Retro [1,4]-Brook Rearrangements of Nonconjugated Secondary α-Lithio Ethers: Proof of Stereospecificity and of Retention of Configuration at the Carbanion Center

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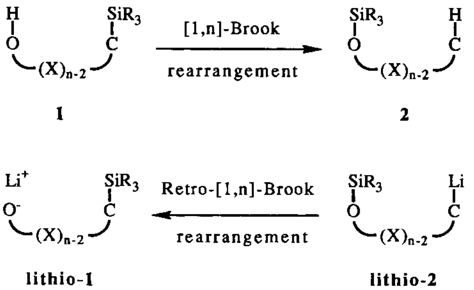
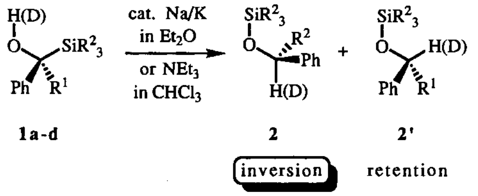
The syntheses of two pairs of diastereomeric γ-(trialkylsilyloxy) α-(tributylstannyl) ethers (*syn*- and *anti*-**6b**, *syn*- and *anti*-**9**) are described. Treatment of each of these compounds with *n*BuLi in THF at −78°C furnished α-lithiated ethers which underwent retro [1,4]-Brook rearrangements at that temperature within 15−30 min. After aqueous workup, the α-silyl ethers *syn*-**14**, *anti*-**14**, *syn*-**11**, and *anti*-**11**, respectively, were isolated isomerically pure in 78−93% yield. Comparison of the stereochemistry of starting materials and products shows that these rearrangements proceed stereospecifically and with retention of configuration at the carbanion center. In a crossover experiment under similar conditions, a 1:1 mixture of the (tributylstannyl) ethers *syn*-**9** and *syn*-**6b** gave, via the intermediacy of a 1:1 mixture of the α-lithiated ethers *syn*-**13** and *syn*-**10**, the α-silyl ethers *syn*-**11** and *syn*-**14** exclusively. They represent the outcome of intramolecular rearrangements rather than intermolecular processes.

In 1958, Brook described [1,2]-silyl C→O migrations: An α-silyl alcohol **1** (n = 2, R = Ph) gave silyl ether **2** (n = 2, R = Ph) either upon reflux in pyridine or, at room temperature, upon exposure to 0.1 M NaOH in EtOH, to Na or Na/K or NaH in Et_2O, or to Ag_2O in benzene[1]. This reaction type − now designated as the [1,2]-Brook rearrangement − tolerates considerable variation of the substituents at the silicon and carbon atom[2]. Analogous [1,*n*]-Brook rearrangements, i.e., [1,*n*]-silyl C→O migrations, are known for $n > 2$, too: β-Silyl alcohols **1** (n = 3) provide silyl ethers **2** (n = 3) by base-catalyzed [1,3]-Brook rearrangements[3]. Similarly, γ-silyl alcohols **1** (n = 4) furnish silyl ethers **2** (n = 4) through base-catalyzed [1,4]-Brook rearrangements[4]. Interestingly, [1,4]-Brook rearrangements were also observed in *alcoholates* provided the "carbanion" which is formed upon cleavage of the C−Si bond bears electron acceptors like $C(=O)NMe_2$[5], C≡N[6], SO_2Ph[4], $Ph_2P(=O)$[7], or $(SiMe_3)_2$[7].



The opposite rearrangement, i.e., O→C silyl migrations of *O*-silyl organolithium compounds **lithio-2** giving lithium alkoxides **lithio-1**, has been coined "retro Brook rearrangement". It was discovered by West et al. first for the [1,3][8] and subsequently for the [1,2] mode[9]. Homologous *overall* retro [1,4]- and [1,5]-Brook rearrangements were found by Simchen and Pfletschinger[10]; mechanistically, however, they represent intermolecular silyl-transfer reactions rather than rearrangements. The latter may have been first encountered by Evans et al.[11].

