09 (d, *J* = 6.1 Hz, 3H), 1.06 (s, 9H), 1.02 (s, 3H), 1.01 (s, 3H), 0.96-0.83 (m, 1H), 0.76 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 136.0, 135.0, 134.7, 129.6, 129.5, 127.6, 127.5, 77.5, 70.1, 48.7, 40.2, 38.5, 27.2, 23.4, 22.3, 22.0, 19.4, 14.3.

MS (70 eV, EI) *m/z* (%): 397 (2) [M–Me]$^{+\bullet}$, 323 (4), 283 (5), 231 (23), 213 (59), 199 (68), 183 (24), 125 (67), 83 (61), 69 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2968 (w), 2932 (w), 2858 (w), 1472 (w), 1462 (w), 1427 (w), 1376 (w), 1363 (w), 1128 (w), 1110 (m), 1075 (m), 1050 (m), 995 (w), 821 (w), 738 (w), 701 (vs), 687 (w).

HRMS (EI) *m/z*: calcd for $C_{25}H_{37}O_2Si^{+\bullet}$ [M–H]$^{+\bullet}$: 397.2563, found: 397.2556.



syn-**6-6f**

According to general procedure, *syn*-**6-2a** (140 mg, 0.30 mmol, d.r. = 97:3) as a starting material and ethyl (2-bromomethyl)acrylate (**6-7f**: 0.21 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/45 to afford *syn*-**6-6f** (84 mg, 62% yield, d.r. = 85:15) as colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.[138]

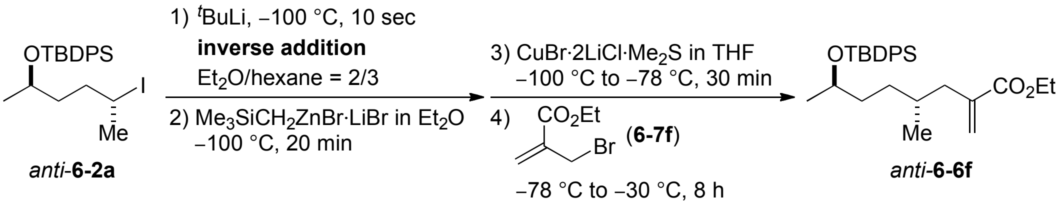
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.73-7.66 (m, 4H), 7.45-7.34 (m, 6H), 6.16-6.12 (m, 1H), 5.44-5.40 (m, 1H), 4.19 (q, *J* = 7.1 Hz, 1H), 3.82 (qt, *J* = 5.9 and 5.7 Hz, 1H), 2.27 (dd, *J* = 13.7 and 5.9 Hz, 1H), 2.01 (dd, *J* = 13.7 and 8.1 Hz, 1H), 1.58-1.24 (m, 5H), 1.29 (t, *J* = 7.1 Hz, 1H), 1.06 (d, *J* = 6.0 Hz, 3H), 1.05 (s, 9H), 0.78 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 167.6, 139.9, 136.0, 135.0, 134.7, 129.6, 129.5, 127.6, 127.5 125.8, 70.0, 60.7, 39.7, 36.8, 32.18, 32.16, 27.2, 23.4, 19.42, 19.41, 14.4.

MS (70 eV, EI) *m/z* (%): 437 (3) [M–Me]$^{+\bullet}$, 395 (100), 349 (10), 289 (4), 227 (7), 197 (34), 181 (45), 135 (13), 121 (39), 109 (7), 69 (16).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2960 (w), 2931 (w), 2857 (w), 1716 (m), 1472 (w), 1462 (w), 1427 (w), 1377 (w), 1323 (w), 1303 (w), 1190 (w), 1155 (w), 1132 (w), 1109 (m), 1065 (w), 1027 (w), 996 (w), 940 (w), 821 (w), 739 (w), 700 (vs), 686 (w), 611 (w).

HRMS (EI) *m/z*: calcd for $C_{28}H_{39}O_3Si^{+\bullet}$ [M–H]$^{+\bullet}$: 451.2668, found: 451.2645.



anti-**6-6f**

According to general procedure, *anti*-**6-2a** (140 mg, 0.30 mmol, d.r. = 99:1) as a starting material and ethyl (2-bromomethyl)acrylate (**6-7f**: 0.21 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/45 to afford *anti*-**6-6f** (85 mg, 63% yield, d.r. = 85:15) as colorless oil. The relative configuration was determined with NMR spectroscopy by the analogy with *anti*- and *syn*-**6-6b**.[138]

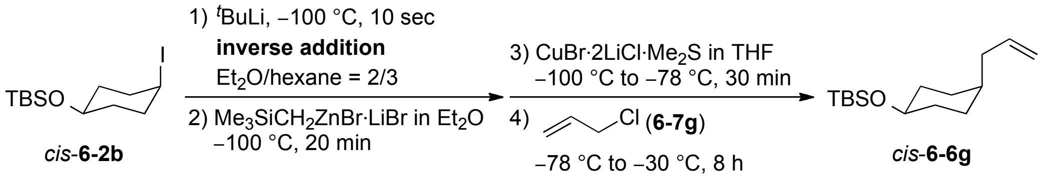
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.73-7.64 (m, 4H), 7.45-7.33 (m, 6H), 6.14 (s, 1H), 5.43 (s, 1H), 4.18 (q, J = 7.0 Hz, 1H), 3.81 (qt, J = 5.9 and 5.5 Hz, 1H), 2.27 (dd, J = 13.7 and 5.8 Hz, 1H), 1.99 (dd, J = 13.7 and 8.1 Hz, 1H), 1.58-1.42 (m, 3H), 1.39-1.25 (m, 2H), 1.28 (t, J = 7.2 Hz, 1H), 1.07-1.01 (m, 3H), 1.05 (s, 9H), 0.77 (d, J = 6.6 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 167.6, 139.9, 136.0, 135.1, 134.7, 129.6, 129.5, 127.6, 127.5, 125.8, 70.0, 60.7, 39.8, 36.9, 32.3, 32.0, 27.2, 23.3, 19.4, 14.4.

MS (70 eV, EI) *m/z* (%): 395 (75) [M–^{t}Bu]$^{+\bullet}$, 349 (15), 317 (9), 289 (9), 235 (7), 227 (22), 199 (100), 183 (27), 135 (24), 81 (16), 55 (25).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2960 (w), 2931 (w), 2857 (w), 1716 (m), 1472 (w), 1462 (w), 1427 (w), 1377 (w), 1324 (w), 1304 (w), 1190 (w), 1156 (w), 1131 (w), 1104 (m), 1065 (w), 1027 (w), 996 (w), 940 (w), 821 (w), 739 (w), 700 (vs), 687 (w), 611 (w).

HRMS (EI) *m/z*: calcd for **$C_{28}H_{41}O_3Si^{+\bullet}$** [M+H]$^{+\bullet}$: 453.2825, found: 453.2823.



cis-**6-6g**

According to general procedure, *cis*-**6-2b** (102 mg, 0.30 mmol, d.r. = 99:1) as a starting material and allyl chloride (**6-7g**: 0.12 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with *i*-hexane to afford pure *cis*-**6-6g** (54 mg, 71% yield) as colorless oil. By the crude NMR diastereoselectivity was determined to be d.r. = 93:7 and calculated combined yield was 75% yield. The relative configuration was determined by coupling constants in ^{1}H NMR spectroscopy.[139]

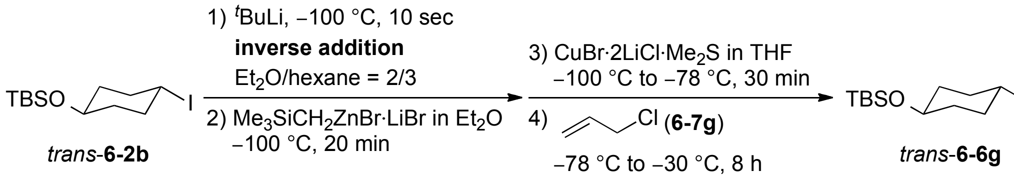
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 5.79 (ddt, *J* = 17.2, 10.1 and 7.2 Hz, 1H), 5.04-4.94 (m, 2H), 3.91 (tt, *J* = 4.4 and 1.8 Hz, 1H), 1.94 (tt, *J* = 6.6 and 1.1 Hz, 2H), 1.70-1.55 (m, 2H), 1.50-1.30 (m, 7H), 0.90 (s, 9H), 0.03 (s, 6H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 138.0, 115.3, 67.4, 41.1, 36.8, 33.3, 27.0, 26.0, 18.3, –4.7.

MS (70 eV, EI) *m/z* (%): 197 (13) [M–^{t}Bu]$^{+•}$, 121 (4), 75 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2927 (w), 2855 (w), 1641 (w), 1472 (w), 1462 (w), 1442 (w), 1376 (w), 1360 (w), 1252 (w), 1142 (w), 1095 (w), 1051 (s), 1019 (m), 1005 (w), 993 (w), 938 (w), 908 (m), 888 (s), 857 (m), 834 (s), 771 (vs), 675 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{30}OSi^{+•}$** [M]$^{+•}$: 254.2066, found: 254.2066.



trans-**6-6g**

According to general procedure, *trans*-**6-2b** (102 mg, 0.30 mmol, d.r. = 98:2) as a starting material and allyl chloride (**6-7g**: 0.12 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/200 to afford pure *trans*-**6-6g** (64 mg, 84% yield) as colorless oil. Diastereoselectivity was determined by the crude NMR to be d.r. = 98:2. The relative configuration was determined by coupling constants in ^{1}H NMR spectroscopy.[139]

^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 5.85-5.70 (m, 1H), 5.01-4.91 (m, 2H), 3.51 (tt, *J* = 10.6 and 4.3 Hz, 1H), 1.94 (tt, *J* = 6.9 and 1.2 Hz, 2H), 1.90-1.78 (m, 2H), 1.78-1.68 (m, 2H), 1.36-1.18 (m, 3H), 1.02-0.86 (m, 2H), 0.88 (s, 9H), 0.05 (s, 6H).

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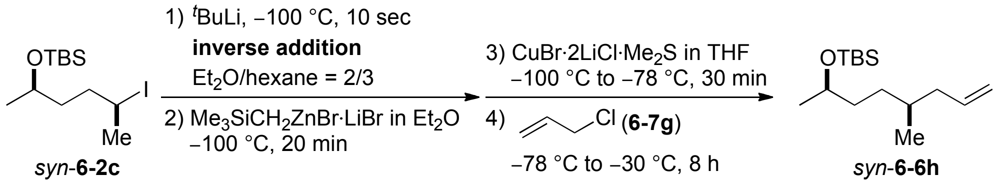
[139] ^{1}H NMR studies of six-membered cyclic compounds in their chair conformations revealed that the spin-spin coupling constants between axial protons and the neighboring protons is larger (approximately 2 to 3 times) than those between equatorial protons and the neighboring protons due to their dihedral angle. In addition, the NMR studies also indicated that the signals of axial protons usually appear at higher field than those of equatorial protons.
a) R. U. Lemieux, H. J. Bernstein, W. G. Schneider, *J. Am. Chem. Soc.* **1958**, *80*, 6098; b) F. R. Jensen, D. S. Noyce, C. H. Sederholm, A. J. Berlin, *J. Am. Chem. Soc.* **1962**, *84*, 386; c) P. M. P. Garcia, T. D. Franco, A. Orsino, P. Ren, X. Hu, *Org. Lett.* **2012**, *14*, 4286.

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 137.6, 115.6, 72.0, 41.3, 36.8, 36.0, 31.3, 26.1, 18.4, –4.4.

MS (70 eV, EI) *m/z* (%): 197 (61) $[M-{}^{t}Bu]^{+\bullet}$, 121 (8), 75 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2928 (w), 2856 (w), 1641 (w), 1472 (w), 1462 (w), 1450 (w), 1377 (w), 1360 (w), 1249 (w), 1095 (s), 1074 (m), 1005 (w), 994 (w), 966 (w), 910 (w), 866 (s), 833 (vs), 771 (s), 667 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{30}OSi^{+\bullet}$** $[M]^{+\bullet}$: 254.2066, found: 254.2059.



syn-**6-6h**

According to general procedure, *syn*-**6-2c** (103 mg, 0.30 mmol, d.r. = 99:1) as a starting material and allyl chloride (**6-7g**: 0.12 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 1/600 to afford pure *syn*-**6-6h** (46 mg, 60% yield, d.r. = 92:8) as colorless oil. The relative configuration was assigned by assuming that the reactions of alkyl copper reagents with allyl chloride proceed with retention of the configuration according to *cis*- and *trans*-**6-6g**.[138]

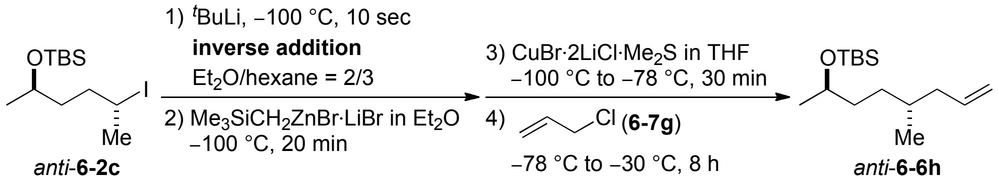
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 5.77 (ddt, J = 16.9, 10.3 and 7.2 Hz, 1H), 5.02-4.93 (m, 2H), 3.74 (qt, J = 6.1 and 6.0 Hz, 1H), 2.11-2.00 (m, 1H), 1.94-1.83 (m, 1H), 1.50-1.14 (m, 5H), 1.11 (d, J = 6.1 Hz, 3H), 0.88 (s, 9H), 0.86 (d, J = 6.7 Hz, 3H), 0.04 (s, 6H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 137.8, 115.7, 69.1, 41.5, 37.2, 33.0, 32.7, 26.1, 24.0, 19.6, 18.3, –4.2, –4.6.

MS (70 eV, EI) *m/z* (%): 241 (2) $[M-Me]^{+\bullet}$, 199 (100), 181 (8), 159 (20), 143 (12), 75 (73).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 2857 (w), 1641 (w), 1472 (w), 1462 (w), 1376 (w), 1361 (w), 1253 (w), 1129 (w), 1079 (w), 1053 (w), 992 (w), 910 (w), 833 (s), 807 (w), 771 (vs).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{31}OSi^{+\bullet}$** $[M]^{+\bullet}$: 255.2144, found: 255.2139.



anti-**6-6h**

According to general procedure, *anti*-**6-2c** (103 mg, 0.30 mmol, d.r. = 98:2) as a starting material and allyl chloride (**6-7g**: 0.12 mL, 1.5 mmol) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/600 to afford pure *anti*-**6-6h** (42 mg, 55% yield, d.r. = 92:8) as colorless oil. The relative configuration was assigned by assuming that the reactions of alkyl copper reagents with allyl chloride proceed with retention of the configuration according to *cis*- and *trans*-**6-6g**.[138]

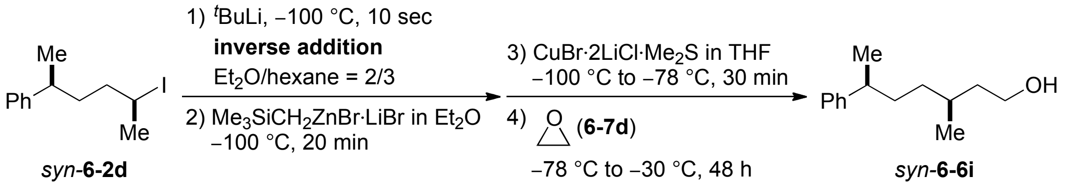
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.76 (ddt, J = 16.9, 10.3 and 7.2 Hz, 1H), 5.02-4.92 (m, 2H), 3.77-3.68 (m, 1H), 2.08-1.98 (m, 1H), 1.93-1.83 (m, 1H), 1.50-1.16 (m, 5H), 1.11 (d, J = 6.1 Hz, 3H), 0.87 (s, 9H), 0.86 (d, J = 6.5 Hz, 3H), 0.03 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 137.8, 115.6, 69.1, 41.6, 37.3, 33.0, 32.7, 26.1, 24.0, 19.7, 18.3, –4.3, –4.6.

MS (70 eV, EI) *m/z* (%): 199 (5) $[M–{}^tBu]^{+\bullet}$, 157 (100), 113 (12), 83 (7).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2929 (w), 2857 (w), 1641 (w), 1472 (w), 1462 (w), 1376 (w), 1361 (w), 1253 (w), 1130 (w), 1080 (w), 1053 (w), 992 (w), 910 (w), 833 (s), 807 (w), 771 (vs).

HRMS (EI) *m/z*: calcd for $C_{15}H_{31}OSi^{+\bullet}$ $[M]^{+\bullet}$: 255.2144, found: 255.2144.



syn-**6-6i**

According to general procedure, *syn*-**6-2d** (87 mg, 0.30 mmol, d.r. = 95:5) as a starting material and a THF solution of ethylene oxide (**6-7d**: 1.5 mL, 2.5-3.3 M in THF, >4.0 mmol, Aldrich) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 4/5 to afford *syn*-**6-6i** (25 mg, 40% yield, d.r. = 89:11) as colorless oil. The relative configuration was assigned by assuming that the reactions of alkyl copper reagents with ethylene oxide proceed with retention of the configuration according to *syn*- and *anti*-**6-6d**.[138]

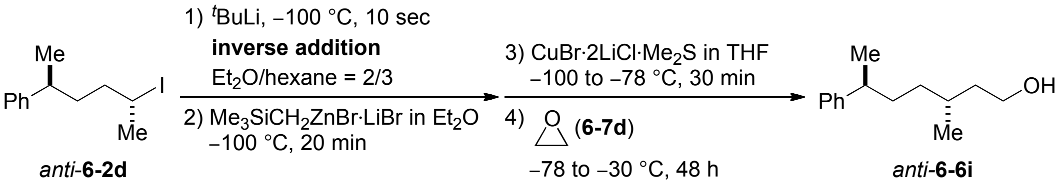
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.33-7.26 (m, 2H), 7.21-7.14 (m, 3H), 3.68-3.55 (m, 2H), 2.64 (qt, J = 7.2 and 6.2 Hz, 1H), 1.70-1.48 (m, 4H), 1.47-1.09 (m, 4H), 1.24 (d, J = 6.9 Hz, 3H), 1.05-0.93 (m, 1H), 0.86 (d, J = 6.6 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 147.8, 128.4, 127.1, 125.9, 61.3, 40.3, 40.0, 35.6, 35.1, 29.6, 22.8, 19.7.

MS (70 eV, EI) *m/z* (%): 206 (6) $[M]^{+\bullet}$, 173 (6), 131 (11), 118 (23), 105 (100), 91 (12), 55 (7).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3328 (br w), 2956 (w), 2925 (w), 2870 (w), 1493 (w), 1452 (w), 1376 (w), 1056 (w), 1010 (w), 960 (w), 760 (m), 699 (vs).

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



anti-**6-6i**

According to general procedure, *anti*-**6-2d** (87 mg, 0.30 mmol, d.r. = 93:7) as a starting material and a THF solution of ethylene oxide (**6-7d**: 1.5 mL, 2.5-3.3 M in THF, >4.0 mmol, Aldrich) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et$_2$O/*i*-hexane = 4/5 to afford *anti*-**6-6i** (25 mg, 40% yield, d.r. = 89:11) as colorless oil. The relative configuration was assigned by assuming that the reactions of alkyl copper reagents with ethylene oxide proceed with retention of the configuration according to *syn*- and *anti*-**6-6d**.[138]

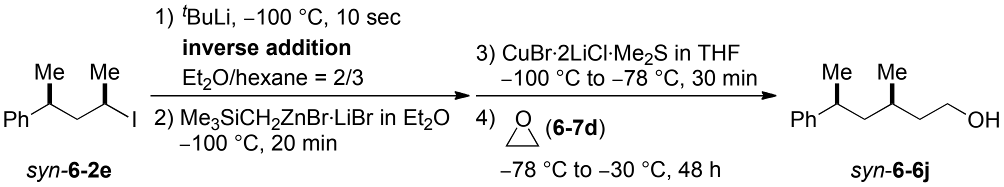
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.32-7.26 (m, 2H), 7.21-7.15 (m, 3H), 3.68-3.56 (m, 2H), 2.64 (qt, J = 7.2 and 7.0 Hz, 1H), 1.71-1.05 (m, 9H), 1.24 (d, J = 6.9 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 148.0, 128.4, 127.1, 125.9, 61.3, 40.4, 39.9, 35.8, 35.3, 29.7, 22.4, 19.8.

MS (70 eV, EI) *m/z* (%): 206 (8) $[M]^{+\bullet}$, 173 (7), 131 (12), 118 (24), 105 (100), 91 (13), 55 (8).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3329 (br w), 2956 (w), 2925 (w), 2870 (w), 1493 (w), 1451 (w), 1376 (w), 1055 (m), 1010 (w), 907 (w), 760 (m), 733 (w), 698 (vs).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{22}O^{+\bullet}$** $[M]^{+\bullet}$: 206.1671, found: 206.1663.



syn-**6-6j**

According to general procedure, *syn*-**6-2e** (82 mg, 0.30 mmol, d.r. = 97:3) as a starting material and a THF solution of ethylene oxide (**6-7d**: 1.5 mL, 2.5-3.3 M in THF, >4.0 mmol, Aldrich) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/2 to afford *syn*-**6-6j** (20 mg, 35% yield, d.r. = 96:4) as colorless oil. The relative configuration was assigned by assuming that the reactions of alkyl copper reagents with ethylene oxide proceed with retention of the configuration according to *syn*- and *anti*-**6-6d**.[138]

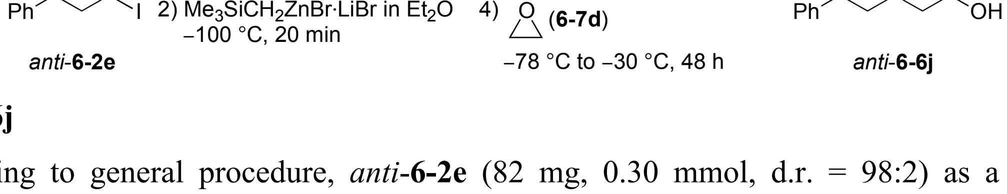
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.32-7.26 (m, 2H), 7.21-7.15 (m, 3H), 3.66-3.54 (m, 1H), 2.86-2.77 (m, 1H), 1.73-1.45 (m, 2H), 1.41-1.30 (m, 3H), 1.23 (d, J = 6.9 Hz, 3H), 0.90 (d, J = 5.9 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 147.5, 128.5, 127.1, 126.0, 61.2, 45.8, 40.4, 37.5, 27.3, 23.6, 19.7.

MS (70 eV, EI) *m/z* (%): 192 (19) $[M]^{+\bullet}$, 174 (24), 159 (100), 145 (23), 131 (18), 118 (63), 105 (63), 91 (58), 79 (22).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3324 (br w), 2956 (w), 2923 (w), 2870 (w), 1493 (w), 1451 (w), 1377 (w), 1053 (m), 1010 (w), 963 (w), 761 (m), 698 (vs).

HRMS (EI) *m/z*: calcd for **$C_{13}H_{20}O^{+\bullet}$** $[M]^{+\bullet}$: 192.1514, found: 192.1507.



anti-**6-6j**

According to general procedure, *anti*-**6-2e** (82 mg, 0.30 mmol, d.r. = 98:2) as a starting material and a THF solution of ethylene oxide (**6-7d**: 1.5 mL, 2.5-3.3 M in THF, >4.0 mmol, Aldrich) as an electrophile were used. The crude product was purified by column chromatography on silica gel with Et_2O/*i*-hexane = 1/2 to afford *anti*-**6-6j** (20 mg, 35% yield, d.r. = 96:4) as colorless oil. The relative configuration was assigned by assuming that the reactions of alkyl copper reagents with ethylene oxide proceed with retention of the configuration according to *syn*- and *anti*-**6-6d**.[138]

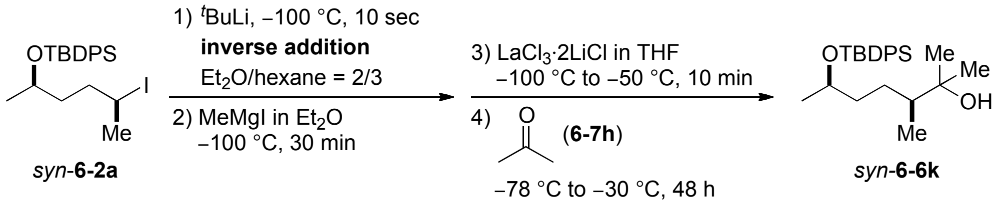
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.32-7.26 (m, 2H), 7.22-7.15 (m, 3H), 3.68 (ddd, J = 10.5, 7.7 and 5.7 Hz, 1H), 3.61 (dt, J = 10.5 and 7.1 Hz, 1H), 2.82 (qt, J = 7.2 and 7.0 Hz, 1H), 1.77-1.61 (m, 1H), 1.60-1.43 (m, 3H), 1.42-1.30 (m, 1H), 1.22 (d, J = 6.9 Hz, 3H), 0.89 (d, J = 6.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 148.1, 128.5, 127.0, 126.0, 61.2, 46.3, 39.9, 37.2, 27.4, 22.1, 20.0.

MS (70 eV, EI) *m/z* (%): 192 (15) $[M]^{+\bullet}$, 174 (23), 159 (89), 145 (20), 131 (14), 118 (42), 105 (100), 91 (33), 79 (22).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3337 (br w), 2957 (w), 2925 (w), 2871 (w), 1493 (w), 1452 (w), 1377 (w), 1054 (m), 1010 (w), 908 (w), 760 (m), 731 (w), 698 (vs).

HRMS (EI) *m/z*: calcd for $C_{13}H_{20}O^{+\bullet}$ $[M]^{+\bullet}$: 192.1514, found: 192.1502.



syn-**6-6k**

A dry and Ar-flushed *Schlenk*-tube was cooled to −100 °C and charged with a solution of ^{t}BuLi (0.38 mL, 2.0 M in *n*-pentane, 0.75 mmol) in mixture of Et_2O (1.3 mL) and *n*-hexane (2.0 mL). A solution of alkyl iodide *syn*-**6-2a** (140 mg, 0.30 mmol, d.r. = 99:1) in Et_2O (0.6 mL) was added dropwise for 1 min. After stirring for 10 sec, an ether solution of MeMgI (1.4 mL, 0.52 M in Et_2O, 0.75 mmol) was added and the reaction mixture was stirred for 30 min at −100 °C. Next, a THF solution of $LaCl_3 \cdot 2LiCl$ (2.3 mL, 0.75 M in THF, 2.3 mmol) was added and the reaction mixture was stirred for 10 min at −78 °C. Then acetone (0.19 mL, 2.3 mmol) was added and the reaction mixture was stirred for 2 h at −30 °C. After quenching the reaction with an aqueous NH_4Cl solution, the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with

EtOAc/*i*-hexane = 1/4 to afford *syn*-**6-6k** (28 mg, 23% yield, d.r. = 92:8) as colorless oil. The relative configuration was determined by the comparing with *anti*-**6-6k**.

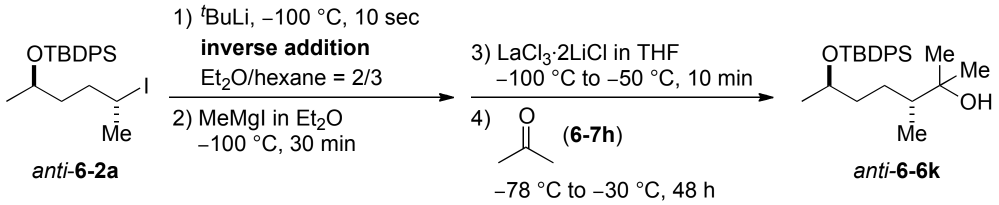
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.71-7.65 (m, 2H), 7.45-7.31 (m, 3H), 3.82 (qt, *J* = 6.0 and 5.9 Hz, 1H), 1.58-1.18 (m, 5H), 1.11 (s, 3H), 1.094 (d, *J* = 6.3 Hz, 3H), 1.086 (s, 3H), 1.05 (s, 9H), 0.98-0.84 (m, 1H), 0.80 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 136.1, 135.0, 134.7, 129.6, 129.5, 127.6, 127.5, 73.6, 70.1, 44.7, 38.4, 27.3, 27.2, 27.0, 26.4, 23.6, 19.4, 14.5.

MS (70 eV, EI) *m/z* (%): 341 (2) [M–^{t}Bu]$^{+\bullet}$, 323 (3), 283 (6), 199 (100), 135 (15), 125 (50), 83 (59), 69 (88).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3381 (br w), 2965 (w), 2931 (w), 2858 (w), 1472 (w), 1462 (w), 1428 (w), 1376 (w), 1130 (w), 1104 (m), 1080 (w), 1051 (w), 996 (w), 942 (w), 909 (w), 822 (w), 738 (w), 700 (vs), 687 (m).

HRMS (EI) *m/z*: calcd for **$C_{21}H_{29}O_2Si^{+\bullet}$** [M–^{t}Bu]$^{+\bullet}$: 341.1937, found: 341.1934.



anti-**6-6k**

A dry and Ar-flushed *Schlenk*-tube was cooled to –100 °C and charged with a solution of ^{t}BuLi (0.38 mL, 2.0 M in *n*-pentane, 0.75 mmol) in mixture of Et$_2$O (1.3 mL) and *n*-hexane (2.0 mL). A solution of alkyl iodide *anti*-**6-2a** (140 mg, 0.30 mmol, d.r. = 99:1) in Et$_2$O (0.6 mL) was added dropwise for 1 min. After stirring for 10 sec, an ether solution of MeMgI (1.4 mL, 0.52 M in Et$_2$O, 0.75 mmol) was added and the reaction mixture was stirred for 30 min at –100 °C. Next, a THF solution of LaCl$_3$·2LiCl (2.3 mL, 0.75 M in THF, 2.3 mmol) was added and the reaction mixture was stirred for 10 min at –78 °C. Then acetone (0.19 mL, 2.3 mmol) was added and the reaction mixture was stirred for 2 h at –30 °C. After quenching the reaction with an aqueous NH$_4$Cl solution, the reaction mixture was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and solvents were evaporated. The crude product was purified by column chromatography on silica gel with EtOAc/*i*-hexane = 1/4 to afford *anti*-**6-6k** (36 mg, 30% yield, d.r. = 95:5) as colorless oil. The relative configuration was determined by further transformation to *anti*-**6-6e'** shown below.

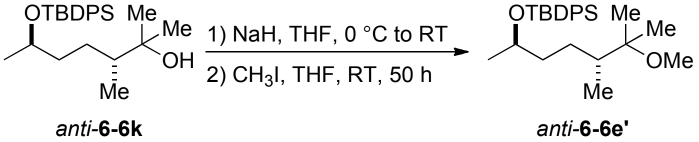
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.71-7.65 (m, 2H), 7.45-7.31 (m, 3H), 3.82 (qt, *J* = 6.0 and 5.9 Hz, 1H), 1.58-1.18 (m, 4H), 1.089 (s, 3H), 1.088 (d, *J* = 6.1 Hz, 3H), 1.07 (s, 3H), 1.05 (s, 9H), 0.97-0.84 (m, 1H), 0.79 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) *δ*: 136.1, 134.9, 134.7, 129.60, 129.55, 127.6, 127.5, 73.6, 70.0, 44.5, 38.3, 27.4, 27.2, 27.0, 26.4, 23.4, 19.4, 14.5.

MS (70 eV, EI) *m/z* (%): 341 (2) $[M–{}^tBu]^{+\bullet}$, 323 (3), 283 (6), 199 (100), 135 (15), 125 (50), 83 (59), 69 (88).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3356 (br w), 2965 (w), 2931 (w), 2858 (w), 1472 (w), 1462 (w), 1427 (w), 1376 (w), 1129 (w), 1104 (m), 1079 (w), 1051 (w), 996 (w), 941 (w), 907 (m), 821 (w), 731 (s), 700 (vs).

HRMS (EI) *m/z*: calcd for **$C_{21}H_{29}O_2Si^{+\bullet}$** $[M–{}^tBu]^{+\bullet}$: 341.1937, found: 341.1932.



anti-**6-6e**'

A dry and Ar-flushed *Schlenk*-tube was charged with a suspension of NaH (1.3 mg, 60% wt, 0.03 mmol) in THF (2.0 mL) and it was cooled down to 0 °C. A solution of *anti*-**6-6k** (13 mg, 0.03 mmol, d.r. = 95:5) in THF (1.0 mL) was added. After stirring for 30 min at room temperature, CH_3I (2.1 μL, 0.03 mmol) was added and the reaction mixture was stirred for 50 h at room temperature. After quenching the reaction with an aqueous NH_4Cl solution, the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was analyzed with NMR to figure out *anti*-**6-6e'** was selectively obtained (d.r. = 94:6).

9.6.3 Deuterolysis experiments

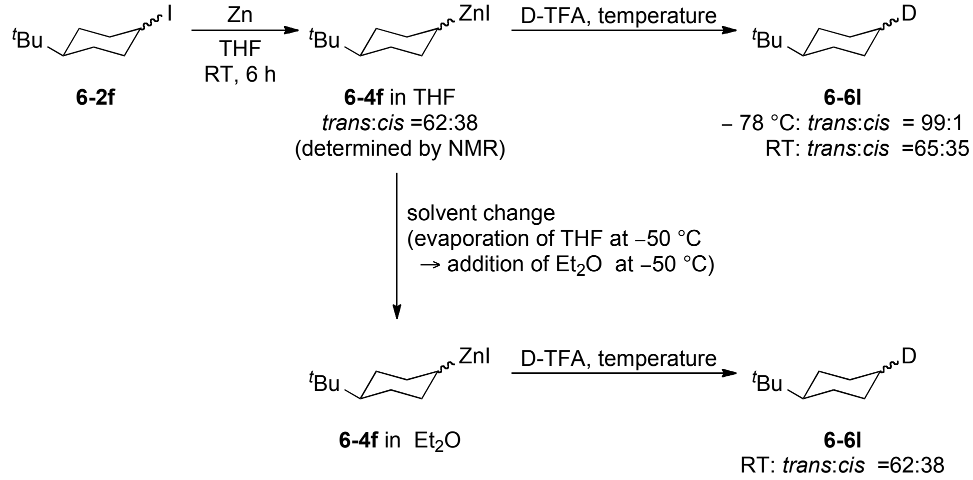
[With solvent switch]

A dry and Ar-flushed *Schlenk*-tube was cooled to −100 °C and charged with a solution of ^{t}BuLi (0.18 mL, 2.1 M in *n*-pentane, 0.38 mmol) in mixture of Et_2O (1.9 mL). A solution of alkyl iodide *trans*-**6-2f** (40 mg, 0.15 mmol, d.r. = 99:1) in Et_2O (0.4 mL) was added dropwise for 1 min. After stirring for 10 sec, an ether solution of ZnI_2 (0.38 mL, 1.0 M in Et_2O, 0.38 mmol) was added and the reaction mixture was stirred for 20 min at −100 °C. Solvents were evaporated at −50 °C and THF (2.3 mL) was added at −50 °C. After warming up to room temperature, the reaction mixture was stirred at room temperature for indicated time (30 sec or 3.5 h). Then, *d*-TFA (0.12 mL, 1.5 mmol) was added at room temperature and the reaction mixture was stirred for 15 min at room temperature. After quenching the reaction with an aqueous $NaHCO_3$ solution, the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was analyzed with D-NMR.

[Without solvent switch]

A dry and Ar-flushed *Schlenk*-tube was cooled to −100 °C and charged with a solution of ^{t}BuLi (0.18 mL, 2.14 M in *n*-pentane, 0.38 mmol) in mixture of Et_2O (1.9 mL). A solution of alkyl iodide *trans*-**6-2f** (40 mg, 0.15 mmol, d.r. = 99:1) in Et_2O (0.4 mL) was added dropwise for 1 min. After stirring for 10 sec, an ether solution of ZnI_2 (0.38 mL, 1.0 M in Et_2O, 0.38 mmol) was added and the reaction mixture was stirred for 20 min at −100 °C. After warming up to room temperature, the reaction mixture was stirred at room temperature for indicated time (30 sec or 3.5 h). Then, *d*-TFA (0.12 mL, 1.5 mmol) was added at room temperature and the reaction mixture was stirred for 15 min at room temperature. After quenching the reaction with an aqueous $NaHCO_3$ solution, the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was analyzed with D-NMR.

[Additional experiments]

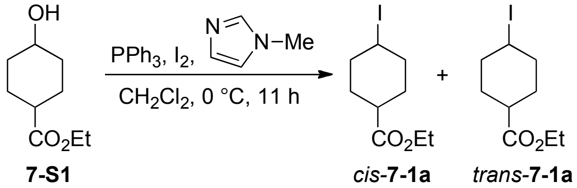


Temperature and solvent effect on deuterolysis reaction was examined.

The THF solution of the cyclohexylzinc compound **6-4f** (*trans*:*cis*= 62:38), prepared by direct insertion of Zn to the corresponding cyclohexyl iodide **6-2f**, was quenched by *d*-TFA at the indicated temperature in THF. At room temperature, stereo-information was retentive although stereoconvergence was observed at –100 °C. Therefore, it is essential to warm the Zn solution to room temperature before quenching reaction with *d*-TFA. The ether solution of diastereomeric mixture of the cyclohexylzinc compound **6-4f** was also prepared by solvent switching and its quenching was still stereoselective at room temperature.

9.7 Stereoconvergent Negishi Cross-Coupling Using Functionalized Cyclohexyl Reagents

9.7.1 Preparation of starting materials



7-1a (CAS: 524734-42-7)[140]

A dry and N_2-flushed *Schlenk*-flask was charged with a solution of I_2 (7.6 g, 30.0 mmol) in CH_2Cl_2 (60 mL) and cooled to 0 °C. PPh_3 (7.2 g, 27.5 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (2.5 mL, 31.7 mmol) was added. After 10 min of further stirring, **7-S1** (4.0 mL, 25.0 mmol) was added and the reaction mixture was stirred overnight at 0 °C. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/30→1/15 to afford **7-1a** (3.1 g, 43% yield) as colorless oil.[139]

cis-**7-1a** (CAS:1442981-32-9)

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.64 (quint, J = 4.2 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 2.40 (tt, J = 9.6 and 4.0 Hz, 1H), 2.18-2.07 (m, 2H), 2.06-1.92 (m, 2H), 1.85-1.67 (m, 4H), 1.26 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 174.8, 60.5, 41.7, 36.1, 32.8, 26.3, 14.4.

MS (70 eV, EI) *m/z* (%): 282 (1) $[M]^{+\bullet}$, 237 (8), 209 (6), 155 (61), 127 (5), 109 (39), 81 (100), 67 (12), 55 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2943 (w), 2865 (w), 1726 (vs), 1441 (w), 1376 (w), 1314 (w), 1236 (m), 1194 (m), 1174 (s), 1151 (s), 1096 (w), 1077 (w), 1038 (s), 1024 (m), 987 (w), 909 (w), 856 (w), 666 (w).

HRMS (EI) *m/z*: calcd for **$C_9H_{15}IO_2^{+\bullet}$** $[M]^{+\bullet}$: 282.0117, found: 282.0109.

trans-**7-1a** (CAS: 1442981-72-7)

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[140] G. L. Lange, C. Gottardo, *Synth. Commun.* **1990**, *20*, 1473.

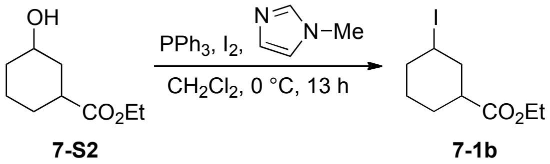
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 4.14 (tt, *J* = 11.4 and 4.0 Hz, 1H), 4.11 (q, *J* = 7.0 Hz, 2H), 2.46-2.36 (m, 2H), 2.37 (tt, *J* = 11.4 and 3.6 Hz, 1H), 2.05-1.83 (m, 4H), 1.63-1.46 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 175.3, 60.6, 41.7, 39.0, 30.8, 28.3, 14.4.

MS (70 eV, EI) *m/z* (%): 282 (1) $[M]^{+\bullet}$, 237 (5), 209 (7), 155 (56), 127 (5), 109 (37), 81 (100), 67 (12), 55 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2941 (w), 2860 (w), 1726 (vs), 1450 (w), 1375 (w), 1340 (w), 1310 (w), 1252 (m), 1187 (s), 1149 (s), 1096 (w), 1076 (w), 1040 (s), 1018 (w), 993 (m), 901 (w), 809 (w), 657 (w).

HRMS (EI) *m/z*: calcd for **$C_9H_{15}IO_2^{+\bullet}$** $[M]^{+\bullet}$: 282.0117, found: 282.0112.



7-1b (CAS: 139125-65-8)

A dry and N$_2$-flushed *Schlenk*-flask was charged with a solution of I$_2$ (6.1 g, 24 mmol) in CH$_2$Cl$_2$ (50 mL) and cooled to 0 °C. PPh$_3$ (5.8 g, 22 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (2.0 mL, 25.4 mmol) was added. After 10 min of further stirring, **7-S2**[141] (3.4 g, 20.0 mmol, CAS: 94160-25-5) was added and the reaction mixture was stirred overnight at 0 °C. The reaction was quenched with saturated NH$_4$Cl aqueous solution and the mixture was extracted with CH$_2$Cl$_2$ three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/40 to afford **7-1b** (1.6 g, 29% yield) as colorless oil.

The peaks of the mixture of the two diastereomers are given.

^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 4.80 (quint, *J* = 4.3 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 4.11 (q, *J* = 7.1 Hz, 0.8H), 4.07 (tt, *J* = 12.4 and 4.0 Hz, 0.4H), 2.80 (tt, *J* = 9.9 and 3.9 Hz, 1H), 2.66 (dtt *J* = 12.9, 3.8 and 1.9 Hz, 0.4H), 2.45-2.37 (m, 0.4H), 2.34 (tt, *J* = 12.2 and 3.6 Hz, 1H), 2.25 (dddd, *J* = 14.5, 5.3, 3.4 and 1.5 Hz, 1H), 2.12-1.25 (m, 9.8H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 1.2H).

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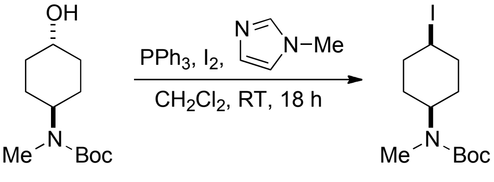
[141] a) H. E. Ungnade, F. V. Morriss, *J. Am. Chem. Soc.* **1948**, *70*, 1898; b) M. Kanazashi, M. Takakusa, *Bull. Chem. Soc. Jpn.* **1954**, *27*, 441.