Scheme 1. Stereochemistry of benzylic [1,2]-Brook rearrangements



	R^1	SiR^2_3	% **2**	ref.
a	H	$SiPh_3$	90±10	12
b[a)]	D	$SiMe_3$	75	13
c	D	SiPhMeNaphth	≈91[b)]	14
c	D		≈61[c)]	14
d	Me		100	15

a) The enantiomer was used.- b) Calculated from the observed ratio **2**:**2'** = 73:27 obtained from the 78:22 mixture of **1b** and its diastereomer (rearranged with Na/K.)- c) Calculated from the observed ratio **2**:**2'** = 54:46 obtained from the 68:32 mixture of **1b** and its diastereomer (rearranged with NEt_3).

The question, whether the C−Si bond of Brook substrates **1** gives the C−H bond of rearrangement product **2** with retention or inversion of configuration, was examined repeatedly. The same is true for the question whether the C−Li bond of retro Brook substrates **lithio-2** is transformed into the C−Si bond of rearrangement product **lithio-1** with retention or inversion of configuration.

In [1,2]-Brook rearrangements, where the SiR_3 group originates from the benzylic carbon atom of α-silyl alcohols **1a−d**, inversion of configuration dominates over retention slightly (ca. 61:39), distinctly, or completely (Scheme 1). Obviously, the steric course de-

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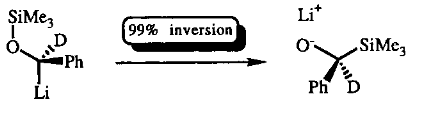
pends markedly both on the substituents and the reaction conditions (compare entry 3 vs. 4).

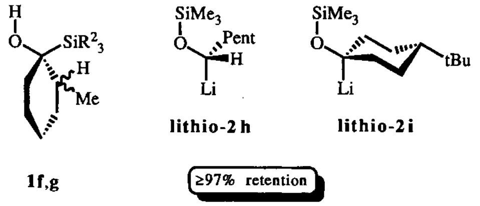
The only stereochemically elucidated retro [1,2]-Brook rearrangement in which an SiR_3 group migrates to a lithiated benzylic carbon atom is **lithio-2e→lithio-1e**. This reaction exhibits complete inversion of configuration[13].



lithio-2e **lithio-1e**

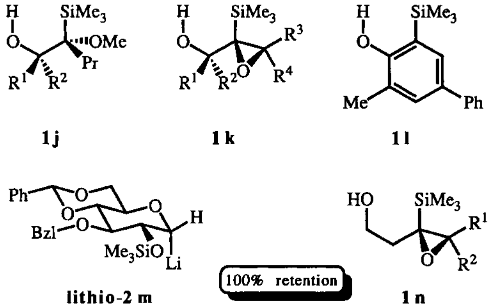
Quite differently, [1,2]-Brook[16] and retro [1,2]-Brook rearrangements[17] occur with more than 97% of retention of configuration when the breaking or forming C–Si bonds involve simple aliphatic instead of benzylic carbon atoms (Scheme 2). An explanation for this difference is missing.

Scheme 2. Stereochemistry of aliphatic [1,2]-Brook and retro [1,2]-Brook rearrangements



The homologs of these rearrangements occur with complete retention of configuration, too (Scheme 3). The cases studied comprise the [1,3]-Brook rearrangements of compounds **1j**[16], **1k**[3a], and **1l**[18], the reto [1,3]-Brook rearrangement of **lithio-2m**[19], and the [1,4]-Brook rearrangement of **1n**[3a].

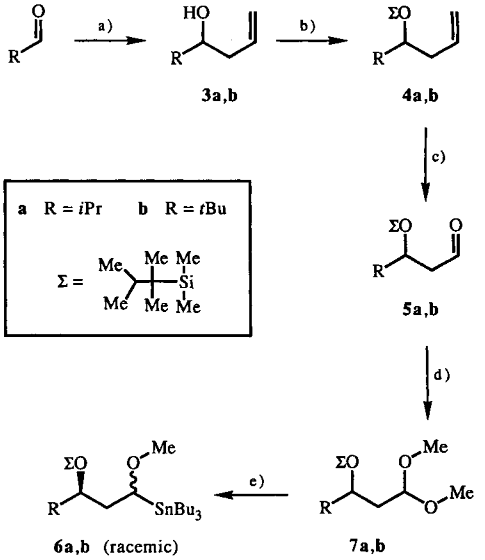
Scheme 3. Stereochemistry of [1,3]-Brook, retro [1,3]-Brook, and [1,4]-Brook rearrangments



The next "unknown" in this series was the stereochemistry of the retro [1,4]-Brook rearrangement[20,33]. Since it aroused our interest also in a different context[21], we studied it and report our results here.

As starting materials for this study we needed the γ-(*tert*-hexyldimethylsilyloxy) α-(tributylstannyl) ethers **6a** and **b**. Their syntheses are outlined in Scheme 4. Adopted is a sequence of steps which furnished related stannylated ethers efficiently in another investigation from this laboratory[22]. The homoallyl alcohols **3a** and **3b** were obtained by addition of allylzinc chloride[23] to isobutyraldehyde and pivalaldehyde, respectively. Protection with chloro-*tert*-hexyldimethylsilane (→ **4a**, **4b**), ozonolysis (→ **5a**, **5b**), acetalization with methanol in the presence of 2,2-dimethoxypropane as a water scavenger (→ **7a**, **7b**), acetal cleavage with acetyl chloride to obtain α-chloro ethers[24] and displacement of chloride by Bu_3Sn^-[24] provided compounds **6a** and **6b** in acceptable overall yields (**a**: 13%; **b**: 19%). Fortunately, the initially isolated diastereomeric mixtures of **6a** and **6b** delivered pure *syn* and *anti* isomers after several passages (**6a**) or one passage (**6b**) through a flash-chromatography column charged with silica gel[25].

Scheme 4

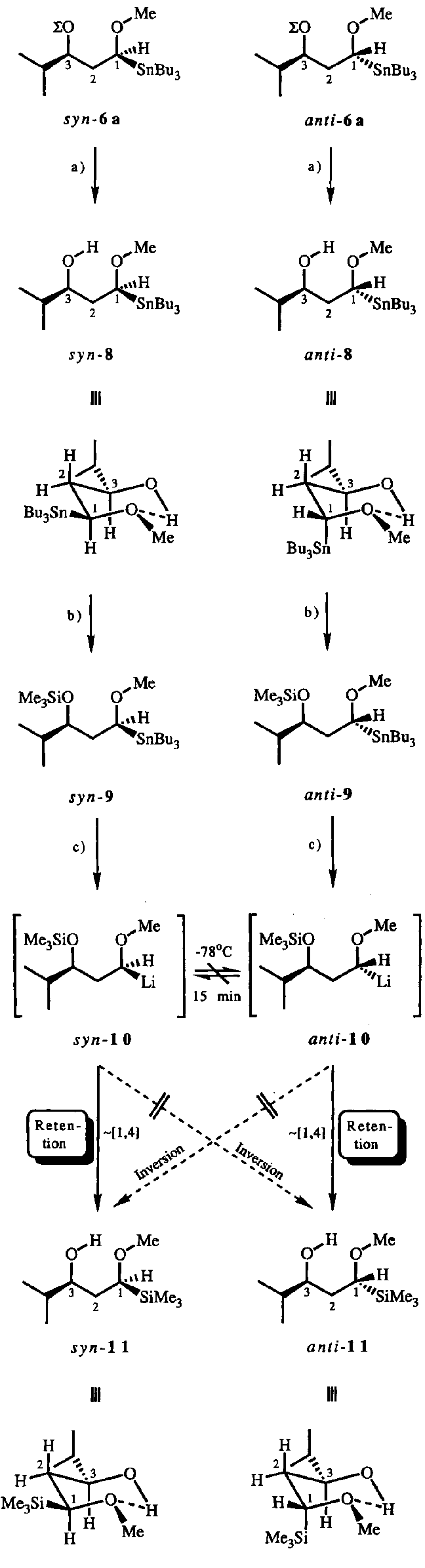


Yield for	3	4	5	6	7
a	74%	77%	60%	60%	65%
b	58%	85%	74%	66%	77%

[a] $CH_2=CHCH_2Br$, Zn, $THF/H_2O/NH_4Cl$. – [b] KH, THF; R_3SiCl, 0°C → room temp. – [c] O_3, CH_2Cl_2, −78°C; Ph_3P, −78°C → room temp. – [d] $(MeO)_2CMe_2$, MeOH, cat. camphersulfonic acid, reflux, 1.5 h. – [e] (1) AcCl, CH_2Cl_2, room temp., 3 h; removal of volatile material under reduced pressure; (2) $LiSnBu_3$, THF, −78°C, 1 h.