^{13}C-NMR (101 MHz, CDCl$_3$) δ: 175.1, 173.7, 60.7, 60.6, 45.5, 42.3, 40.4, 39.8, 38.8, 36.6, 32.6, 28.3, 27.7, 27.6, 26.5, 22.7, 14.4, 14.3.

MS (70 eV, EI) *m/z* (%): 282 (1) $[M]^{+\bullet}$, 237 (8), 209 (5), 155 (54), 127 (4), 109 (34), 81 (100), 67 (11), 55 (7).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2977 (w), 2935 (w), 1726 (vs), 1445 (w), 1374 (w), 1321 (w), 1278 (w), 1243 (m), 1176 (s), 1147 (s), 1095 (w), 1055 (w), 1037 (m), 1027 (m), 983 (w), 856 (w), 847 (w), 679 (w).

HRMS (EI) *m/z*: calcd for **$C_9H_{15}IO_2^{+\bullet}$** $[M]^{+\bullet}$: 282.0117, found: 282.0119.



trans-**7-S3** *cis*-**7-1c**

cis-**7-1c** (CAS: 1537869-33-2)

A dry and N$_2$-flushed *Schlenk*-flask was charged with a solution of I$_2$ (6.1 g, 24 mmol) in CH$_2$Cl$_2$ (50 mL) and cooled to 0 °C. PPh$_3$ (5.8 g, 22 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (2.0 mL, 25.4 mmol) was added. After 10 min of further stirring, *trans*-**7-S3**[142] (4.6 g, 20.0 mmol, CAS: 400899-99-2) was added and the reaction mixture was stirred overnight at 0 °C. The reaction was quenched with saturated NH$_4$Cl aqueous solution and the mixture was extracted with CH$_2$Cl$_2$ three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/2 to afford *cis*-**7-1c** (4.3 g, 63% yield) as white solid.

m.p.: 67.8-69.0 °C.

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.79 (br s, 1H), 4.00 (br s, 1H), 2.80 (s, 3H), 2.20-1.85 (m, 4H), 1.70-1.48 (m, 4H), 1.46 (s, 9H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 155.6, 79.4, 53.0, 35.8, 34.9, 28.6, 26.1.

MS (70 eV, EI) *m/z* (%): 339 (9) $[M]^{+\bullet}$, 284 (28), 266 (10), 239 (4), 209 (10), 156 (100), 112 (37), 101 (4), 81 (74), 70 (18), 57 (74).

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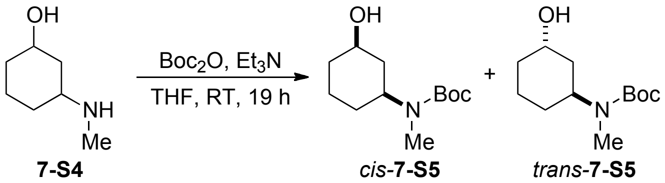
[142] K. Seifert, A. Büttner, S. Rigol, N. Eukert, E. Wandel, A. Giannis, *Bioorg. Med. Chem.* **2012**, *20*, 6465.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2982 (w), 2958 (w), 2930 (w), 1676 (vs), 1475 (w), 1431 (m), 1402 (w), 1360 (s), 1353 (m), 1320 (s), 1254 (m), 1161 (s), 1129 (vs), 1068 (w), 1048 (m), 1030 (w), 1021 (w), 992 (m), 896 (s), 841 (w), 766 (m), 697 (w).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{22}IO_2N^{+\bullet}$** [M]$^{+\bullet}$: 339.0695, found: 339.0690.



7-S5 (CAS: 1332632-81-1)

A 250 mL flask was charged with a solution of **7-S4**[143] (2.0 g, 15.2 mmol, CAS: 89854-96-6) in THF (35 mL) and cooled to 0 °C. Et_3N (1.2 mL, 16.7 mmol) and Boc_2O (3.8 mL, 16.7 mmol) were added and the resulting solution was stirred for 19 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/3 to afford **7-S5** (2.9 g, 83% yield) as colorless oil.

cis-**7-S5** (CAS: 610302-04-0)

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 4.18-3.75 (br s, 1H), 3.75-3.58 (m, 1H), 2.72 (s, 3H), 2.04-1.89 (m, 2H), 1.88-1.02 (m, 7H), 1.45 (s, 9H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 155.7, 79.6, 70.0, 52.3, 39.8, 34.9, 29.0, 28.63, 28.57, 28.4, 22.2.

MS (70 eV, EI) *m/z* (%): 229 (4) [M]$^{+\bullet}$, 173 (25), 156 (18), 130 (26), 114 (5), 98 (5), 86 (59), 76 (8), 70 (14), 57 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3406 (br w), 2934 (w), 2860 (w), 1688 (m), 1667 (s), 1480 (w), 1451 (w), 1402 (m), 1364 (m), 1316 (m), 1251 (w), 1153 (vs), 1066 (m), 1042 (m), 959 (m), 939 (w), 875 (m), 837 (w), 773 (w).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{19}O_2N^{+\bullet}$** [M]$^{+\bullet}$: 229.1678, found: 229.1674.

trans-**7-S5** (CAS: 1537869-34-3)

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[143] T. Lehmann-Lintz, A. Heckel, J. Kley, E. Langkopf, N. Redemann, A. Sauer, L. Thomas, D. Wiedenmayer, M. Austen, J. Danilewicz, M. Schneider, K. Schreiter, P. Black, W. Blackaby, I. Linney, *PCT Int. Appl.*, 2011104334, September 01, 2011.

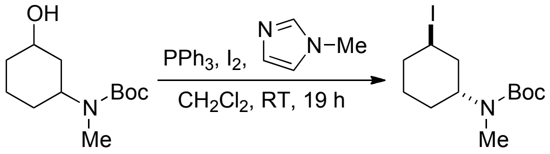
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 4.40-4.15 (m, 2H), 2.69 (s, 3H), 1.89-1.04 (m, 9H), 1.43 (s, 9H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 155.9, 79.4, 67.0, 49.4, 36.8, 31.8, 30.2, 28.6, 19.8.

MS (70 eV, EI) *m/z* (%): 229 (6) $[M]^{+\bullet}$, 173 (32), 155 (28), 130 (25), 114 (5), 98 (10), 86 (57), 76 (7), 70 (15), 57 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3422 (br w), 2974 (w), 2932 (w), 1664 (s), 1480 (w), 1447 (w), 1400 (w), 1364 (m), 1316 (m), 1245 (w), 1178 (w), 1149 (vs), 1117 (s), 1056 (w), 1031 (w), 978 (m), 895 (w), 882 (m), 772 (w).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{19}O_2N^{+\bullet}$** $[M]^{+\bullet}$: 229.1678, found: 229.1666.



7-S5 *trans*-**7-1d**

trans-**7-1d** (CAS: 1537869-33-2)

A dry and N$_2$-flushed *Schlenk*-flask was charged with a solution of I$_2$ (3.8 g, 15.1 mmol) in CH$_2$Cl$_2$ (30 mL) and cooled to 0 °C. PPh$_3$ (3.7 g, 13.9 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (1.3 mL, 16.0 mmol) was added. After 10 min of further stirring, **7-S5** (2.9 g, 12.6 mmol) was added and the reaction mixture was stirred overnight at 0 °C. The reaction was quenched with saturated NH$_4$Cl aqueous solution and the mixture was extracted with CH$_2$Cl$_2$ three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/7 to afford *trans*-**7-1d** (1.6 g, 38% yield) as a yellow solid.

m.p.: 46.5-48.7 °C.

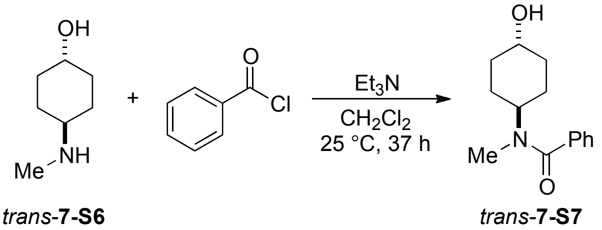
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 4.96-4.83 (br s, 1H), 4.36 (tt, *J* = 11.8 and 3.3 Hz, 1H), 2.70 (s, 3H), 2.10-1.10 (m, 8H), 1.45 (s, 9H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 155.6, 79.6, 51.9, 39.6, 35.6, 33.9, 30.1, 28.7, 22.6.

MS (70 eV, EI) *m/z* (%): 339 (2) $[M]^{+\bullet}$, 284 (3), 266 (50), 212 (50), 156 (100), 112 (35), 81 (17), 70 (15), 57 (64).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2933 (w), 1740 (w), 1686 (vs), 1146 (w), 1401 (w), 1363 (s), 1325 (m), 1285 (w), 1241 (s), 1182 (m), 1155 (s), 1139 (s), 1128 (s), 1078 (w), 1055 (w), 1046 (w), 976 (w), 887 (w), 856 (w), 839 (w), 772 (w).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{23}IO_2N^{+\bullet}$** [M+H]$^{+\bullet}$: 340.0773, found: 340.0776.



trans-**7-S7** (CAS: 60481-81-4)

A 250 mL flask was charged with a solution of *trans*-**7-S6**[141] (2.3 g, 18.0 mmol, CAS: 22348-44-3) in CH_2Cl_2 (100 mL). Et_3N (2.6 mL, 36.0 mmol) and benzoyl chloride (2.3 mL, 19.8 mmol) were added at 25 °C and the resulting solution was stirred for 37 h. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc to afford *trans*-**7-S7** (3.9 g, 92% yield) as a white solid.

m.p.: 152.5-153.7 °C.

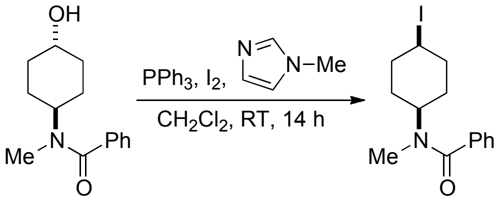
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.46-7.30 (m, 5H), 4.66-4.40 (m, 0.5H), 3.70-3.35 (m, 1.55H), 3.08-2.63 (m, 3H), 2.20-0.97 (m, 8H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ: 171.8, 137.1, 129.5, 128.7, 126.6, 69.9, 54.8, 34.3, 32.3, 27.9.

MS (70 eV, EI) *m/z* (%): 233 (28) [M]$^+$, 215 (7), 174 (18), 160 (5), 136 (30), 127 (6), 105 (100), 77 (33), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3366 (br w), 2934 (w), 1593 (s), 1574 (m), 1501 (w), 1444 (m), 1413 (m), 1326 (w), 1309 (w), 1188 (w), 1072 (s), 1023 (w), 984 (w), 903 (w), 793 (m), 784 (w), 739 (m), 703 (vs).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{19}O_2N^{+\bullet}$** [M+H]$^{+\bullet}$: 233.1416, found: 233.1413.



trans-**7-S7** *cis*-**7-1e**

cis-**7-1e** (CAS: 1537869-37-6)

A dry and N_2-flushed *Schlenk*-flask was charged with a solution of I_2 (5.0 g, 19.9 mmol) in CH_2Cl_2 (40 mL) and cooled to 0 °C. PPh_3 (4.9 g, 18.3 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (1.7 mL, 21.1 mmol) was added. After 10 min of further stirring, *trans*-**7-S7** (3.9 g, 16.6 mmol) was added and the reaction mixture was stirred overnight at 0 °C. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/5→1/4 to afford *cis*-**7-1e** (2.8 g, 49% yield) as white solid.

m.p.: 89.6-92.6 °C.

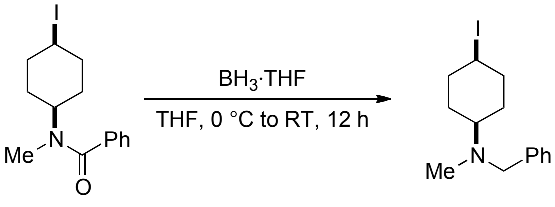
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.42-7.28 (m, 5H), 4.95-4.55 (m, 1.6H), 3.68-3.35 (m, 0.4H), 3.17-2.73 (m, 3H), 2.35-1.90 (m, 4H), 1.87-1.14 (m, 4H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 171.6, 137.1, 129.4, 128.6, 126.6, 54.6, 35.5, 32.8, 26.1.

MS (70 eV, EI) *m/z* (%): 343 (27) $[M]^{+\bullet}$, 216 (60), 136 (18), 105 (100), 77 (30), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2935 (w), 1620 (vs), 1578 (w), 1500 (w), 1485 (w), 1441 (m), 1434 (m), 1406 (m), 1373 (w), 1350 (w), 1325 (m), 1249 (w), 1196 (m), 1182 (w), 1149 (m), 1071 (s), 1054 (w), 1027 (w), 1018 (w), 1005 (m), 975 (w), 922 (w), 902 (w), 848 (m), 789 (m), 721 (s), 698 (vs), 668 (w).

HRMS (EI) *m/z*: calcd for $C_{14}H_{18}ION^{+\bullet}$ $[M]^{+\bullet}$: 343.0433, found: 343.0430.



cis-**7-1e** *cis*-**7-1f**

cis-**7-1f**

A dry and N_2-flushed 100 mL *Schlenk*-flask was charged with a solution of *cis*-**7-1e** (2.4 g, 7.0 mmol) in THF (20 mL) and cooled to 0 °C. BH_3·THF (16.8 mL, 1 M solution in THF, 16.8 mmol) was added and the resulting solution was stirred for 12 h at 0 °C to room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C and was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography two times on silica gel with Et_2O/*i*-hexane = 1/2 to afford *cis*-**7-1f** (0.86 g, 37% yield) as pale yellow oil.

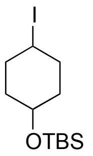
^{1}H-NMR (300 MHz, CDCl3) δ: 7.38-7.20 (m, 5H), 4.78 (quint, *J* = 3.3 Hz, 1H), 3.63 (s, 2H), 2.54 (tt, *J* = 10.9 and 3.6 Hz, 1H), 2.26 (s, 3H), 2.28-2.10 (m, 2H), 1.93 (ddd, *J* = 15.0, 11.7 and 3.5 Hz, 2H), 1.81-1.70 (m, 2H), 1.59 (ddt, *J* = 15.0, 11.7 and 3.5 Hz, 2H).

^{13}C-NMR (75 MHz, CDCl3) δ: 140.1, 128.9, 128.4, 126.9, 61.3, 58.0, 37.9, 36.1, 35.8, 25.2.

MS (70 eV, EI) *m/z* (%): 329 (16) $[M]^{+\bullet}$, 202 (100), 160 (36), 146 (41), 132 (7), 91 (96), 65 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3024 (w), 2934 (w), 2860 (w), 2832 (w), 2784 (w), 1493 (w), 1451 (w), 1438 (w), 1348 (w), 1245 (m), 1163 (w), 1120 (w), 1071 (w), 1037 (w), 1026 (m), 987 (w), 967 (w), 904 (w), 874 (w), 840 (w), 735 (s), 697 (vs), 676 (m).

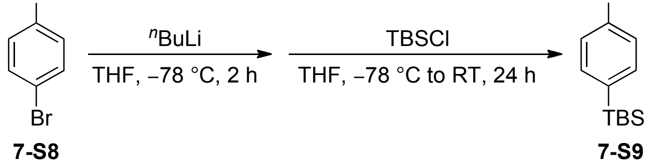
HRMS (EI) *m/z*: calcd for $\mathbf{C_{14}H_{20}IN^{+\bullet}}$ $[M]^{+\bullet}$: 329.0640, found: 329.0654.



7-1g

7-1g (CAS:1285537-44-1)

It was prepared in the same way as **6-2b**.



7-S9 (CAS: 1537869-41-2)

A N_2-flushed 1 L *Schlenk*-flask was charged with a solution of **7-S8** (13.0 g, 75.0 mmol) in THF (220 mL) and cooled to –78 °C. Then ^{n}BuLi (65.2 mL, 2.5 M in *n*-hexane, 165.0 mmol) was added dropwise and this solution was stirred for 2 h at –78 °C. Then, TBSCl (27.1 g, 180.0 mmol) was added and the solution was stirred for 24 h at –78 °C to room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution at 0 °C. The mixture was concentrated by evaporation and was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography two times on silica gel with *i*-hexane to afford **7-S9** (8.7 g, 36% yield) as white paste.

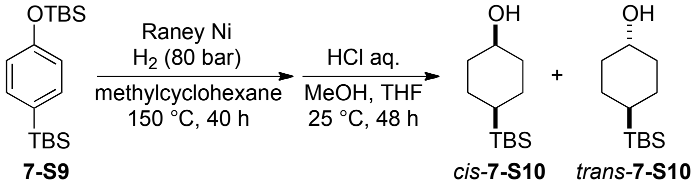
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.37 (d, J = 8.3 Hz, 2H), 6.83 (d, J = 8.3 Hz, 2H), 0.99 (s, 9H), 0.86 (s, 9H), 0.24 (s, 6H), 0.21 (s, 6H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 156.5, 135.9, 129.4, 119.4, 26.6, 25.8, 18.4, 17.1, –4.2, –5.9.

MS (70 eV, EI) *m/z* (%): 322 (4) $[M]^{+\bullet}$, 307 (2), 265 (100), 193 (3), 73 (2).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2953 (w), 2927 (w), 2855 (w), 1592 (m), 1500 (m), 1471 (w), 1462 (w), 1361 (w), 1253 (s), 1176 (w), 1107 (m), 1006 (w), 913 (s), 820 (s), 800 (vs), 779 (s), 768 (s), 676 (m), 665 (m).

HRMS (EI) *m/z*: calcd for $C_{18}H_{34}OSi_2^{+\bullet}$ $[M]^{+\bullet}$: 322.2148, found: 322.2150.



7-S10

7-S9 (8.7 g, 27.0 mmol) and Raney Ni (0.30 g) in methylcyclohexanol (25 mL) was mixed in the autoclave. Then the inside atmosphere was replaced to H_2 (80 bar) and the mixture was stirred for 40 h at 150 °C. Then, the catalyst was filtered off with Celite and the solvents were evaporated. Then MeOH (50 mL), THF (40 mL) and 2 M HCl aqueous solution (30 mL) were added and stirred for 48 h at room temperature. This solution was neutralized with saturated $NaHCO_3$ aqueous solution. The reaction mixture was reduced by evaporation and was extracted with EtOAc three times. This combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography two times on silica gel with EtOAc/*i*-hexane = 1/5 to afford **7-S10** (3.6 g, 63% yield in two steps) as colorless oil.

cis-**S10** (CAS: 1537869-44-5)

^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 4.09-4.03 (m, 1H), 1.81-1.70 (m, 2H), 1.62-1.46 (m, 6H), 0.89 (s, 9H), 0.76 (tt, *J* = 11.8 and 3.3 Hz, 1H), –0.09 (s, 6 H).

^{13}C-NMR (101 MHz, CDCl$_3$) *δ*: 66.7, 34.4, 27.4, 23.3, 22.3, 17.4, –7.3.

MS (70 eV, EI) *m/z* (%): 213 (0.1) [M–H]$^+$ 157 (4), 139 (4), 81 (5), 75 (100), 59 (8).

IR (ATR) $\widetilde{\nu}$ (cm^{-1}): 3334 (br, w), 2924 (m), 2854 (w), 1470 (w), 1463 (w), 1361 (w), 1246 (m), 1085 (w), 1000 (m), 951 (w), 861 (w), 823 (vs), 798 (m), 770 (s), 734 (m), 671 (w).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{26}OSi^{+\bullet}$** [M]$^{+\bullet}$: 214.1753, found: 214.1752.

trans-**S10** (CAS: 1537869-42-3)

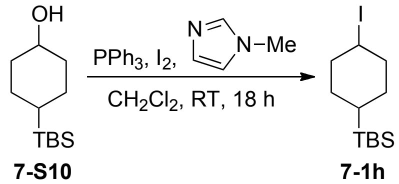
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 3.49 (tt, *J* = 10.6 and 4.4 Hz, 1H), 2.07-1.97 (m, 2H), 1.85-1.77 (m, 2H), 1.23-1.10 (m, 4H), 0.89 (s, 9H), 0.59 (tt, *J* = 12.7 and 3.2 Hz, 1H), –0.11 (s, 6H).

^{13}C-NMR (101 MHz, CDCl$_3$) *δ*: 71.2, 37.6, 27.4, 27.2, 22.6, 17.4, –7.3.

MS (70 eV, EI) *m/z* (%): 214 (7) [M]$^+$, 157 (100), 139 (31), 123 (4), 111 (9), 97 (4), 85 (4), 81 (83), 75 (97), 67 (5), 59 (34).

IR (ATR) $\widetilde{\nu}$ (cm^{-1}): 3350 (br w), 2925 (m), 2853 (w), 1470 (w), 1463 (w), 1448 (w), 1361 (w), 1247 (w), 1048 (w), 1007 (w), 968 (w), 907 (m), 824 (m), 800 (m), 768 (m), 730 (vs), 655 (w).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{26}OSi^{+\bullet}$** [M]$^{+\bullet}$: 214.1753, found: 214.1741.



7-1h

A dry and N$_2$-flushed *Schlenk*-flask was charged with a solution of I$_2$ (5.1 g, 20.3 mmol) in CH$_2$Cl$_2$ (40 mL) and cooled to 0 °C. PPh$_3$ (5.0 g, 18.6 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (1.7 mL, 21.5 mmol) was added. After 10 min of further stirring, **7-S10** (3.6 g, 16.9 mmol) was added and the reaction mixture was stirred overnight at 0 °C. The reaction was quenched with saturated NH$_4$Cl aqueous solution and the mixture was extracted with CH$_2$Cl$_2$ three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with *i*-hexane to afford **7-1h** (1.4 g, 25% yield) as pale yellow oil.