In order to unravel the stereochemistry of silyl ethers *syn*- and *anti*-**6** – still unknown at this point – they were separately desilylated with Bu_4NF in refluxing THF. The resulting alcohols *syn*-**8** and *anti*-**8** disclosed their configurations readily: As established for other β-hydroxy ethers[21,22,26] and similarly for β-hydroxy alcohols[27], they should form hydrogen bonds in chair-like six-membered rings (cf. Scheme 5). This premise makes the coupling pattern of the 2-H_2 resonance in the ^{1}H-NMR spectra a straightforward criterion for the differentiation of *syn*- vs. *anti*-**8**: Compound *syn*-**8** should exist as *one* conformer (formula in Scheme 5) with one axial 2-H and one equatorial 2-H. The former exhibits two large $J_{ax,ax}$ and the latter two small $J_{eq,ax}$ couplings (2-H_{ax}: 11.9, 9.7 Hz; 2-H_{eq}: 2.6, 2.4 Hz). *anti*-**8** may

Scheme 5

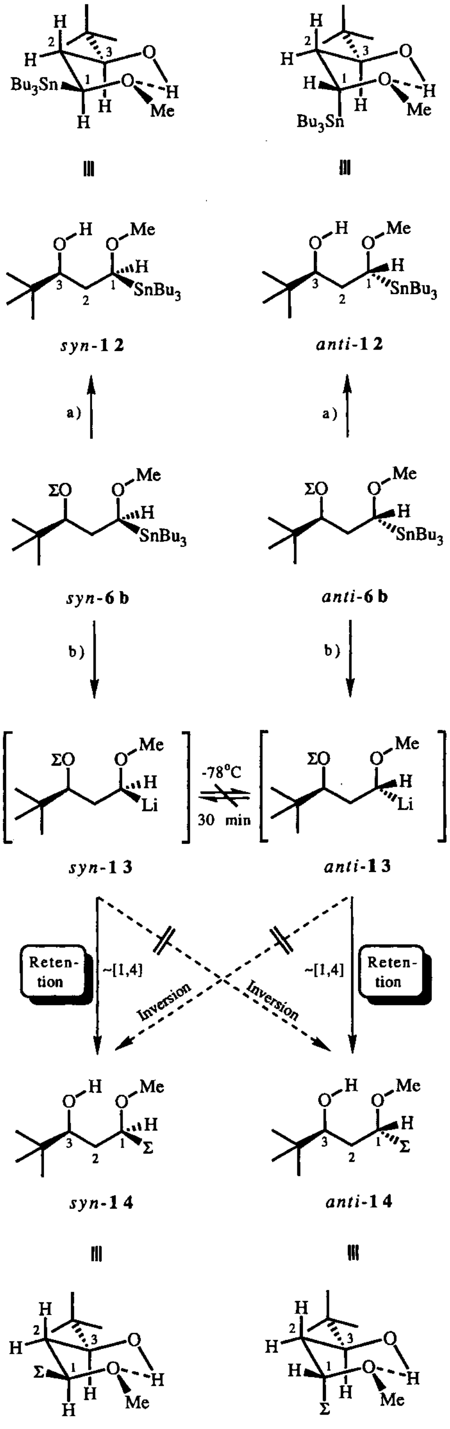


[a] 1 M Bu_4NF in THF, 60°C, 6 h; 85% *syn*-**8**, 81% *anti*-**8**. — [b] $Me_3SiOSO_2CF_3$, 2,6-lutidine, CH_2Cl_2, 0°C, 80 min; 90% *syn*-**9**, 95% *anti*-**9**. — [c] *n*BuLi, THF, −78°C, 15 min; H_2O/NH_4Cl; 82% *syn*-**11**, 78% *anti*-**11**.

consist of *two* equilibrating chair conformers (only one formula shown in Scheme 5 for clarity). The distinction between axial 2-H and equatorial 2-H is less pronounced; in essence, each 2-H signal is associated with one large and one small J_{vic} value (2-H¹: 6.6, 2.0 Hz; 2-H²: 9.5, 3.7 Hz).

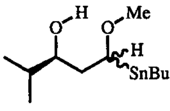
This assignment is underscored by the ^{13}C-NMR argument of Hoffmann and Weidmann[26a]: According to them,

Scheme 6



[a] 1 M Bu_4NF in THF, 60°C, 4.5 h; 61% *syn*-**12**, 86% *anti*-**12**. — [b] *n*BuLi, THF, −78°C, 30 min; H_2O/NH_4Cl; 93% *syn*-**13**, 86% *anti*-**13**.

Table 1. Selected ^{1}H- (400 MHz) and ^{13}C-NMR data (50 MHz) in CDCl$_3$ of the newly prepared γ-alkoxy alcohols; *J* values in Hz



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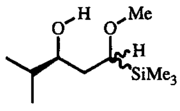

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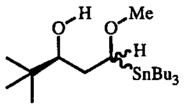

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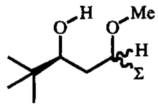

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	δ(C-1)	δ(C-3)	δ(C-1) +δ(C-3)	δ(1-H)	δ(2-H^{ax})	δ(2-H^{eq})	δ(3-H)	$J_{2\text{-H}^{ax},1}$	$J_{2\text{-H}^{ax},3}$	$J_{2\text{-H}^{eq},1}$	$J_{2\text{-H}^{eq},3}$
syn-**8**			161.32	3.97	1.94	1.71	3.53	11.9	9.7	2.6	2.4
-**11**			157.73	3.18	1.62	1.54	3.58	11.2	9.2	3.5	2.4
-**12**	83.62	81.40	165.02	3.95	1.88	1.77	3.40	11.5	9.9	2.8	1.8
-**14**			160.91	3.27	1.59	1.70	3.41	10.9	10.0	3.3	1.5

	δ(C-1)	δ(C-3)	δ(C-1) +δ(C-3)	δ(1-H)	δ(2-H^1)	δ(2-H^2)	δ(3-H)	$J_{2\text{-H}^1,1}$	$J_{2\text{-H}^1,3}$	$J_{2\text{-H}^2,1}$	$J_{2\text{-H}^2,3}$
anti-**8**			156.60	4.05	1.80	2.02	3.48	6.6	2.0	3.7	9.5
-**11**			150.60	3.22	1.63	1.75	3.59	7.4	2.2	3.7	10.0
-**12**	80.37	79.34	159.71	4.04	1.75	2.01	3.40	5.9	1.8	3.8	10.5
-**14**			152.10	3.41	1.58	1.85	3.56	6.1	1.8	4.0	11.0

in β-hydroxy ethers, the sum of the ^{13}C-NMR shifts of the two main-chain carbon nuclei bearing the oxygen atoms is greater in *syn* than in *anti* diastereomers. In fact, δ(^{13}C-1) + δ(^{13}C-3) = 161.32 is greater in the compound already designated *syn*-**8** than in *anti*-**8** [δ(^{13}C-1) + δ(^{13}C-3) = 156.60].

Now that their stereochemistry was established *syn*- and *anti*-**8** were silylated[28] giving the α-(tributylstannyl) γ-(trimethylsilyloxy) ethers *syn*- and *anti*-**9**, respectively (Scheme 5). Each of these compounds was exposed at −78 °C in THF to a small excess of *n*BuLi (1.1 equiv.). Presumably, each is converted by tin/lithium exchange into the corresponding lithio ether *syn*- and *anti*-**10**, respectively, with retention of configuration[29]. The lithium-bearing carbon atom of these intermediates should be pyramidal[30] and configuratively stable during the 15 min[31] which the ensueing rearrangement required for going to completion. After aqueous workup, the α-silyl ether *syn*-**11** was isolated *isomerically pure* (82% yield) starting from *syn*-**9**, as was *anti*-**11** (78% yield) starting from *anti*-**9**. *Thus, both retro [1,4]-Brook rearrangements occurred stereoselectively and with retention of configuration at the carbanion center.*