The peaks of a mixuture of the two diastereomers are given.

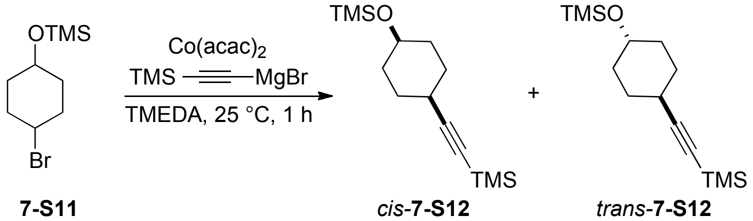
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 4.98-4.88 (m, 1H), 4.18 (tt, *J* = 12.2 and 4.0 Hz, 0.3H), 2.53-2.41 (m, 0.6H), 2.14-2.02 (m, 2H), 2.05-1.05 (m, 10.4H), 0.91 (s, 9H), 0.88 (s, 2.7H), 0.87-0.73 (m, 1.3H), –0.04 (s, 6H), –0.12 (s, 1.8H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 42.4, 38.5, 37.6, 31.5, 31.4, 27.5, 27.4, 24.7, 23.6, 22.7, 17.5, 17.4, –7.3, –7.4.

MS (70 eV, EI) *m/z* (%): 324 (1) $[M]^{+\bullet}$, 267 (33), 197 (26), 185 (47), 115 (50), 81 (100), 72 (57), 59 (32).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2926 (w), 2853 (w), 1470 (w), 1463 (w), 1445 (w), 1435 (w), 1361 (w), 1246 (m), 1180 (w), 1131 (w), 1052 (w), 1043 (w), 1007 (w), 991 (m), 936 (w), 876 (w), 825 (vs), 799 (m), 771 (m), 745 (w), 712 (w), 682 (w), 664 (m).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{25}ISi^{+\bullet}$** $[M]^{+\bullet}$: 324.0770, found: 324.0771.



7-S12

A dry and Ar-flushed 100 mL *Schlenk*-flask was charged with a solution of ^{n}BuMgCl (43.8 mL, 1.4 M in THF, 63.0 mmol) and trimethylsilylacetylene (8.8 mL, 63.0 mmol) was added at 25 °C. The solution was stirred for 2 h at 25 °C. Then the solvent was removed under vacuum and TMEDA (35 mL) was added. In another dry and Ar-flushed 250 mL *Schlenk*-flask was charged with Co(acac)$_2$ (3.0 g, 8.4 mmol) and heated very gently with a heat-gun at high vacuum (1 mbar). After the flushing Ar, TMEDA (15 mL) was added and this mixture was stirred for 3 min at room temperature. Then, **7-S11**[144] (5.4 g, 21.0 mmol, CAS: 66957-15-1) and the prepared solution of ((trimethylsilyl)ethynyl)magnesium bromide was added and the reaction mixture was stirred for 1 h at 25 °C. The reaction was poured into saturated NH$_4$Cl aqueous solution and the mixture was extracted with Et$_2$O three times. The combined

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[144] T. A. Grese, S. Cho, H. U. Bryant, H. W. Cole, A. L. Glasebrook, D. E. Magree, D. L. Phillips, E. R. Rowley, L. L. Short, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 201.

organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/100 to afford **7-S12** (5.5 g, 97% yield) as brown oil.

cis-**S-12**

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.69-3.54 (m, 1H), 2.63-2.46 (m, 1H), 1.94-1.32 (m, 8H), 0.14 (s, 9H), 0.11 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 110.8, 84.9, 69.6, 32.3, 28.9, 28.2, 0.44.

MS (70 eV, EI) *m/z* (%): 268 (4) $[M]^{+•}$, 253 (33), 240 (10), 195 (14), 178 (5), 171 (7), 163 (9), 155 (9), 147 (100), 129 (77), 119 (7), 109 (9), 101 (7), 91 (4), 81 (8), 73 (38), 59 (7).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2171 (w), 2139 (w), 1444 (w), 1377 (w), 1247 (m), 1091 (w), 1046 (w), 1016 (w), 975 (w), 884 (w), 831 (vs), 757 (m), 695 (w), 668 (m).

HRMS (EI) *m/z*: calcd for $C_{14}H_{28}OSi^{+•}$ $[M]^{+•}$: 268.1679, found: 268.1663.

trans-**S-12**

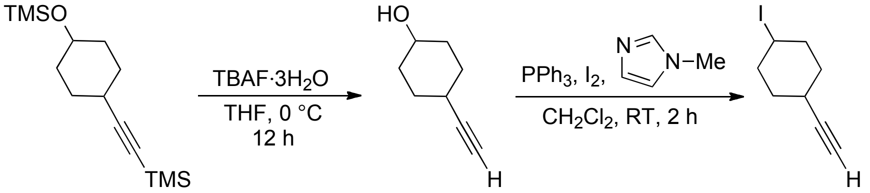
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.57 (tt, *J* = 9.2 and 3.8 Hz, 1H), 2.24 (tt, *J* = 10.1 and 3.2 Hz, 1H), 2.07-1.73 (m, 4H), 1.50-1.15 (m, 4H), 0.12 (s, 9H), 0.09 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 110.1, 84.0, 70.1, 34.7, 30.9, 29.6, 0.38.

MS (70 eV, EI) *m/z* (%): 268 (2) $[M]^{+•}$, 253 (26), 240 (9), 195 (14), 178 (16), 163 (21), 147 (66), 129 (100), 119 (10), 109 (13), 101 (11), 91 (3), 83 (10), 73 (67), 59 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2940 (w), 2167 (w), 1452 (w), 1376 (w), 1248 (m), 1093 (m), 1045 (w), 1028 (w), 963 (w), 883 (w), 832 (vs), 757 (m), 696 (w), 667 (w).

HRMS (EI) *m/z*: calcd for $C_{14}H_{28}OSi^{+•}$ $[M]^{+•}$: 268.1679, found: 268.1683.



7-S12 **7-S13** **7-1i**

7-1i

A 250 mL flask was charged with a solution of **7-S12** (5.5 g, 20.4 mmol) in THF (120 mL) and cooled to 0 °C. Then TBAF·$3H_2O$ (19.3 g, 61.2 mmol) was added portionwise and the solution was stirred for 12 h at 0 °C. The reaction was quenched with saturated NH_4Cl aqueous solution and it was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated carefully. The crude product was purified by chromatography on silica gel with Et_2O/*n*-pentane = 2/1 to afford **7-S13** (2.0 g, CAS: 141895-72-9) with some other unidentified alcohols. A N_2-flushed 100 mL *Schlenk*-flask was charged with a solution of I_2 (2.9 g, 11.5 mmol) in CH_2Cl_2 (25 mL) and cooled to 0 °C. PPh_3 (2.9 g, 11.0 mmol) was added at 0 °C in twice and the resulting suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (0.9 mL, 11.0 mmol) was added. After 10 min of further stirring, the crude product containing **7-S13** (1.2 g) in CH_2Cl_2 (5 mL) was added and the mixture was stirred for 2 h at 0 °C. The reaction was quenched with saturated NH_4Cl aqueous solution and was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with *i*-hexane to afford the title compound **7-1i** (0.32 g, 11% yield in two steps) still with a little impurity as yellow oil.

The peaks of the mixture of the diastereomers are given.

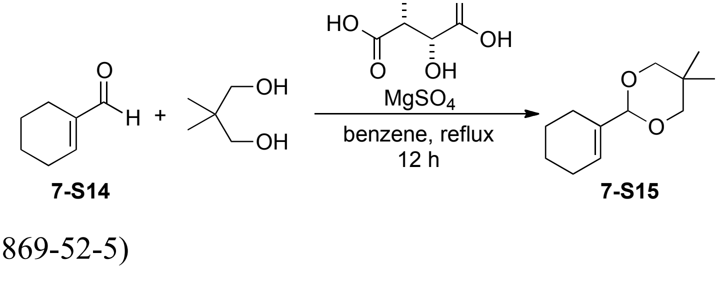
^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: 4.67-4.04 (m, 1.7H), 2.11 (d, *J* = 2.4 Hz, 1H), 2.05 (d, *J* = 2.4 Hz, 0.7H), 2.95-1.34 (m, 15.3H).

^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 87.6, 87.0, 69.6, 68.9, 37.4, 35.8, 32.8, 31.4, 30.9, 27.6, 27.1.

MS (70 eV, EI) *m/z* (%): 234 (5) $[M+H]^{+\bullet}$, 206 (13), 127 (5), 107 (30), 91 (41), 79 (100), 67 (32), 53 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3289 (w), 2940 (w), 2855 (w), 2113 (w), 1446 (w), 1438 (w), 1353 (w), 1296 (w), 1251 (w), 1220 (m), 1155 (m), 1073 (w), 1048 (w), 1020 (w), 1002 (w), 988 (m), 937 (w), 896 (w), 845 (w), 794 (w), 683 (w).

HRMS (EI) *m/z*: calcd for **$C_8H_{12}I^{+\bullet}$** $[M]^{+\bullet}$: 234.9984, found: 234.9962.



7-S15 (CAS: 1537869-52-5)

A 250 mL 2-neck flask equipped with a reflux condenser, a *Dean-Stark*-condenser and a drying tube with $CaCl_2$, was charged with **7-S14**[145] (5.0 g, 45.4 mmol, CAS: 1192-88-7),

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[145] J. Rodriguez, P. Brun, B. Waegell, *J. Organometallic. Chem.* **1989**, *359*, 343.

$MgSO_4$ (5.5 g, 45.4 mmol), *L*-tartaric acid (42 mg, 0.27 mmol) and benzene (60 mL). 2,2-dimethylpropane-1,3-diol (12.8 g, 123.0 mmol) was added portionwise at 25°C and the reaction mixture was heated to reflux for 12 h. After cooling to 0 °C, $NaHCO_3$ (45 mg, 0.54 mmol) was added as a solid and the reaction mixture was stirred for additional 30 min. The reaction mixture was filtrated over $NaHCO_3$ and the remaining solid was washed with CH_2Cl_2. The solvents of the combined organic phase were evaporated and the crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/15 to afford **7-S15** (8.4 g, 94% yield) as colorless oil.

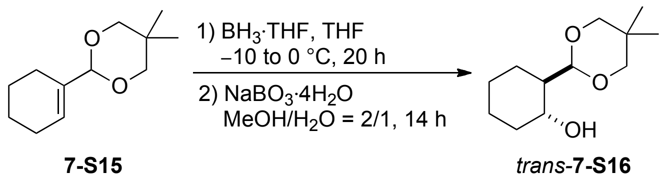
^{1}H-NMR (300 MHz, C_6D_6) δ: 5.99 (ttd, J = 3.7, 1.9 and 0.6 Hz, 1H), 4.67 (s, 1H), 3.49 (d, J = 10.8 Hz, 2H), 3.21 (d, J = 10.5 Hz, 2H), 2.35 (ddt, J = 8.4, 6.2 and 2.2 Hz, 2H), 1.91 (ddt, J = 9.1, 6.1 and 2.9 Hz, 2H), 1.42-1.61 (m, 4H), 1.18 (s, 3H), 0.34 (s, 3H).

13C-NMR (75 MHz, C_6D_6) δ: 136.5, 125.4, 104.4, 77.2, 30.0, 25.1, 23.7, 23.1, 22.9, 22.7, 21.7.

MS (70 eV, EI) *m/z* (%): 196 (100) $[M]^+$, 181 (4), 167 (63), 155 (5), 141 (11), 128 (11), 111 (41), 93 (12), 81 (54), 69 (41), 55 (25).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2929 (w), 2839 (w), 1470 (w), 1390 (m), 1362 (w), 1299 (w), 1184 (m), 1099 (vs), 1078 (w), 1031 (w), 1014 (w), 979 (m), 922 (w), 911 (m), 837 (w), 800 (w), 780 (w).

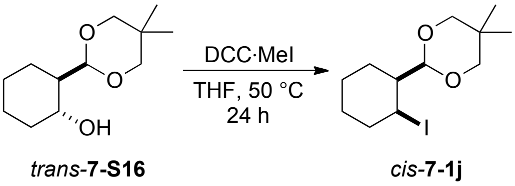
HRMS (EI) *m/z*: calcd for $C_{12}H_{20}O_2^{+\bullet}$ $[M]^{+\bullet}$: 196.1463, found: 196.1461.



trans-**7-S16** (CAS: 1537869-53-6)

A dry N_2-flushed 250 mL *Schlenk*-flask was charged with a solution of **7-S15** (2.4 g, 12.4 mmol) in THF (20 mL). It was cooled to –10 °C and BH_3·THF (13.6 mL, 1.0 M in THF, 13.6 mmol) was added slowly. The reaction mixture was allowed to warm to 0 °C and stirred for 20 h at 0 °C. After completion of the hydroboration a suspension of $NaBO_3$·4H_2O (7.6 g, 49.6 mmol) in MeOH (14 mL) and H_2O (7 mL) was added carefully. The resulting reaction mixture was stirred for 14 h at 25°C. After filtration, the filtrate was dried over Na_2SO_4 and washed with EtOAc. The solvents were evaporated and the crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/1→2/1 to afford *trans*-**7-S16** (1.9 g, 71% yield) as colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 4.41 (d, *J* = 4.6 Hz, 1H), 3.80-3.47 (br s, 1H), 3.67 (t, *J* = 9.8 Hz, 1H), 3.42 (dd, *J* = 15.1 and 11.1 Hz, 2H), 2.06-1.94 (m, 1H), 1.82-1.52 (m, 4H), 1.20-1.00 (m, 4H), 1.19 (s, 3H), 0.72 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$) *δ*: 105.7, 77.6, 77.3, 70.8, 48.2, 34.5, 30.5, 26.4, 25.2, 24.4, 23.1, 21.9.
MS (70 eV, EI) *m/z* (%): 213 (3) $[M–H]^{+•}$, 196 (5), 129 (5), 115 (100), 99 (4), 93 (5), 81 (16), 69 (51), 57 (12).
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3293 (br w), 2924 (m), 2851 (w), 1449 (w), 1393 (m), 1160 (w), 1115 (s), 1089 (s), 1080 (m), 1062 (m), 1042 (s), 1020 (vs), 985 (m), 968 (m), 926 (w), 904 (w), 850 (w), 835 (w), 797 (w), 784 (w), 676 (w).
HRMS (EI) *m/z*: calcd for $C_{12}H_{21}O_3^{+•}$ $[M–H]^{+•}$: 213.1491, found: 213.1488.



cis-**7-1j** (CAS: 1537869-54-7)

A dry and N_2-flushed *Schlenk*-flask was charged with freshly prepared DCC·MeI[146] (11.5 g, 33.2 mmol). A solution of *trans*-**7-S16** (3.6 g, 16.6 mmol) in THF (65 mL) was added at room temperature and the reaction mixture was heated to 50 °C for 24 h. The reaction mixture was diluted with Et_2O. The layers were separated and the organic phase was washed with H_2O and the combined aqueous phase was extracted with Et_2O. Then the combined organic phase was washed with saturated $NaHSO_3$ aqueous solution and was dried over $MgSO_4$. The solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O /*i*-hexane = 1/50 and the obtained eluent was left at 70 °C under 1×10^{-3} bar to remove the impurity and to afford the title compound *cis*-**7-1j** (1.3 g, 24% yield) as white solid.

m.p.: 77.8-79.1 °C.

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[146] R. Scheffold, E. Saladin, *Angew. Chem. Int. Ed.* **1972**, *11*, 229.

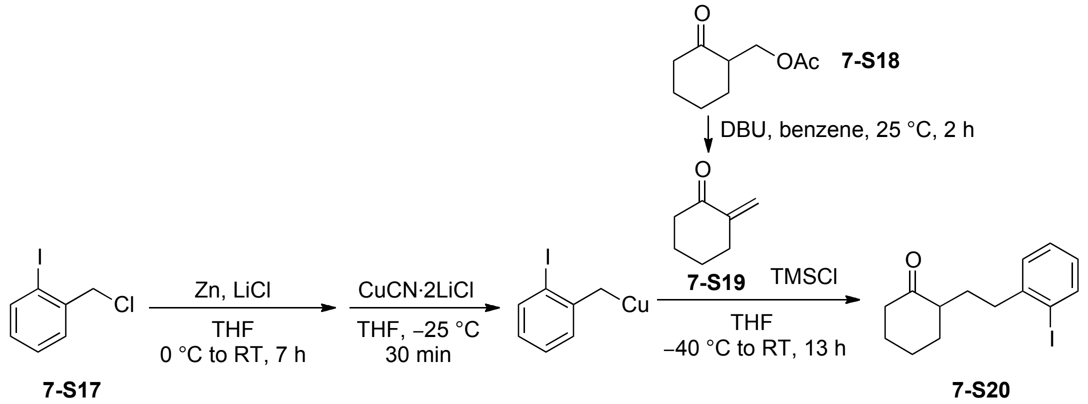
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 4.85 (s, 1H), 4.06 (d, J = 7.5 Hz, 1H), 3.66-3.55 (m, 2H), 3.43 (dd, J = 11.2 and 4.9 Hz, 1H), 2.16 (dd, J = 12.8 Hz, 1H), 1.83-1.52 (m, 4H), 1.41-1.25 (m, 2H), 1.17 (s, 3H), 0.81-0.72 (m, 1H), 0.72 (s, 3H).

^{13}C-NMR (101 MHz, CDCl$_3$) δ: 106.6, 77.50, 77.47, 46.4, 40.7, 36.3, 30.5, 25.2, 23.8, 23.3, 22.6, 22.0.

MS (70 eV, EI) *m/z* (%): 323 (5) [M–H]$^{+\bullet}$, 197 (100), 167 (5), 129 (8), 115 (86), 93 (31), 83 (79), 69 (85), 55 (28).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2952 (w), 2946 (w), 2936 (w), 2844 (w), 1467 (w), 1449 (w), 1435 (w), 1390 (w), 1360 (w), 1300 (w), 1256 (w), 1232 (w), 1193 (w), 1166 (m), 1149 (m), 1128 (w), 1098 (s), 1069 (m), 1037 (s), 1021 (vs), 993 (m), 976 (s), 948 (m), 919 (w), 903 (w), 892 (m), 864 (w), 834 (w), 786 (w), 671 (w).

HRMS (EI) *m/z*: calcd for **$C_{12}H_{21}O_3^{+\bullet}$** [M–H]$^{+\bullet}$: 323.0508, found: 323.0500.



7-S20 (CAS:1537869-55-8)

A 100 mL *Schlenk*-flask was charged with **7-S18**[147] (2.1 g, 12.1 mmol, CAS: 7500-52-9) in benzene (40 mL) and DBU (1.8 mL, 12.1 mmol) was added. After stirring for 2 h at 25°C, *i*-hexane (20 mL) was added to the reaction mixture and this solution was washed with H_2O two times, 2M HCl aqueous solution and H_2O again. The solution was dried over $MgSO_4$ and solvents were evaporation carefully and this crude product of **7-S19** (CAS: 3045-98-5) was used without further purification. LiCl (0.70 g, 16.5 mmol) was placed in a dry Ar-flushed 20 mL *Schlenk*-flask and it was dried for 5 min at 400 °C (heat-gun) under high vacuum (1 mbar). Then Zn powder (1.1 g, 16.5 mmol) was added and the mixture was dried for 5 min at 400 °C (heat-gun) at high vacuum (1 mbar). After flushing Ar, THF (3.5 mL) was added, followed by activation with 1,2-dibromoethane (50 μL, 0.59 μmol) and TMSCl (20 μL,

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[147] Sparrow, K.; Barker, D.; Brimble, M. A. *Tetrahedron* **2011**, *67*, 7989.

0.17 µmol). The mixture was stirred for 5 min at room temperature. After cooling it to 0 °C, **7-S17** (2.8 g, 11.0 mmol) in THF (4.0 mL) was added and the mixture was stirred at 0 °C for 20 min, and then it was warmed up to 25°C. After stirring for 7 h at 25°C, the remaining Zn powder was removed with membrane filter (25 mm with 1 µm glass fiber membrane) and the solution was added to CuCN·2LiCl (11.0 mL, 1.0 M in THF, 11.0 mmol) solution dropwise at –25 °C. This mixture was stirred for 30 min at –25 °C to afford the corresponding organocopper reagent.[148] The solution was cooled to –40 °C and the mixture of **7-S19** and TMSCl (3.47 mL, 27.5 mmol) in THF (15 mL) was added dropwise for 10 min. The mixture was warmed up gradually to 25°C and stirred for 13 h. The reaction mixture was quenched with the mixture of NH_4Cl and NH_3 aqueous solution and resulting precipitate was filtered off. The obtained blue solution was extracted with Et_2O and the organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/6 to afford **7-S20** (1.4 g, 40% yield in two steps) as yellow oil with a little impurity.

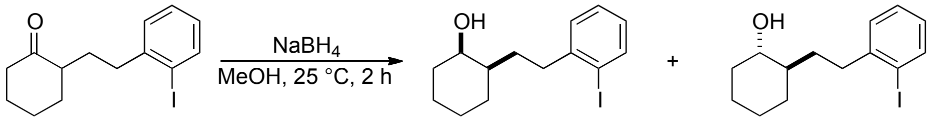
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.79 (d, J = 7.9 Hz, 1H), 7.35-7.11 (m, 2H), 6.87 (dd, J = 7.9 and 6.7 Hz, 1H), 2.72 (t, J = 8.1 Hz, 2H), 2.52-1.32 (m, 12H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 213.1, 145.1, 139.6, 129.6, 128.5, 127.9, 100.7, 50.3, 42.3, 38.4, 34.2, 30.3, 28.2, 25.1.

MS (70 eV, EI) *m/z* (%): 328 (1) $[M]^{+\bullet}$, 230 (7), 217 (14), 201 (23), 128 (4), 115 (6), 98 (100), 83 (11), 70 (10), 55 (8).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2935 (w), 2860 (w), 2251 (w), 1704 (w), 1465 (w), 1448 (w), 1434 (w), 1130 (w), 1010 (w), 905 (s), 724 (vs).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{14}H_{17}IO^{+\bullet}}$ $[M]^{+\bullet}$: 328.0324, found: 328.0313.



7-S20 *cis*-**7-S21** *trans*-**7-S21**

7-S21

A 100 mL flask was charged with a solution of **7-S20** (1.7 g, 5.2 mmol) in MeOH (35 mL) and $NaBH_4$ (0.23 g, 6.2 mmol) was added slowly. The reaction mixture was stirred for 2 h at 25°C. The reaction mixture was quenched with saturated NH_4Cl aqueous solution and it was

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[148] A. Metzger, Schade, M. A.; Knochel, P. *Org. Lett.* **2008**, *10*, 1107.

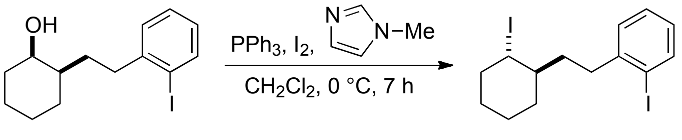
extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/3.5 to afford *cis*-**7-S21** (0.62 g, 37% yield) as the first eluent and white solid and *trans*-**7-S21** (0.73 g, 43% yield) as the second eluent and white solid.

cis-**7-S21** (CAS: 1537869-57-0)
m.p.: 88.1-90.3 °C
^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: 7.79 (d, *J* = 8.1 Hz, 1H), 7.35-7.11 (m, 2H), 6.87 (dd, *J* = 7.9 and 6.8 Hz, 1H), 4.00-3.95 (m, 1H), 2.72 (t, *J* = 8.1 Hz, 2 H), 2.52-1.32 (m, 12 H).
^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 145.4, 139.6, 129.4, 128.5, 127.7, 100.7, 69.4, 41.3, 38.7, 33.1, 26.8, 25.3, 20.7.
MS (70 eV, EI) *m/z* (%): 312 (5) $[M–H_2O]^+$, 262 (47), 230 (100), 217 (33), 203 (22), 183 (46), 170 (4), 152 (14), 143 (6), 128 (23), 117 (23), 108 (23), 91 (42), 77 (15), 67 (15), 57 (14).
IR (ATR) $\widetilde{\nu}$ (cm^{-1}): 3373 (br w), 2914 (w), 2845 (w), 1465 (w), 1435 (w), 1323 (w), 1281 (w), 1185 (w), 1160 (w), 1139 (w), 1080 (w), 1064 (w), 1042 (w), 1010 (m), 972 (m), 946 (w), 937 (m), 891 (m), 848 (w), 814 (w), 757 (s), 748 (vs), 720 (w).
HRMS (DEI) *m/z*: calcd for $\mathbf{C_{14}H_{19}IO^{+\bullet}}$ $[M]^{+\bullet}$: 330.0481, found: 330.0457.

trans-**7-S21** (CAS: 1537869-56-9)
m.p.: 68.9-70.8 °C
^{1}H-NMR (600 MHz, $CDCl_3$) *δ*: 7.80 (d, *J* = 8.0 Hz, 1H), 7.31-7.19 (m, 2 H), 6.86 (dd, *J* = 7.9 and 7.0 Hz, 1H), 3.30 (td, *J* = 9.7 and 4.2 Hz, 1H), 2.83 (ddd, *J* = 13.4, 11.9 and 5.0 Hz, 1H), 2.65 (ddd, *J* = 13.3, 11.7 and 5.0 Hz, 1H), 2.06-1.92 (m, 3H), 1.82-1.62 (m, 2H), 1.44 (dddd, *J* = 13.4, 11.5, 8.5 and 5.0 Hz, 1H), 1.34 (dddd, *J* = 15.4, 12.4, 5.9 and 2.8 Hz, 1H), 1.30-1.26 (m, 2H), 1.13 (dtt, *J* = 12.7, 12.5 and 3.8 Hz, 1H), 1.08 (ddd, *J* = 13.1, 11.9 and 3.5 Hz, 1H).
^{13}C-NMR (150 MHz, $CDCl_3$) *δ*: 145.6, 139.6, 129.4, 128.5, 127.7, 100.7, 74.6, 45.2, 38.2, 35.8, 33.2, 30.3, 25.7, 25.0.
MS (70 eV, EI) *m/z* (%): 312 (3) $[M–H_2O]^{+\bullet}$, 244 (3), 230 (100), 217 (19), 203 (16), 185 (14), 143 (5), 128 (8), 117 (19), 104 (11), 91 (28), 77 (11), 67 (8), 55 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3341 (br w), 2921 (m), 2853 (w), 1561 (w), 1464 (w), 1447 (w), 1433 (w), 1350 (w), 1299 (w), 1132 (w), 1059 (m), 1038 (m), 1008 (w), 941 (w), 845 (w), 746 (vs), 717 (w).

HRMS (DEI) *m/z*: calcd for $\mathbf{C_{14}H_{19}IO^{+\bullet}}$ [M]$^{+\bullet}$: 330.0481, found: 330.0457.



cis-**7-S21** *trans*-**7-1k**

trans-**7-1k** (CAS: 1537869-58-1)

A dry and N_2-flushed *Schlenk*-flask was charged with a solution of I_2 (0.57 g, 2.3 mmol) in CH_2Cl_2 (10 mL) and cooled to 0 °C. PPh_3 (0.56 g, 2.1 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (0.19 mL, 2.4 mmol) was added. After 10 min of further stirring, *cis*-**7-S21** (0.62 g, 1.9 mmol) was added and the reaction mixture was stirred overnight at 0 °C. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with *i*-hexane to afford *trans*-**7-1k** (1.4 g, 25% yield) as white solid.

m.p.: 39.3-39.8 °C.

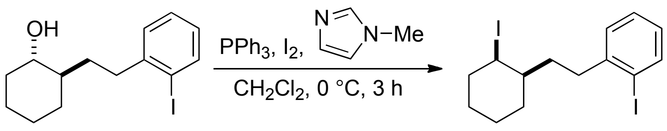
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.80 (d, J = 7.9 Hz, 1H), 7.33-7.19 (m, 2H), 6.88 (dd, J = 7.9 and 6.7 Hz, 1H), 4.08 (td, J = 10.9 and 4.0 Hz, 1H), 2.78 (ddd, J = 13.2, 12.1 and 5.1 Hz, 1H), 2.61 (ddd, J = 13.3, 11.7 and 5.3 Hz, 1H), 2.56-2.45 (m, 1H), 2.22-1.95 (m, 3H), 1.90-1.72 (m, 2H), 1.66-1.16 (m, 5H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 145.0, 139.6, 129.5, 128.6, 127.9, 100.7, 46.6, 42.1, 41.4, 38.8, 37.7, 32.0, 29.0, 25.7.

MS (70 eV, EI) *m/z* (%): 440 (1) [M]$^{+\bullet}$, 313 (16), 231 (5), 217 (70), 186 (100), 158 (4), 144 (9), 129 (10), 117 (14), 104 (11), 90 (19), 77 (9), 55 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2927 (w), 2850 (w), 1560 (w), 1463 (w), 1441 (w), 1431 (w), 1255 (w), 1149 (w), 1076 (w), 1041 (w), 1008 (m), 972 (w), 947 (w), 911 (w), 854 (w), 790 (w), 780 (w), 748 (vs), 715 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{14}H_{18}I_2^{+\bullet}}$ [M]$^{+\bullet}$: 439.9498, found: 439.9502.



trans-**7-S21** *cis*-**7-1k**

cis-**7-1k** (CAS: 1537869-59-2)

A dry and N_2-flushed *Schlenk*-flask was charged with a solution of I_2 (0.60 g, 2.4 mmol) in CH_2Cl_2 (10 mL) and cooled to 0 °C. PPh_3 (0.59 g, 2.2 mmol) was added at 0 °C and the resulting yellow suspension was stirred for 1.5 h at 0 °C. Then *N*-methylimidazole (0.20 mL, 2.5 mmol) was added. After 10 min of further stirring, *trans*-**7-S21** (0.66 g, 2.0 mmol) was added and the reaction mixture was stirred overnight at 0 °C. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with CH_2Cl_2 three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with *i*-hexane to afford *cis*-**7-1k** (1.4 g, 25% yield) as white solid.

m.p.: 37.8-38.8 °C.

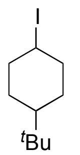
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.80 (d, *J* = 7.9 Hz, 1H), 7.35-7.14 (m, 2H), 6.92-6.84 (m, 1H), 4.83-4.77 (m, 1H), 2.74 (ddd, *J* = 13.7, 11.1 and 6.4 Hz, 1H), 2.64 (ddd, *J* = 13.4, 10.9 and 6.0 Hz, 1H), 2.35-2.09 (m, 1 H), 1.96-1.18 (m, 9H), 0.69-0.43 (m, 1H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 144.9, 139.6, 129.5, 128.5, 127.9, 100.7, 47.7, 42.4, 39.1, 37.7, 36.8, 29.2, 25.6, 23.0.

MS (70 eV, EI) *m/z* (%): 440 (1) $[M]^{+\bullet}$, 313 (16), 231 (4), 217 (64), 186 (100), 158 (4), 143 (9), 129 (9), 117 (12), 104 (11), 90 (21), 77 (11), 55 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2925 (w), 2850 (w), 1585 (w), 1561 (w), 1464 (w), 1451 (w), 1442 (w), 1432 (m), 1348 (w), 1334 (w), 1254 (w), 1151 (w), 1081 (w), 1056 (w), 1045 (w), 1008 (s), 954 (w), 939 (w), 900 (w), 886 (w), 831 (w), 817 (w), 743 (vs), 716 (w).

HRMS (EI) *m/z*: calcd for $C_{14}H_{18}I_2^{+\bullet}$ $[M]^{+\bullet}$: 439.9498, found: 439.9508.



7-1l

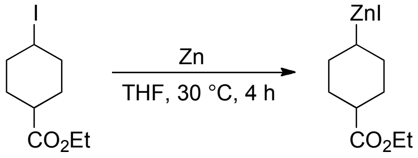
7-1l (CAS: 85592-89-8)

It was prepared according to the previous literature.[22]

9.7.2 Preparation of alkylzinc reagents

[General Procedure]

Zn powder (3 equiv, Aldrich) was placed in a dry and Ar-flushed 50 mL *Schlenk*-tube and dried for 5 min at 400 °C (heat-gun) under high vacuum (1 mbar). After cooling to room temperature, it was evacuated and refilled with Ar three times. THF (to make 0.50 M solution of starting alkyl iodides) was added and the mixture was gently heated to activate the Zn surface. Then alkyl iodides (1 equiv) was added neat at room temperature. The resulting mixture was stirred for indicated time and temperature. The remaining Zn powder was removed with a membrane filter (25 mm with 1 μm glass fiber membrane) and the solution was transferred to another dry Ar-flushed *Schlenk*-tube. The concentration of the cyclohexylzinc reagent was determined by titration of a small aliquot with I_2.[103]



7-1a **7-2a**

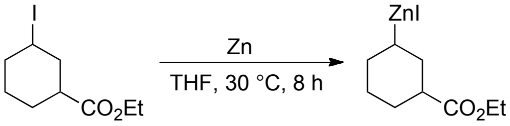
7-2a (CAS: 1354817-61-0)

According to the general procedure, **7-1a** (2.3 g, 8.1 mmol) was used and the reaction mixture was stirred at 30 °C for 4 h to obtain **7-2a** (82% yield, 0.41 M in THF). A dry and Ar-flushed 10 mL *Schlenk*-tube was charged with **7-2a** (0.59 mL, 0.41 M in THF, 0.24 mmol) and the solvent was removed at 0 °C under high vacuum (1 mbar) for 2 h. The obtained oily compounds was dissolved with THF-d_8 and the NMR measurement was performed at –80 °C.

The peaks of the mixture of the diastereomers are given.

^{1}H-NMR (400 MHz, THF-d_8) δ: 3.974 (q, J = 7.2 Hz, 1.2H), 3.967 (q, J = 7.1 Hz, 0.8H), 2.22 (tt, J = 12.0 and 3.1 Hz, 0.6H), 2.14 (tt, J = 12.1 and 3.4 Hz, 0.4H), 2.04-1.13 (m, 11.4H), 0.53 (tt, J = 13.1 and 2.8 Hz, 0.6H).

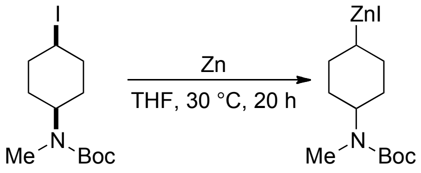
^{13}C-NMR (100 MHz, THF-d_8) δ: 176.0, 175.8, 60.3, 60.0, 44.6, 43.3, 32.9, 32.6, 32.3, 31.1, 29.6, 27.8, 26.2, 14.3.



7-1b **7-2b**

7-2b (CAS: 1537869-15-0)

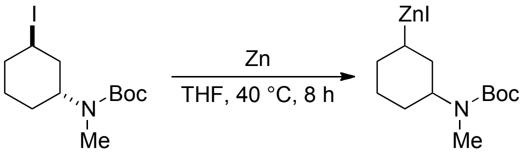
According to the general procedure, **7-1b** (1.6 g, 5.7 mmol) was used and the reaction mixture was stirred at 30 °C for 8 h to obtain **7-2b** (82% yield, 0.41 M in THF).



cis-**7-1c** **7-2c**

7-2c

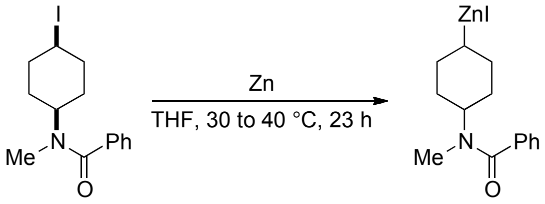
According to the general procedure, *cis*-**7-1c** (0.85 g, 2.5 mmol) was used and the reaction mixture was stirred at 30 °C for 20 h to obtain **7-2c** (84% yield, 0.42 M in THF).



trans-**7-1d** **7-2d**

7-2d

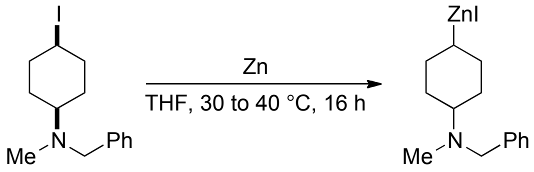
According to the general procedure, *trans*-**7-1d** (0.68 g, 2.0 mmol) was used and the reaction mixture was stirred at 30 °C for 20 h to obtain **7-2d** (84% yield, 0.42 M in THF).



cis-**7-1e** **7-2e**

7-2e (CAS: 1537869-18-3)

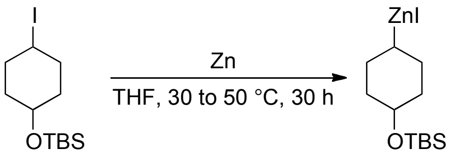
According to the general procedure, *cis*-**7-1e** (0.38 g, 1.1 mmol) was used and the reaction mixture was stirred at 30 to 40 °C for 23 h to obtain **7-2e** (60% yield, 0.30 M in THF).



cis-**7-1f** **7-2f**

7-2f (CAS: 1537869-19-4)

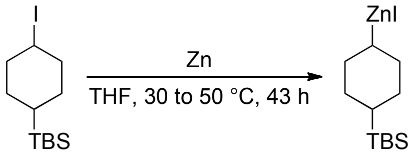
According to the general procedure, *cis*-**7-1f** (0.49 g, 1.5 mmol) was used and the reaction mixture was stirred at 30 to 40 °C for 23 h to obtain **7-2f** (71% yield, 0.35 M in THF).



7-1g **7-2g**

7-2g (CAS: 1285537-35-0)

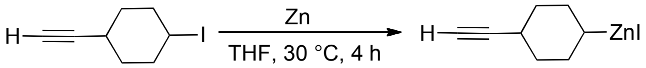
According to the general procedure, **7-1g** (0.68 g, 2.0 mmol) was used and the reaction mixture was stirred at 30 to 50 °C for 30 h to obtain **7-2g** (83% yield, 0.42 M in THF).



7-1h **7-2h**

7-2h

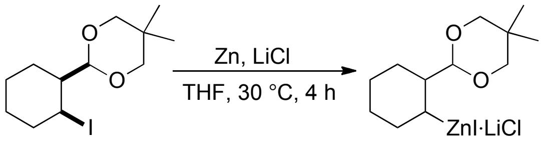
According to the general procedure, **7-1h** (0.49 g, 1.5 mmol) was used and the reaction mixture was stirred at 30 to 50 °C for 43 h to obtain **7-2h** (66% yield, 0.33 M in THF).



7-1i **7-2i**

7-2i

According to the general procedure, **7-1i** (0.42 g, 1.8 mmol) was used and the reaction mixture was stirred at 30 °C for 4 h to obtain **7-2i** (73% yield, 0.33 M in THF).

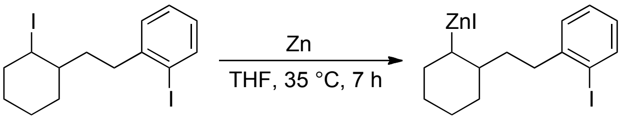


cis-**7-1j** **7-2j**

7-2j

A dry and Ar-flushed 25 mL *Schlenk*-flask was charged with LiCl (0.13 g, 3.0 mmol) and Zn powder (0.39 g, 6.0 mmol) and they were dried for 5 min at 400 °C (heat-gun) at high vacuum (1 mbar). THF (3 mL) was added, followed by activation with 1,2-dibromoethane (13 µL, 0.15 mmol). The mixture was gently heated to activate the Zn surface. A solution of *cis*-**7-1j**

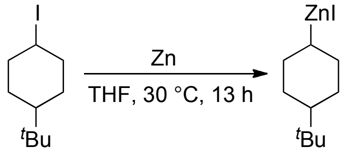
(0.86 g, 2.0 mmol) in THF (1 mL) was added dropwise and the reaction mixture was stirred for 4 h at 30 °C. The remaining Zn powder was removed with a membrane filter (25 mm with 1 µm glass fiber membrane) and the solution was transferred to another dry Ar-flushed *Schlenk*-tube. The concentration of the cyclohexylzinc reagent was determined by titration of a small aliquot with I_2 (73% yield, 0.37 M in THF).[103]



7-1k **7-2k**

7-2k

According to the general procedure, **7-1k** (0.53 g, 1.2 mmol) was used and the reaction mixture was stirred at 35 °C for 7 h to obtain **7-2k** (84% yield, 0.42 M in THF).



7-1l **7-2l**

7-2l (CAS: 1285537-33-8)

According to the general procedure, **7-1l** (1.1 g, 4.0 mmol) was used and the reaction mixture was stirred at 30 °C for 13 h to obtain **7-2l** (84% yield, 0.42 M in THF). A dry and Ar-flushed 10 mL *Schlenk*-tube was charged with the solution of **7-2l** (0.60 mL, 0.42 M solution in THF, 0.25 mmol) and the solvent was removed at 0 °C under high vacuum (1 mbar) for 2 h. The obtained oily compounds was dissolved with THF-d_8 (0.5 mL) and the NMR measurement was performed at 0 °C.

The peaks of the mixture of the diastereomers are given.

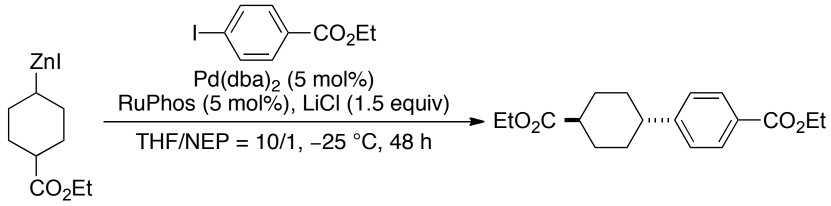
^{1}H-NMR (400 MHz, THF-d_8) δ: 1.99 (td, J = 13.0 and 3.1 Hz, 2H), 1.81-1.61 (m, 2.8H), 1.48 (tdd, J = 13.0, 12.8 and 2.6 Hz, 1.2H), 1.31 (tdd, J = 12.3, 12.2 and 2.9 Hz, 1.2H), 1.25 (quint, J = 1.9 Hz, 0.4H) 1.01 (tt, J = 12.0 and 2.8 Hz, 0.4H), 0.98 (tt, J = 11.8 and 2.9 Hz, 0.6H), 0.84 (s, 3.6H), 0.80 (s, 5.4H), 0.55 (tt, J = 13.3 and 3.2 Hz, 0.6H).

^{13}C-NMR (100 MHz, THF-d_8) δ: 50.2, 49.9, 34.5, 34.1, 33.2, 32.9, 31.6, 29.3, 29.3, 28.3, 28.0, 27.6.

9.7.3 Cross-coupling reaction

[General Procedure]

LiCl (32 mg, 0.75 mmol) was placed in a dry and Ar-flushed 10 mL *Schlenk*-tube and dried over 5 min at 400 °C (heat-gun) at high vacuum (1 mbar). After cooling to room temperature, $Pd(dba)_2$[149] (14.4 mg, 0.025 mmol), RuPhos[150] (11.7 mg, 0.025 mmol) and aryl iodide (0.35 mmol) was added under Ar atmosphere and it was evacuated and refilled with Ar three times. Then THF (0.35 mL) was added and the resulting solution was stirred at 25°C for 10 min. The solution was cooled to –25 °C and *N*-ethylpyrrolidone (0.22 mL, 10 vol%) was added. Subsequently, the solution of alkylzinc reagents (0.50 mmol) was added slowly with syringe pump for 100 min and the resulting mixture was stirred for 48 h at –25 °C. The reaction mixture was quenched with saturated NH_4Cl aqueous solution and it was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel.



7-2a **7-3aa**

7-3aa

According to the general procedure, **7-2a** (1.9 mL, 0.27 M in THF, 0.50 mmol) and methyl 4-iodobenzoate (92 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with CH_2Cl_2/*i*-hexane = 1/1→5/4 to afford the *trans* diastereomer **7-3aa** (81 mg, 80% yield, d.r. = 96:4) as brown solid.

m.p.: 63.7-65.1 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.95 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.89 (s, 3H), 2.57 (tt, J = 11.5 and 3.3 Hz, 1H), 2.34 (tt, J = 11.9 and 3.5 Hz, 1H), 2.18-2.06 (m, 2H), 2.03-1.91 (m, 2H), 1.60 (tdd, J = 12.8, 12.1 and 3.0 Hz, 2H), 1.48 (tdd, J = 12.7, 12.0 and 3.2 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H).

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[149] Bis(dibenzylideneacetone)palladium (0): a) Y. Takahashi, T. Ito, S. Sakai, Y. Ishii, *J. Chem. Soc. D,* **1970**, 1065; b) T. Ukai, H. Kawazura, Y. Ishii, J. J. Bonnet, J. A. Ibers, *J. Organomet. Chem.* **1974**, *65*, 253.

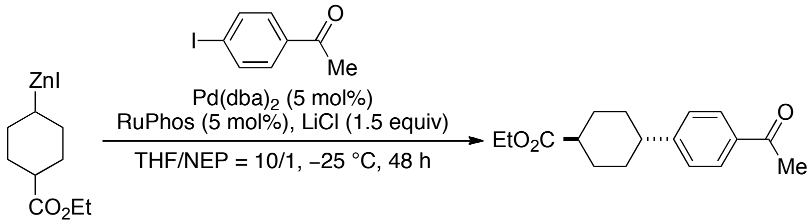
[150] M. D. Charles, P. Schultz, S. L. Buchwald, *Org. Lett.* **2005**, *7*, 3965.

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 175.9, 167.2, 152.3, 129.9, 128.2, 126.9, 60.4, 52.1, 43.8, 43.1, 33.1, 29.3, 14.4.

MS (70 eV, EI) *m/z* (%): 290 (100) [M]$^{+\bullet}$, 259 (26), 244 (61), 229 (36), 216 (81), 201 (59), 185 (21), 175 (5), 157 (80), 149 (51), 131 (59), 115 (28), 103 (18), 91 (24), 77 (16), 59 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2934 (w), 2859 (w), 1729 (vs), 1717 (s), 1608 (w), 1437 (w), 1412 (w), 1377 (w), 1317 (m), 1277 (s), 1249 (s), 1238 (m), 1192 (w), 1171 (s), 1159 (s), 1105 (s), 1036 (w), 1024 (w), 1016 (s), 955 (w), 899 (w), 866 (w), 856 (w), 840 (w), 820 (w), 756 (m), 706 (s), 665 (w).

HRMS (EI) *m/z*: calcd for $C_{17}H_{22}O_4^{+\bullet}$ [M]$^{+\bullet}$: 290.1518, found: 290.1515.



7-2a **7-3ab**

7-3ab

According to the general procedure, **7-2a** (1.9 mL, 0.27 M in THF, 0.50 mmol) and 1-(4-iodophenyl)ethanone (86 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/20→1/15 to afford the *trans* diastereomer **7-3ab** (69 mg, 72 % yield, d.r. = 94:6) as white solid.

m.p.: 42.6-43.9 °C.

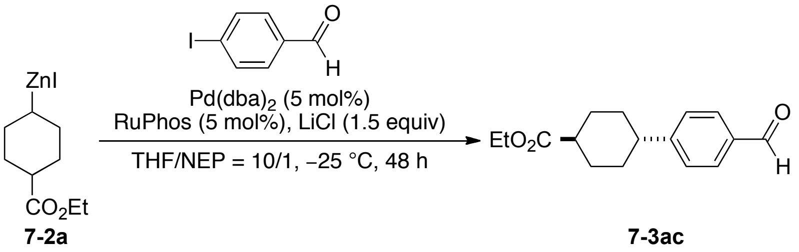
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.88 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 2.66-2.50 (m, 1H), 2.56 (s, 3H), 2.34 (tt, J = 12.0 and 3.6 Hz, 1H), 2.18-2.06 (m, 2H), 2.02-1.90 (m, 2H), 1.59 (tdd, J = 12.8, 12.0 and 3.0 Hz, 2H), 1.48 (tdd, J = 12.7, 12.0 and 2.9 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 197.9, 175.9, 152.6, 135.4, 128.7, 127.1, 60.4, 43.8, 43.2, 33.1, 29.2, 26.6, 14.4.

MS (70 eV, EI) *m/z* (%): 274 (100) [M]$^{+\bullet}$, 259 (24), 231 (8), 200 (60), 185 (21), 157 (36), 147 (5), 131 (28), 115 (14), 105 (14), 91 (14), 77 (10), 55 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2935 (w), 2855 (w), 2221 (w), 1716 (s), 1681 (m), 1673 (m), 1605 (m), 1448 (w), 1415 (w), 1374 (w), 1358 (w), 1318 (w), 1268 (m), 1254 (m), 1200 (w), 1174 (vs), 1138 (m), 1118 (m), 1097 (w), 1040 (m), 1023 (m), 956 (w), 902 (w), 843 (m), 825 (m), 784 (w), 755 (w), 713 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{17}H_{22}O_3}^{+\bullet}$ [M]$^{+\bullet}$: 274.1569, found: 274.1566.



7-3ac

According to the general procedure, **7-2a** (1.2 mL, 0.41 M in THF, 0.50 mmol) and 4-iodobenzaldehyde (81 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/25→1/20 to afford the *trans* diastereomer **7-3ac** (67 mg, 73 % yield, d.r. = 96:4) as colorless solid.

m.p.: 42.6-43.9 °C.

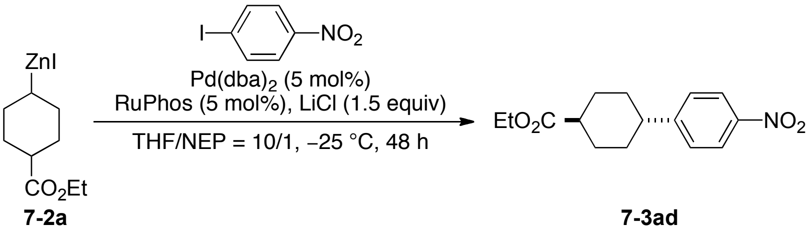
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 9.95 (s, 1H), 7.80 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.60 (tt, *J* = 11.6 and 3.2 Hz, 1H), 2.34 (tt, *J* = 12.0 and 3.5 Hz, 1H), 2.18-2.05 (m, 2H), 2.04-1.92 (m, 2H), 1.60 (tdd, *J* = 13.1, 12.0 and 2.9 Hz, 2H), 1.49 (tdd, *J* = 13.0, 12.0 and 3.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 192.0, 175.8, 154.2, 134.9, 130.1, 127.6, 60.4, 44.0, 43.0, 33.0, 29.2, 14.3.

MS (70 eV, EI) *m/z* (%): 260 (100) [M]$^{+\bullet}$, 231 (4), 214 (18), 186 (81), 171 (5), 157 (30), 143 (5), 131 (27), 119 (16), 103 (9), 91 (43), 77 (9), 67 (4), 55 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2932 (w), 2857 (w), 2221 (w), 1724 (m), 1697 (s), 1605 (s), 1574 (w), 1450 (w), 1375 (w), 1306 (w), 1255 (w), 1238 (w), 1211 (m), 1167 (s), 1138 (w), 1114 (w), 1096 (w), 1041 (m), 1026 (w), 912 (w), 865 (w), 823 (s), 728 (vs).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{16}H_{20}O_3}^{+\bullet}$ [M]$^{+\bullet}$: 260.1412, found: 260.1412.



7-3ad

According to the general procedure, **7-2a** (1.2 mL, 0.41 M in THF, 0.50 mmol) and 4-iodo-4-nitrobenzene (87 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/20 to afford the *trans* diastereomer **7-3ad** (72 mg, 74 % yield, d.r. = 96:4) as ivory solid.

m.p.: 83.9-85.5 °C.

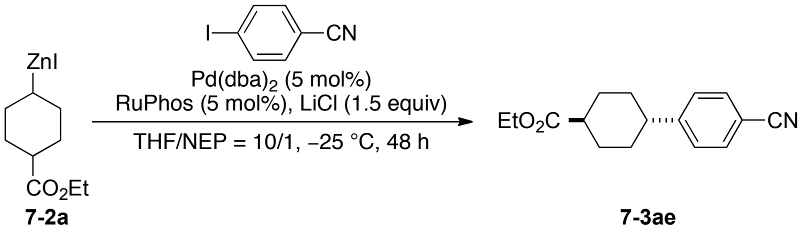
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 8.14 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 8.7 Hz, 2H), 4.14 (q, J = 7.1 Hz, 2H), 2.64 (tt, J = 11.9 and 3.3 Hz, 1H), 2.35 (tt, J = 12.0 and 3.6 Hz, 1H), 2.19-2.09 (m, 2H), 2.03-1.94 (m, 2H), 1.61 (tdd, J = 12.7, 12.2 and 2.7 Hz, 2H), 1.49 (tdd, J = 13.1, 12.1 and 2.8 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, CDCl$_3$) δ: 175.7, 154.6, 146.6, 127.7, 123.9, 60.5, 43.8, 42.9, 33.0, 29.1, 14.4.

MS (70 eV, EI) *m/z* (%): 277 (25) [M]$^+$, 260 (28), 247 (11), 231 (29), 214 (23), 203 (100), 186 (75), 172 (5), 156 (29), 141 (8), 132 (20), 115 (32), 106 (15), 91 (19), 77 (17), 67 (5), 55 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2936 (w), 2855 (w), 1723 (m), 1603 (w), 1594 (w), 1511 (s), 1476 (w), 1461 (w), 1447 (m), 1384 (w), 1343 (vs), 1283 (w), 1261 (m), 1238 (w), 1201 (w), 1168 (w), 1119 (m), 1103 (w), 1044 (w), 1027 (w), 1012 (w), 872 (w), 856 (m), 836 (w), 788 (w), 743 (w), 702 (m), 675 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{19}NO_4^{+\bullet}$** [M]$^{+\bullet}$: 277.1314, found: 277.1315.



7-3ae

According to the general procedure, **7-2a** (1.9 mL, 0.27 M in THF, 0.50 mmol) and 4-iodobenzonitrile (80 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/8 to afford the *trans* diastereomer **7-3ae** (63 mg, 70 % yield, d.r. = 94:6) as ivory solid.

m.p.: 61.2-63.5 °C.

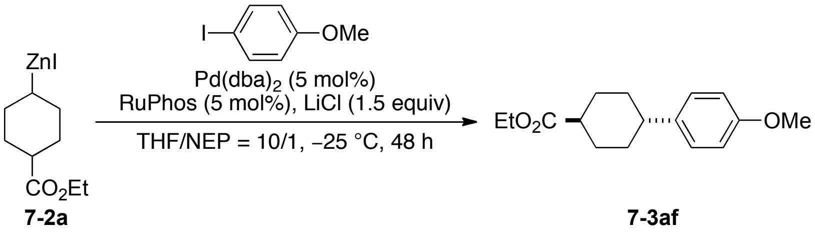
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.57 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.57 (tt, *J* = 11.8 and 3.2 Hz, 1H), 2.33 (tt, *J* = 11.9 and 3.5 Hz, 1H), 2.18-2.06 (m, 2H), 2.01-1.90 (m, 2H), 1.59 (tdd, *J* = 13.1, 12.1 and 3.0 Hz, 2H), 1.46 (tdd, *J* = 13.1, 12.1 and 3.0 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 175.7, 152.4, 132.4, 127.7, 119.1, 110.1, 60.4, 43.9, 42.9, 33.0, 29.1, 14.4.

MS (70 eV, EI) *m/z* (%): 257 (37) $[M]^{+\bullet}$, 211 (100), 193 (5), 182 (74), 168 (30), 154 (18), 142 (25), 129 (44), 116 (65), 101 (18), 89 (9), 81 (5), 73 (6), 55 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2985 (w), 2939 (w), 2858 (w), 2201 (w), 1711 (vs), 1606 (w), 1504 (w), 1449 (w), 1393 (w), 1374 (w), 1320 (w), 1254 (w), 1240 (w), 1206 (w), 1174 (s), 1161 (m), 1117 (w), 1096 (w), 1035 (w), 1016 (m), 902 (w), 854 (m), 846 (w), 833 (s), 785 (w), 752 (w), 731 (w).

HRMS (EI) *m/z*: calcd for $\mathbf{C_{16}H_{19}NO_2^{+\bullet}}$ $[M]^{+\bullet}$: 257.1416, found: 257.1413.



7-3af

According to the general procedure, **7-2a** (1.9 mL, 0.50 mmol; 0.27 M in THF) and 4-iodoanisole (82 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/20 to afford the *trans* diastereomer **7-3af** (68 mg, 74 % yield, d.r. = 97:3) as brown solid.

m.p.: 47.0-48.2 °C.

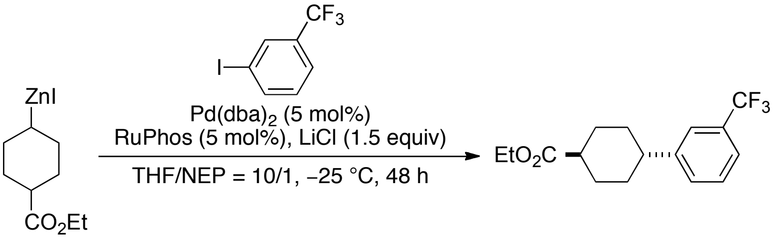
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.12 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 2.47 (tt, *J* = 11.8 and 3.3 Hz, 1H), 2.33 (tt, *J* = 11.9 and 3.5 Hz, 1H), 2.16-2.04 (m, 2H), 2.00-1.90 (m, 2H), 1.58 (tdd, *J* = 12.6, 12.2 and 2.5 Hz, 2H), 1.44 (tdd, *J* = 12.6, 12.1 and 2.6 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 176.2, 158.0, 139.3, 127.7, 113.9, 60.3, 55.4, 43.2, 42.9, 33.7, 29.5, 14.4.

MS (70 eV, EI) *m/z* (%): 262 (68) $[M]^{+\bullet}$, 217 (13), 188 (85), 173 (12), 159 (8), 147 (100), 134 (40), 121 (50), 108 (6), 91 (17), 77 (7), 65 (5), 55 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2935 (w), 2857 (w), 1725 (s), 1607 (w), 1512 (s), 1464 (w), 1143 (w), 1376 (w), 1315 (w), 1284 (w), 1247 (s), 1198 (w), 1171 (m), 1157 (vs), 1134 (m), 1113 (m), 1093 (m), 1031 (s), 1021 (s), 898 (w), 863 (w), 845 (w), 828 (m), 806 (s), 795 (w), 790 (w), 758 (w), 713 (w).

HRMS (EI) *m/z*: calcd for **$C_{16}H_{22}O_3^{+\bullet}$** [M]$^{+\bullet}$: 262.1569, found: 262.1562.



7-2a **7-3ag**

7-3ag

According to the general procedure, **7-2a** (1.9 mL, 0.27 M in THF, 0.50 mmol) and 1-iodo-3-(trifluoromethyl)benzene (95 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/20 to afford the *trans* diastereomer **7-3ag** (72 mg, 68 % yield, d.r. = 93:7) as brown oil.

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.48-7.36 (m, 4H), 4.15 (q, J = 7.1 Hz, 2H), 2.59 (tt, J = 11.8 and 3.3 Hz, 1H), 2.35 (tt, J = 11.9 and 3.5 Hz, 1H), 2.20-2.06 (m, 2H), 2.04-1.92 (m, 2H), 1.61 (tdd, J = 12.7, 12.0 and 2.9 Hz, 2H), 1.49 (tdd, J = 12.7, 12.0 and 3.3 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H).

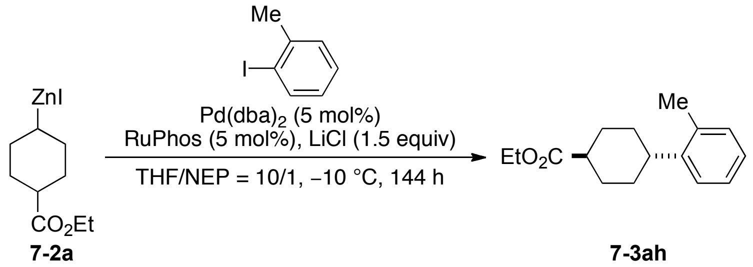
^{13}C-NMR (75 MHz, CDCl$_3$) δ: 175.9, 147.8, 130.8 (q, J = 31.9 Hz, 1C), 130.4 (q, J = 1.3 Hz, 1C), 128.9, 124.4 (q, J = 272.3 Hz, 1C), 123.6 (q, J = 3.8 Hz, 1C), 123.1 (q, J = 3.8 Hz, 1C), 60.4, 43.6, 43.0, 33.3, 29.3, 14.4.

^{19}F-NMR (282 MHz, CDCl$_3$) δ: –62.6

MS (70 eV, EI) *m/z* (%): 300 (25) [M]$^{+\bullet}$, 281 (21), 254 (100), 226 (58), 211 (19), 197 (8), 185 (21), 172 (44), 159 (57), 151 (6), 129 (9), 115 (8), 101 (11), 81 (5), 73 (5), 55 (9).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2932 (w), 2860 (w), 1727 (s), 1451 (w), 1376 (w), 1328 (s), 1278 (w), 1256 (w), 1237 (w), 1194 (w), 1160 (s), 1119 (vs), 1073 (s), 1041 (w), 1027 (w), 908 (w), 894 (w), 801 (w), 751 (w), 702 (s), 665 (w).

HRMS (EI) *m/z*: calcd for **$C_{16}H_{19}F_3O_2^{+\bullet}$** [M]$^{+\bullet}$: 300.1337, found: 300.1322.



7-3ah

According to the general procedure, **7-2a** (1.4 mL, 0.37 M in THF, 0.50 mmol) and 2-iodotoluene (76 mg, 0.35 mmol) were used and the reaction mixture was stirred at –10 ºC for 144 h. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/40 to afford the *trans* diastereomer **7-3ah** (62 mg, 72 % yield, d.r. = 97:3) as colorless oil.

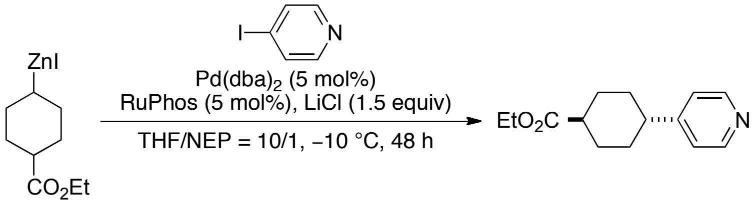
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.23-7.06 (m, 4 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 2.75 (tt, *J* = 11.7 and 3.2 Hz, 1 H), 2.39 (tt, *J* = 12.1 and 3.6 Hz, 1 H), 3.34 (s, 3 H), 2.18-2.08 (m, 2 H), 1.97-1.86 (m, 2 H), 1.64 (tdd, *J* = 12.6, 12.1 and 2.5 Hz, 2 H), 1.49 (tdd, *J* = 12.8, 11.9 and 2.5 Hz, 2 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

^{13}C-NMR (101 MHz, CDCl$_3$) *δ*: 176.1, 144.9, 135.3, 130.5, 126.3, 125.9, 125.2, 60.3, 43.4, 39.3, 32.6, 29.7, 19.4, 14.4.

MS (70 eV, EI) *m/z* (%): 246 (100) $[M]^{+\bullet}$, 231 (14), 217 (3), 200 (71), 185 (16), 172 (71), 157 (51), 143 (27), 131 (55), 118 (45), 105 (72), 91 (27), 70 (11), 65 (5), 55 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2932 (w), 2859 (w), 1728 (vs), 1490 (w), 1450 (w), 1377 (w), 1314 (w), 1258 (w), 1238 (m), 1172 (s), 1139 (m), 1119 (w), 1096 (w), 1040 (s), 1026 (m), 902 (w), 864 (w), 748 (s), 725 (m).

HRMS (EI) *m/z*: calcd for **$C_{16}H_{22}O_3^{+\bullet}$** $[M]^{+\bullet}$: 246.1620, found: 246.1614.



7-3ai

According to the general procedure, **7-2a** (1.4 mL, 0.37 M in THF, 0.50 mmol) and 4-iodopyridine (72 mg, 0.35 mmol) were used and the reaction mixture was stirred at –10 °C for 48 h. The crude product was purified by chromatography on silica gel with

EtOAc/*i*-hexane = 1/1 to afford the *trans* diastereomer **7-3ai** (56 mg, 69 % yield, d.r. = 97:3) as yellow oil.

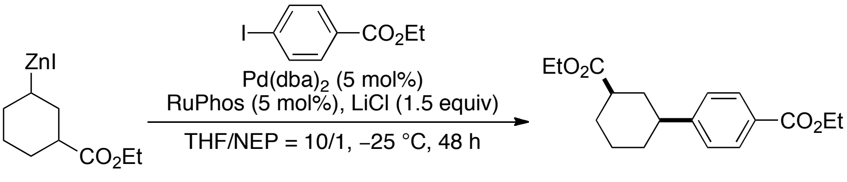
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 8.48 (d, *J* = 5.5 Hz, 2H), 7.09 (d, *J* = 5.5 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.49 (tt, *J* = 11.9 and 3.6 Hz, 1H), 2.32 (tt, *J* = 11.9 and 3.6 Hz, 1H), 2.19-2.08 (m, 2H), 2.03-1.93 (m, 2H), 1.60 (tdd, *J* = 12.9, 12.5 and 2.8 Hz, 2H), 1.47 (tdd, *J* = 12.7, 12.6 and 3.0 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 175.7, 155.5, 150.0, 122.3, 60.4, 43.0, 42.9, 32.5, 29.1, 14.3.

MS (70 eV, EI) *m/z* (%): 233 (100) $[M]^{+\bullet}$, 220 (23), 204 (25), 187 (19), 178 (21), 160 (64), 144 (21), 132 (38), 118 (30), 106 (59), 93 (33), 77 (18), 65 (15), 55 (16).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2933 (w), 2855 (w), 1726 (vs), 1598 (w), 1525 (m), 1450 (w), 1376 (w), 1348 (m), 1315 (w), 1300 (w), 1241 (m), 1219 (w), 1203 (w), 1165 (s), 1136 (m), 1104 (m), 1076 (w), 1039 (m), 1026 (m), 971 (w), 919 (w), 910 (w), 899 (w), 861 (w), 829 (w), 806 (w), 783 (w), 766 (w), 736 (m), 713 (w), 693 (m), 678 (w).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{19}NO_2^{+\bullet}$** $[M]^{+\bullet}$: 233.1416, found: 233.1412.



7-2b **7-3ba**

7-3ba

According to the general procedure, **7-2b** (1.2 mL, 0.41 M in THF, 0.50 mmol) and methyl 4-iodobenzoate (92 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/40→1/25 to afford the *cis* diastereomer **7-3ba** (81 mg, 80 % yield, d.r. = 95:5) as pale yellow oil.

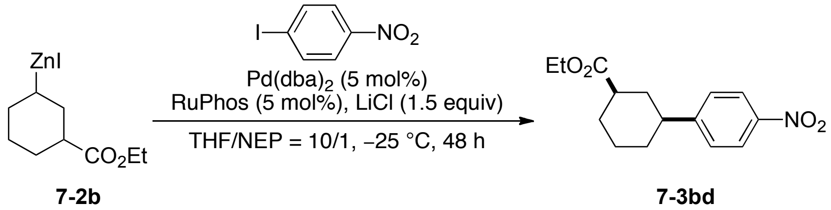
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 7.96 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 2.61 (tt, *J* = 11.9 and 3.3 Hz, 1H), 2.45 (tt, *J* = 12.0 and 3.5 Hz, 1H), 2.13 (dtt, *J* = 12.9, 3.6 and 2.0 Hz, 1H), 2.10-1.83 (m, 3H), 1.60 (td, *J* = 12.7 and 12.4 Hz, 1H), 1.55-1.33 (m, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 175.6, 167.2, 152.0, 129.9, 128.3, 127.0, 60.4, 52.1, 43.82, 43.78, 36.1, 33.4, 28.6, 25.9, 14.3.

MS (70 eV, EI) *m/z* (%): 290 (100) $[M]^{+\bullet}$, 259 (54), 244 (29), 230 (16), 216 (81), 201 (23), 190 (79), 175 (14), 167 (6), 157 (41), 149 (59), 141 (11), 131 (6), 115 (41), 101 (18), 91 (26), 77 (17), 67 (7), 59 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2932 (w), 2857 (w), 1718 (vs), 1610 (w), 1435 (w), 1417 (w), 1375 (w), 1311 (w), 1275 (s), 1247 (m), 1199 (m), 1178 (m), 1109 (s), 1099 (s), 1030 (w), 1019 (m), 966 (w), 850 (w), 835 (w), 816 (w), 771 (m), 732 (w), 706 (m).

HRMS (EI) *m/z*: calcd for $C_{17}H_{22}O_4^{+\bullet}$ $[M]^{+\bullet}$: 290.1518, found: 290.1513.



7-3bd

According to the general procedure, **7-2b** (1.2 mL, 0.41 M in THF, 0.50 mmol) and 1-iodo-3-nitrobenzene (97 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/40→1/30 to afford the *cis* diastereomer **3bd** (72 mg, 74 % yield, d.r. = 97:3) as pale yellow oil.

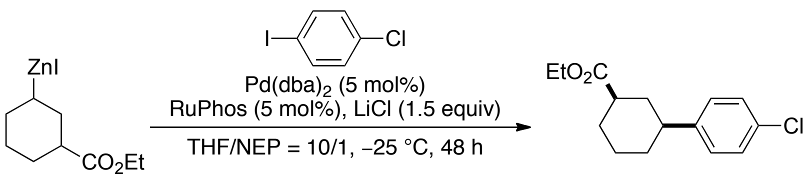
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 8.14 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.7 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 2.68 (tt, J = 11.2 and 3.1 Hz, 1H), 2.47 (tt, J = 11.9 and 3.5 Hz, 1H), 2.14 (dtt, J = 11.0, 3.9 and 2.2 Hz, 1H), 2.10-1.83 (m, 3H), 1.60 (td, J = 12.6 and 12.5 Hz, 1H), 1.54-1.33 (m, 3H), 1.24 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 175.4, 154.3, 146.6, 127.8, 123.9, 60.5, 43.7, 43.6, 35.9, 33.3, 28.6, 25.8, 14.3.

MS (70 eV, EI) *m/z* (%): 277 (39) $[M]^{+\bullet}$, 260 (53), 247 (15), 231 (46), 214 (13), 203 (100), 186 (70), 177 (51), 168 (13), 141 (16), 129 (47), 101 (45), 91 (32), 77 (30), 67 (12), 55 (27).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2932 (w), 2857 (w), 1725 (s), 1595 (w), 1514 (s), 1447 (w), 1376 (w), 1343 (vs), 1248 (w), 1205 (m), 1171 (m), 1130 (w), 1110 (m), 1030 (m), 869 (w), 846 (m), 825 (w), 783 (w), 749 (w), 736 (w), 698 (m).

HRMS (EI) *m/z*: calcd for $C_{15}H_{19}NO_4^{+\bullet}$ $[M]^{+\bullet}$: 277.1314, found: 277.1318.



7-2b **7-3bj**

7-3bj

According to the general procedure with small modifications, a solution of Pd(dba)$_2$, RuPhos and 4-iodochlorobenzene (84 mg, 0.35 mmol) in THF (0.35 mL) was prepared at –25 °C and it was stirred at –25 °C for 25 min before the addition of **7-2b** (1.22 mL, 0.41 M in THF, 0.50 mmol). In addition, this cross-coupling reaction was stopped in 38 h. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 0/100→1/25→1/20→1/10 to afford the *cis* diastereomer **7-3bj** (74 mg, 79 % yield, d.r. = 94:6) as colorless oil.

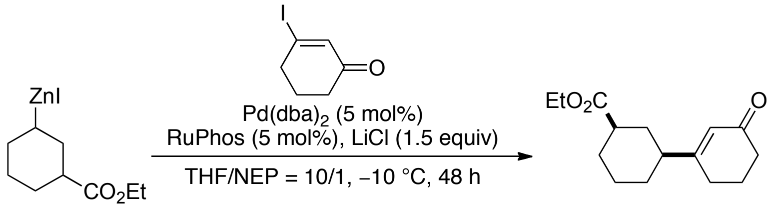
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.25 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 8.6 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 2.53 (tt, J = 11.9 and 3.2 Hz, 1H), 2.44 (tt, J = 12.0 and 3.3 Hz, 1H), 2.10 (dtt, J = 13.0, 3.5 and 1.9 Hz, 1H), 2.09-1.78 (m, 3H), 1.55 (td, J = 12.6 and 12.5 Hz, 1H), 1.52-1.29 (m, 3H), 1.24 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 175.7, 145.2, 131.9, 128.6, 128.3, 60.4, 43.9, 43.2, 36.4, 33.6, 28.6, 25.9, 14.4.

MS (70 eV, EI) *m/z* (%): 266 (81) $[M]^{+\bullet}$, 221 (14), 192 (89), 185 (5), 177 (5), 164 (14), 151 (36), 138 (34), 125 (100), 115 (39), 101 (68), 89 (12), 81 (11), 73 (15), 63 (4), 55 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2930 (w), 2857 (w), 1726 (vs), 1492 (m), 1461 (w), 1447 (w), 1410 (w), 1375 (w), 1313 (w), 1296 (w), 1279 (w), 1259 (w), 1245 (w), 1203 (m), 1163 (s), 1130 (m), 1115 (w), 1089 (m), 1030 (m), 1013 (m), 819 (s), 783 (w), 755 (w), 718 (w).

HRMS (EI) *m/z*: calcd for **$C_{15}H_{19}ClO_3^{+\bullet}$** $[M]^{+\bullet}$: 266.1074, found: 266.1078.



7-2b **7-3bk**

7-3bk

According to the general procedure, **7-2b** (1.5 mL, 0.34 M in THF, 0.50 mmol) and 3-iodocyclohex-2-enone (78 mg, 0.35 mmol) were used and this reaction mixture were stirred at –10 °C for 48 h. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/20→1/10→1/3 to afford the *cis* diastereomer **7-3bk** (68 mg, 78 % yield, d.r. = 96:4) as pale yellow oil.

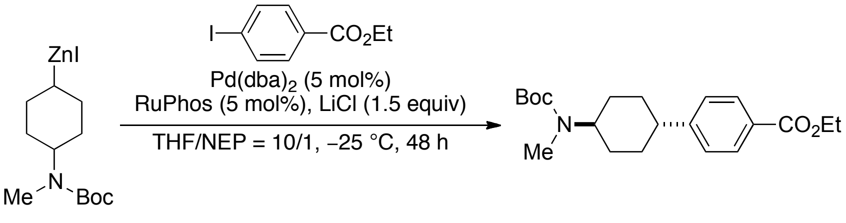
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 5.87 (s, 1 H), 4.12 (q, J = 7.1 Hz, 2 H), 2.42-2.27 (m, 5 H), 2.19-1.85 (m, 6 H), 1.85-1.93 (m, 1 H), 1.48-1.14 (m, 3 H), 1.30-1.14 (m, 1 H), 1.25 (t, J = 7.1 Hz, 3 H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 200.2, 175.4, 169.4, 124.7, 60.5, 45.3, 43.4, 37.7, 33.2, 30.3, 28.7, 28.2, 25.5, 23.0, 14.4.

MS (70 eV, EI) *m/z* (%): 250 (100) $[M]^+$, 221 (4), 205 (20), 193 (4), 176 (69), 159 (28), 148 (37), 133 (33), 123 (59), 110 (68), 95 (77), 79 (59), 67 (43), 55 (32).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2932 (w), 2860 (w), 1726 (s), 1665 (vs), 1620 (w), 1448 (w), 1375 (w), 1344 (w), 1325 (w), 1291 (w), 1252 (m), 1204 (m), 1191 (m), 1172 (s), 1136 (m), 1029 (m), 993 (w), 966 (w), 910 (w), 887 (w), 859 (w), 758 (w), 730 (w).

HRMS (EI) *m/z*: calcd for $C_{15}H_{22}O_3^{+\bullet}$ $[M]^{+\bullet}$: 250.1569, found: 250.1561.



7-2c **7-3ca**

7-3ca

According to the general procedure, **7-2c** (1.2 mL, 0.42 M in THF, 0.50 mmol) and methyl 4-iodobenzoate (92 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/8 to afford the *trans* diastereomer **7-3ca** (95 mg, 78 % yield, d.r. = 99:1) as colorless oil.

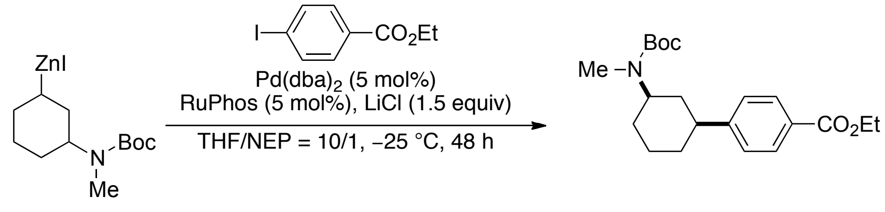
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.95 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 4.25-3.80 (br s, 1H), 3.89 (s, 3H), 2.76 (s, 3H), 2.51 (tt, J = 11.8 and 3.4 Hz, 1H), 2.02-1.89 (m, 2H), 1.88-1.76 (m, 2H), 1.68-1.51 (m, 4H), 1.47 (s, 9H).

^{13}C-NMR (101 MHz, CDCl$_3$) δ: 167.2, 155.8, 152.2, 129.9, 128.2, 126.9, 79.4, 54.0, 52.1, 43.8, 32.3, 30.2, 28.7, 28.5.

MS (70 eV, EI) *m/z* (%): 347 (5) $[M]^{+\bullet}$, 316 (10), 291 (14), 274 (11), 260 (14), 247 (30), 232 (100), 216 (46), 204 (12), 178 (8), 157 (14), 141 (4), 131 (12), 114 (10), 103 (4), 91 (5), 70 (6), 57 (95).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2925 (w), 1718 (s), 1681 (vs), 1608 (w), 1481 (w), 1448 (m), 1437 (m), 1404 (w), 1385 (w), 1365 (m), 1323 (m), 1273 (s), 1179 (m), 1149 (s), 1108 (s), 1091 (s), 1048 (w), 1018 (w), 986 (m), 906 (w), 879 (w), 855 (w), 839 (w), 818 (w), 768 (s), 704 (s), 666 (w).

HRMS (EI) *m/z*: calcd for $C_{20}H_{29}NO_4^{+\bullet}$ $[M]^{+\bullet}$: 347.2097, found: 347.2092.



7-2d **7-3da**

7-3da

According to the general procedure, **7-2d** (1.3 mL, 0.38 M in THF, 0.50 mmol) and methyl 4-iodobenzoate (92 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/8 to afford the *cis* diastereomer **7-3da** (102 mg, 84 % yield, d.r. = 99:1) as a colorless oil. The relative configuration was assigned by analogy with **3ca** and by comparison of NMR spectra with those of **3aa** and **3ba**.

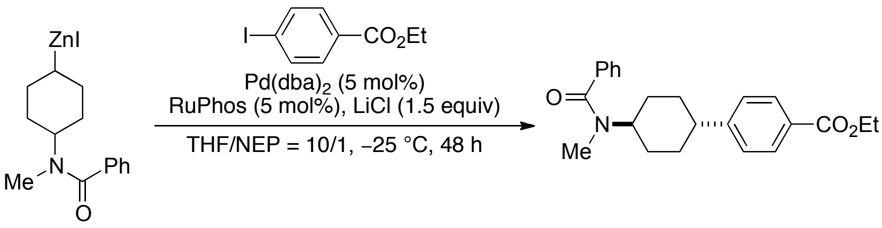
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.95 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 4.31-3.90 (br s, 1H), 3.89 (s, 3H), 2.75-2.61 (m, 1H), 2.74 (s, 3H), 2.00-1.68 (m, 4H), 1.62-1.15 (m, 4H), 1.46 (s, 9H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 167.2, 155.7, 151.8, 129.9, 128.2, 126.9, 79.5, 54.0, 52.1, 43.9, 37.8, 33.0, 29.7, 28.6, 28.5, 25.5.

MS (70 eV, EI) *m/z* (%): 347 (10) $[M]^{+\bullet}$, 316 (16), 291 (19), 259 (8), 247 (60), 232 (41), 216 (68), 204 (85), 149 (11), 131 (13), 115 (10), 105 (5), 91 (10), 70 (42), 57 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2913 (m), 2848 (w), 1723 (s), 1685 (s), 1610 (w), 1471 (w), 1435 (w), 1390 (w), 1363 (m), 1314 (m), 1277 (vs), 1254 (m), 1228 (w), 1199 (w), 1177 (s), 1150 (s), 1110 (s), 1019 (s), 974 (w), 884 (w), 876 (w), 851 (w), 770 (m), 716 (m), 706 (m).

HRMS (EI) *m/z*: calcd for $C_{20}H_{29}NO_4^{+\bullet}$ $[M]^{+\bullet}$: 347.2097, found: 347.2085.



7-2e **7-3ea**

7-3ea

According to the general procedure, **7-2e** (1.7 mL, 0.30 M in THF, 0.50 mmol) and methyl 4-iodobenzoate (92 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane = 1/10→1/5→1/1 to afford the *trans* diastereomer **7-3ea** (94 mg, 76 % yield, d.r. = 99:1) as white solid. The relative configuration was assigned by analogy with **7-3ca**.

m.p.: 187.6-189.2 °C.

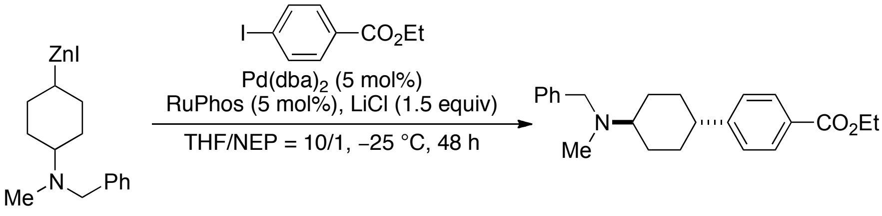
^{1}H-NMR (300 MHz, CDCl$_3$) *δ*: 8.03-7.84 (br s, 2H), 7.45-7.34 (br s, 5H), 7.30-7.09 (br s, 2H), 4.79-4.47 (br s, 0.5H), 3.87 (s, 3H), 3.71-3.45 (br s, 0.5H), 3.13-2.69 (m, 3H), 2.65-2.36 (br s, 1H), 2.14-1.50 (br s, 7H), 1.49-1.11 (br s, 1H).

^{13}C-NMR (75 MHz, CDCl$_3$) *δ*: 171.7, 167.1, 151.7, 137.2, 129.8, 129.4, 128.6, 128.3, 126.8, 126.2, 55.1, 52.0, 43.6, 32.9, 32.2, 30.0, 27.6.

MS (70 eV, EI) *m/z* (%): 351 (74) $[M]^{+\bullet}$, 336 (5), 320 (9), 304 (6), 291 (3), 245 (6), 216 (17), 201 (5), 185 (5), 174 (21), 162 (14), 149 (5), 136 (52), 115 (5), 105 (100), 77 (31), 57 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2939 (w), 1705 (m), 1613 (s), 1572 (w), 1498 (s), 1481 (w), 1448 (w), 1433 (w), 1417 (w), 1404 (w), 1369 (w), 1327 (w), 1270 (s), 1181 (w), 1110 (m), 1098 (m), 1065 (m), 1025 (w), 1017 (w), 1008 (w), 972 (w), 921 (w), 902 (w), 853 (w), 818 (w), 790 (m), 782 (w), 763 (m), 731 (m), 706 (m), 698 (vs).

HRMS (EI) *m/z*: calcd for $C_{22}H_{25}NO_3^{+\bullet}$ $[M]^{+\bullet}$: 351.1834, found: 351.1833.



7-2f **7-3fa**

7-3fa

According to the general procedure, **7-2f** (1.4 mL, 0.35 M in THF, 0.50 mmol) and methyl 4-iodobenzoate (92 mg, 0.35 mmol) were used and **7-2f** was added one time instead of dropwise addition. The crude product was purified by chromatography on silica gel with EtOAc/*i*-hexane/Et_3N = 1/10/0.4 was used for column chromatography and Et_2O/*i*-hexane/Et_3N = 1/4/0.16 was used for the subsequent preparative TLC to afford the *trans* diastereomer **7-3fa** (90 mg, 76 % yield, d.r. = 99:1) as white solid. The relative configuration was further confirmed by X-ray crystallography of single crystal recrystallized from CH_2Cl_2/*n*-heptane.

m.p.: 93.5-94.2 °C.

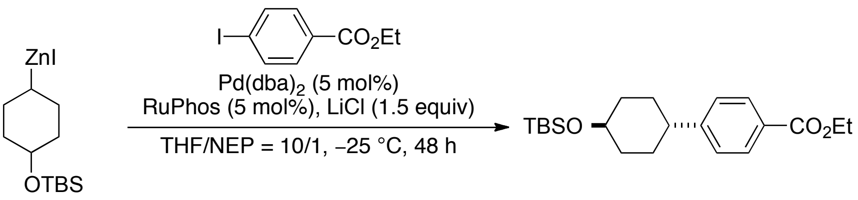
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, J = 8.2 Hz, 2 H), 7.37-7.28 (m, 5 H), 7.27 (d, J = 8.3 Hz, 2 H), 3.90 (s, 3 H), 3.62 (s, 2 H), 2.57 (tt, J = 11.2 and 3.2 Hz, 1 H), 2.55 (tt, J = 11.4 and 3.5 Hz, 1 H), 2.25 (s, 3H), 2.10-1.93 (m, 4 H), 1.61-1.44 (m, 4 H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 167.2, 152.7, 140.3, 129.8, 128.9, 128.4, 128.0, 127.0, 126.9, 62.0, 58.1, 52.1, 44.6, 37.9, 33.6, 28.6.

MS (70 eV, EI) *m/z* (%): 337 (12) $[M]^{+\bullet}$, 306 (5), 160 (100), 146 (28), 132 (5), 120 (4), 91 (33), 77 (2), 65 (2).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2926 (w), 1717 (s), 1606 (w), 1449 (w), 1436 (w), 1416 (w), 1356 (w), 1309 (w), 1275 (s), 1191 (w), 1182 (w), 1155 (w), 1112 (m), 1104 (m), 1088 (w), 1038 (w), 1026 (w), 1017 (w), 964 (w), 856 (w), 818 (w), 780 (w), 772 (w), 766 (w), 758 (m), 741 (m), 706 (m), 699 (vs), 680 (w).

HRMS (ESI) *m/z*: calcd for $C_{22}H_{28}NO_2^{+\bullet}$ $[M+H]^{+\bullet}$: 338.2120, found: 338.2112.



7-2g **7-3ga**

7-3ga

According to the typical procedure, **7-2g** (1.2 mL, 0.42 M in THF, 0.50 mmol) and methyl 4-iodobenzoate (92 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with Et_2O/*i*-hexane = 1/18 to afford the *trans* diastereomer **7-3ga** (92 mg, 75 % yield, d.r. = 97:3) as white solid.

m.p.: 63.4-64.1 °C.

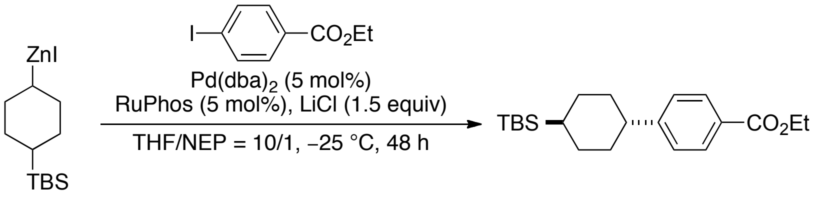
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.95 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H), 3.89 (s, 3H), 3.64 (tt, J = 10.2 and 4.4 Hz, 1H), 2.52 (tt, J = 11.6 and 3.5 Hz, 1H), 2.05-1.83 (m, 4H), 1.50 (dt, J = 12.8 and 10.6 Hz, 2H), 1.47 (dt, J = 11.7 and 10.5 Hz, 2H), 0.91 (s, 9H), 0.08 (s, 6H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 167.2, 152.5, 129.8, 128.1, 127.0, 71.4, 52.1, 43.7, 36.3, 32.6, 26.1, 18.4, –4.4.

MS (70 eV, EI) *m/z* (%): 348 (1) $[M]^{+\bullet}$, 333 (3), 317 (5), 291 (86), 215 (100), 201 (7), 185 (40), 149 (5), 131 (13), 115 (4), 103 (3), 75 (23).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2928 (w), 2854 (w), 1720 (m), 1610 (w), 1438 (w), 1377 (w), 1359 (w), 1273 (m), 1246 (w), 1186 (w), 1110 (m), 1089 (s), 1021 (w), 1004 (w), 991 (w), 961 (w), 900 (w), 858 (m), 841 (s), 832 (s), 769 (vs), 703 (m), 675 (w), 663 (w).

HRMS (EI) *m/z*: calcd for $C_{20}H_{32}O_3Si^{+\bullet}$ $[M]^{+\bullet}$: 348.2121, found: 348.2123.



7-2h **7-3ha**

7-3ha

According to the general procedure, **7-2h** (1.5 mL, 0.33 M in THF, 0.50 mmol) and methyl 4-iodobenzoate (92 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/70→1/35 to afford the *trans* diastereomer **7-3ha** (81 mg, 70 % yield, d.r. = 98:2) as colorless oil.

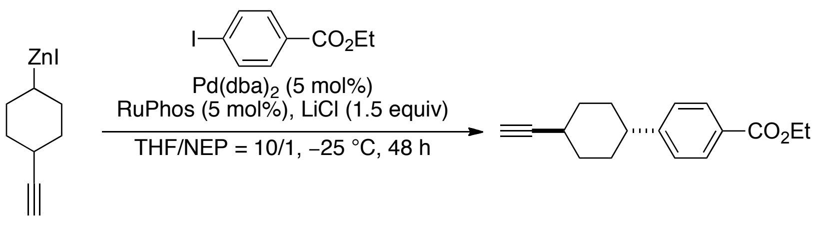
^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.96 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 3.90 (s, 3H), 2.54 (tt, J = 11.7 and 3.0 Hz, 1H), 1.99-1.84 (m, 4H), 1.43 (dtd, J = 12.3, 12.0 and 2.5 Hz, 2H), 1.33 (dtd, J = 12.6, 12.6 and 2.5 Hz, 2H), 0.93 (s, 9H), 0.80 (tt, J = 12.3 and 2.5 Hz, 1H), –0.06 (s, 6H).

^{13}C-NMR (101 MHz, CDCl$_3$) δ: 167.3, 153.6, 129.9, 127.9, 127.0, 52.0, 44.9, 35.7, 28.9, 27.5, 23.4, 17.5, –7.3.

MS (70 eV, EI) *m/z* (%): 332 (4) $[M]^{+\bullet}$, 301 (5), 275 (100), 215 (4), 193 (18), 185 (94), 162 (3), 145 (7), 131 (16), 115 (4), 103 (4), 75 (21), 59 (17).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2925 (w), 2850 (w), 1716 (m), 1609 (w), 1436 (w), 1276 (s), 1246 (w), 1180 (w), 1111 (w), 1019 (w), 907 (m), 826 (m), 801 (w), 762 (m), 729 (vs), 708 (m).

HRMS (ESI) *m/z*: calcd for **$C_{20}H_{33}O_2Si^{+\bullet}$** [M+H]$^{+\bullet}$: 333.2250, found: 333.2243.



7-2i **7-3ia**

7-3ia

According to the general procedure, **7-2i** (1.5 mL, 0.33 M in THF, 0.50 mmol) and methyl 4-iodobenzoate (92 mg, 0.35 mmol) were used. The crude product was purified by chromatography on silica gel with Et$_2$O /*i*-hexane = 1/30→1/20 to afford the *trans* diastereimer **7-3ia** (50 mg, 59 % yield) as white solid and the *cis* diastereomer, methyl 4-(*cis*-4-ethynylcyclohexyl)benzoate (7 mg, 8 % yield) as white solid with a small amount of **7-3ia**. The diastereoselectivity was determined to be d.r. = 88:12 from GC analysis of the crude product.

methyl 4-(*cis*-4-ethynylcyclohexyl)benzoate

m.p.: 80.5-81.0 °C.

^{1}H-NMR (599 MHz, CDCl$_3$) *δ*: 7.97 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 3.90 (s, 3H), 2.89 (dt, *J* = 6.5 and 3.2 Hz, 1H), 2.55 (tt, *J* = 11.8 and 3.4 Hz, 1H), 2.13 (d, *J* = 2.5 Hz, 1H), 1.97-1.87 (m, 4H), 1.77-1.70 (m, 2H), 1.64 (tt, *J* = 13.8 and 3.8 Hz, 2H).

^{13}C-NMR (101 MHz, CDCl$_3$) *δ*: 167.3, 152.9, 129.9, 128.1, 127.1, 87.4, 69.9, 52.1, 44.4, 31.0, 29.3, 26.3.

MS (70 eV, EI) *m/z* (%): 242 (72) [M]$^{+\bullet}$, 227 (16), 214 (74), 201 (17), 183 (51), 175 (12), 162 (18), 155 (54), 141 (41), 131 (100), 115 (66), 103 (39), 91 (68), 77 (51), 67 (8), 59 (23), 51 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3260 (w), 2932 (m), 2920 (m), 2849 (w), 1708 (s), 1607 (w), 1512 (m), 1446 (w), 1433 (m), 1415 (w), 1393 (w), 1364 (w), 1340 (m), 1315 (w), 1296 (w), 1276 (s), 1192 (w), 1181 (m), 1108 (s), 1064 (w), 1019 (m), 1003 (w), 962 (w), 937 (w), 847 (m), 833 (w), 780 (w), 761 (m), 753 (m), 705 (s), 696 (vs), 679 (m).

HRMS (ESI) *m/z*: calcd for **$C_{16}H_{18}O_2^{+\bullet}$** [M]$^{+\bullet}$: 242.1307, found: 242.1309.

7-3ia

m.p.: 129.2-130.5 °C.

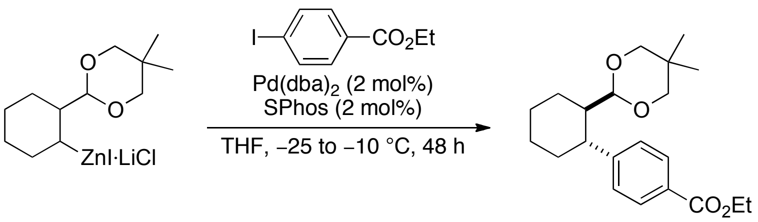
^{1}H-NMR (599 MHz, CDCl$_3$) δ: 7.94 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 3.88 (s, 3H), 2.55 (tt, J = 11.8 and 3.4 Hz, 1H), 2.30 (ttd, J = 11.8, 3.6 and 2.4 Hz, 1H), 2.16-2.09 (m, 2H), 2.07 (d, J = 2.4 Hz, 1H), 1.95-1.87 (m, 2H), 1.54 (tdd, J = 12.5, 12.1 and 3.1 Hz, 2H), 1.45 (tdd, J = 12.7, 12.1 and 3.1 Hz, 2H).

^{13}C-NMR (151 MHz, CDCl$_3$) δ: 167.2, 152.4, 129.9, 128.2, 126.9, 88.6, 68.1, 52.1, 43.7, 33.4, 33.2, 29.2.

MS (70 eV, EI) *m/z* (%): 242 (8) [M]$^+$, 227 (5), 214 (100), 201 (14), 189 (32), 183 (32), 173 (11), 162 (7), 155 (47), 141 (19), 129 (100), 115 (46), 103 (28), 91 (51), 77 (41), 67 (13), 59 (19), 51 (11).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3251 (w), 2950 (w), 2923 (w), 2852 (w), 1703 (s), 1607 (m), 1433 (m), 1414 (w), 1314 (w), 1255 (w), 1279 (vs), 1191 (w), 1179 (m), 1114 (m), 1107 (s), 1016 (m), 960 (w), 940 (w), 897 (w), 859 (w), 841 (w), 818 (w), 777 (m), 761 (m), 708 (s), 683 (m).

HRMS (ESI) *m/z*: calcd for **$C_{16}H_{18}O_2^{+\bullet}$** [M]$^{+\bullet}$: 242.1307, found: 242.1301.



7-2j **7-3ja**

7-3ja

In a dry and Ar-flushed 10 mL *Schlenk*-tube Pd(dba)$_2$ (11.5 mg, 0.02 mmol), S-Phos[89b] (8.2 mg, 0.02 mmol) and methyl 4-iodobenzoate (183 mg, 0.70 mmol) was added and it was evacuated and refilled with Ar three times. Then THF (1.0 mL) was added and the resulting solution was stirred at room temperature for 10 min. The solution was cooled to –25 °C and, subsequently, the solution **7-2j** (2.7 mL, 0.37 M in THF, 1.0 mmol) was added slowly with syringe pump in 100 min and the resulting mixture was stirred for 24 h at –25 °C. Then the reaction mixture was stirred for further 24 h at –10 °C. The reaction mixture was quenched with saturated NH$_4$Cl aqueous solution and it was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with Et$_2$O/*i*-hexane = 1/10 to afford the *trans* diastereomer **7-3ja** (171 mg, 73% yield, d.r. = 99:1) as white solid.

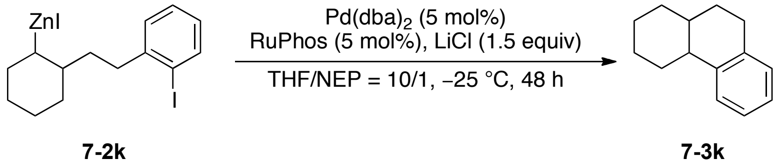
^{1}H-NMR (400 MHz, CDCl$_3$) *δ*: 7.98 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 3.90 (s, 3H), 3.81 (d, *J* = 2.0 Hz, 1H), 3.51 (dd, *J* = 10.9 and 2.6 Hz, 1H), 3.45 (dd, *J* = 10.8 and 2.6 Hz, 1H), 3.14 (d, *J* = 10.8 Hz, 1H), 3.05 (d, *J* = 10.9 Hz, 1H), 2.61 (td, *J* = 11.8 and 3.2 Hz, 1H), 2.13-2.03 (m, 1H), 1.90-1.73 (m, 4H), 1.56-1.27 (m, 4H), 1.11 (s, 3H), 0.59 (s, 3H).

^{13}C-NMR (101 MHz, CDCl$_3$) *δ*: 167.3, 151.4, 129.8, 128.2, 127.8, 101.5, 52.1, 47.3, 45.8, 35.1, 30.3, 26.6, 25.9, 24.4, 22.9, 21.7.

MS (70 eV, EI) *m/z* (%): 331 (5) $[M–H]^{+\bullet}$, 301 (4), 217 (4), 196 (29), 187 (4), 167 (5), 149 (7), 131 (5), 115 (100), 105 (3), 91 (5), 69 (27).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2947 (w), 2925 (w), 2846 (w), 1719 (s), 1609 (w), 1432 (w), 1392 (w), 1286 (w), 1275 (m), 1186 (w), 1155 (m), 1110 (vs), 1098 (s), 1085 (m), 1077 (m), 1029 (w), 1017 (m), 988 (m), 973 (m), 966 (w), 933 (w), 917 (w), 886 (w), 851 (w), 841 (w), 810 (w), 792 (w), 770 (s), 710 (s).

HRMS (ESI) *m/z*: calcd for **$C_{20}H_{27}O_4^{+\bullet}$** $[M–H]^{+\bullet}$: 331.1909, found: 331.1904.



7-3k (CAS: 16306-39-1)

A dry and Ar-flushed 10 mL *Schlenk*-tube was charged with LiCl (25 mg, 0.60 mmol) and dried over 5 min at 400 °C (heat-gun) at high vacuum (1 mbar). After cooling to room temperature, Pd(dba)$_2$ (11.5 mg, 0.02 mmol), RuPhos (9.3 mg, 0.02 mmol) was added under Ar atmosphere and it was evacuated and refilled with Ar three times. After the mixture was cooled to –25 °C, THF (0.35 mL) and *N*-ethylpyrrolidone (0.14 mL, 10 vol%) were added and then **7-2k** (0.95 mL, 0.42 M in THF, 0.95 mmol) was added dropwise for 3 min. The resulting mixture was stirred for 24 h at –25 °C and for another 24 h at 0 °C. The reaction was quenched with saturated NH$_4$Cl aqueous solution and the mixture was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with *i*-hexane to afford **7-3k** and 1-(2-(cyclohex-1-en-1-yl)ethyl)-2-iodobenzene (a β-hydride elimination product). In a dry and Ar-flushed 10 mL *Schlenk*-tube this mixture was treated with BH$_3$·SMe$_2$ in THF (2 mL) at 0 ˚C for 1 h. Then the reaction was quenched with H$_2$O and it was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and the solvents were evaporated. The crude product was purified by chromatography on silica gel with *i*-hexane to afford **7-3k** (34 mg, 46% yield, d.r. = 51:49) as colorless oil. The relative configuration was assigned by the comparison with the reported values.[151]

The peaks of the mixuture of the diastereomers are given.

^{1}H-NMR (300 MHz, CDCl$_3$) δ: 7.37-7.03 (m, 8H), 3.03-1.05 (m, 28H).

^{13}C-NMR (75 MHz, CDCl$_3$) δ: 142.5, 140.8, 137.3, 136.4, 129.2, 129.1, 128.9, 125.7, 125.58, 125.55, 44.0, 40.8, 40.5, 34.6, 34.0, 32.0, 31.6, 31.2, 30.8, 30.1, 29.8, 27.2, 26.5, 26.4, 24.0, 21.7.

MS (70 eV, EI) *m/z* (%): 186 (100) [M]$^+$, 158 (30), 143 (66), 129 (74), 115 (36), 104 (25), 91 (21), 77 (7), 65 (5), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2916 (m), 2849 (w), 1487 (w), 1445 (w), 1433 (w), 763 (w), 757 (m), 732 (vs).

HRMS (EI) *m/z*: calcd for **$C_{14}H_{18}^{+\bullet}$** [M]$^{+\bullet}$: 186.1409, found: 186.1413.

9.7.4 Deuterolysis experiments

[With solvent switch]

A dry and Ar-flushed *Schlenk*-tube was cooled to −100 °C and charged with a solution of ^{t}BuLi (0.18 mL, 2.1 M in *n*-pentane, 0.38 mmol) in mixture of Et$_2$O (1.9 mL). A solution of alkyl iodide *trans*-**7-1l** (40 mg, 0.15 mmol, d.r. = 99:1) in Et$_2$O (0.4 mL) was added dropwise for 1 min. After stirring for 10 sec, an ether solution of ZnI$_2$ (0.38 mL, 1.0 M in Et$_2$O, 0.38 mmol) was added and the reaction mixture was stirred for 20 min at −100 °C. Solvents were evaporated at −50 °C. THF (2.1 mL) and NEP (0.2 mL) were added at −50 °C. After warming up to room temperature, the reaction mixture was stirred at room temperature for indicated time (30 sec or 3.5 h). Then, *d*-TFA (0.12 mL, 1.5 mmol) was added at room temperature and the reaction mixture was stirred for 15 min at room temperature. After quenching the reaction with an aqueous NaHCO$_3$ solution, the reaction mixture was extracted with Et$_2$O three times. The combined organic phase was dried over MgSO$_4$ and solvents were evaporated. The crude product was analyzed with D NMR.

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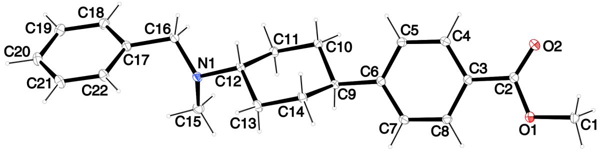
[151] a) K. C. Nicolaou, W. E. Barnette, P. Ma, *J. Org. Chem.* **1980**, *45*, 1463; b) R. C. Bansal, C. E. Browne, E. J. Eisenbraun, C. E. Thomson, *J. Org. Chem.* **1988**, *53*, 452; c) H. Sano, H. Ohtsuka, T. Migita, *J. Am. Chem. Soc.* **1988**, *110*, 2014.

[Without solvent switch]

A dry and Ar-flushed *Schlenk*-tube was cooled to −100 °C and charged with a solution of ^{t}BuLi (0.18 mL, 2.1 M in *n*-pentane, 0.38 mmol) in mixture of Et_2O (1.9 mL). A solution of alkyl iodide *trans*-**7-1l** (40 mg, 0.15 mmol, d.r. = 99:1) in Et_2O (0.4 mL) was added dropwise for 1 min. After stirring for 10 sec, an ether solution of ZnI_2 (0.38 mL, 1.0 M in Et_2O, 0.38 mmol) was added and the reaction mixture was stirred for 20 min at −100 °C. After warming up to room temperature, the reaction mixture was stirred at room temperature for indicated time (30 sec or 3.5 h). Then, *d*-TFA (0.12 mL, 1.5 mmol) was added at room temperature and the reaction mixture was stirred for 15 min at room temperature. After quenching the reaction with an aqueous $NaHCO_3$ solution, the reaction mixture was extracted with Et_2O three times. The combined organic phase was dried over $MgSO_4$ and solvents were evaporated. The crude product was analyzed with D-NMR.

9.7.5 X-ray crystal information



7-3fa (Thermal ellipsoids are drawn at 50% probability level.)

net formula	$C_{22}H_{27}NO_2$
M/g mol^{-1}	337.455
crystal size/mm	0.193 × 0.140 × 0.116
T/K	100(2)
radiation	MoKα
diffractometer	'Bruker D8Venture'
crystal system	monoclinic
space group	*C*2/*c*
a/Å	31.6105(11)
b/Å	6.1248(2)
c/Å	22.3646(8)
α/°	90.00
β/°	124.4190(10)
γ/°	90.00
V/Å^3	3571.9(2)

Z	8
calc. density/g cm^{-3}	1.25505(7)
μ/mm^{-1}	0.079
absorption correction	multi-scan
refls. measured	32178
R_{int}	0.0370
mean σ$(I)/I$	0.0222
θ range	4.12–27.64
observed refls	3670
x,y (weighting scheme)	0.0456, 2.9503
hydrogen refinement	constr
refls in refinement	4087
parameters	228
restraints	0
$R(F_{\text{obs}})$	0.0375
$R_{\text{w}}(F^2)$	0.0985
S	1.048
shift/error$_{\text{max}}$	0.001
max electron density/e Å^{-3}	0.356
min electron density/e Å^{-3}	–0.192