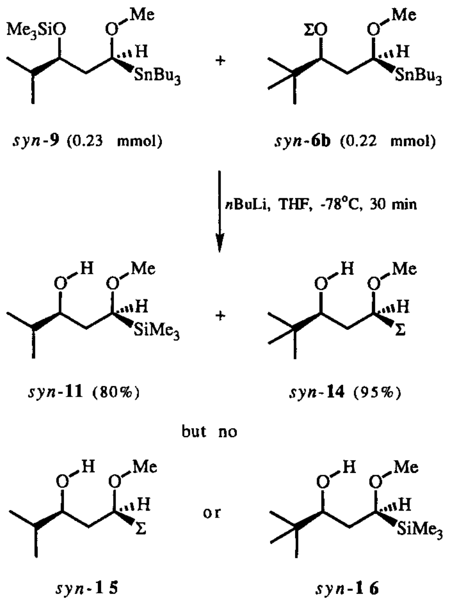
The configurational assignment of *syn*- vs. *anti*-**11** relied on the assumption that these β-hydroxy ethers form hydrogen-bonded six-membered chair-like rings, too (cf. Scheme 5). Accordingly, the ^{1}H- and ^{13}C-NMR data listed in Table 1 allow to unambiguously distinguish *syn*- from *anti*-**11** by applying the same arguments forwarded for the differentiation of *syn*- vs. *anti*-**8**.

We had still to establish that the α-silyl ethers *syn*- and *anti*-**11** result from an intramolecular process, i.e., a genuine rearrangement of the lithio ether intermediates **10**, and not from an intermolecular silyl transfer upon **10**. There was at least one precedent each for γ-lithiated silyl ethers (compare **10**) which give γ-silyl alcohols (compare **11**) through an intramolecular[32] and an intermolecular process[10], respectively. *We* distinguished these possibilities by a cross-over experiment. In order to perform this, it was necessary to first find a second *and sufficiently similar* system which underwent *equally* a (maybe only formal) retro [1,4]-Brook rearrangement. Suitable substrates turned out to be the diastereomeric α-(tributylstannyl) γ-(*tert*-hexyldimethylsilyl) ethers *syn*- and *anti*-**6b** (Scheme 6).

First, their relative configurations were determined after desilylation to the β-alkoxy alcohols *syn*- and *anti*-**12**, respectively. As laid out in detail for the corresponding *normethyl* β-alkoxy alcohols *syn*- and *anti*-**8** we (a) assumed the prevalence of hydrogen-bonded chair-like structures; (b) we deduced the *syn*/*anti* assignment from the J_{vic} values of the protons at C-2 and from the magnitude of the sums δ(^{13}C-1) + δ(^{13}C-3) (cf. Table 1 for relevant data).

Subsequently, *syn*- and *anti*-**6b** were treated in separate experiments at −78 °C with *n*BuLi in THF (Scheme 6). 30 min of reaction time were deemed necessary to allow complete conversion of starting materials and considered short enough to guarantee the configurational stability[31] of the resulting lithio ether intermediates *syn*- and *anti*-**13**, respectively. Each substrate underwent a stereoselective retro [1,4]-Brook rearrangement. *syn*-**6b** led exclusively to compound *syn*-**14** according to the NMR spectra (Table 1; cf. the analogous stereochemical assignment of rearrangement product **11**), since, for example, one of its 2-H signals exhibits two large vicinal coupling constants (10.9, 10.0 Hz) while the other shows two considerably smaller ones (3.3, 1.5 Hz). Similarly, *anti*-**6b** rearranged cleanly to compound *anti*-**14** where both 2-H signals display one large and one small J_{vic} value (2-H^1: 6.1, 1.8 Hz; 2-H^2: 11.0, 4.0 Hz). This means that this new set of retro [1,4]-Brook rearrangements is stereospecific and occurs with retention of configuration at the carbanion center *as did the previous set from Scheme 5.*

The stage was now set for the intended cross-over experiment: The α-stannylated ethers *syn*-**9** and *syn*-**6b** were treated as a 1:1 mixture with *n*BuLi under the previous conditions (THF, −78 °C, 30 min). Thereupon, we isolated *only* compounds *syn*-**11** (80%) and *syn*-**14** (95%). Both result from intramolecular reactions. Careful analysis of the crude reaction mixture by GLC revealed no peak between *syn*-**11** (retention time 13.1 min) and *syn*-**14** (retention time 20.4 min) except one for Bu_4Sn (19.7 min). *There* one would have expected additional peaks if an intermolecular silyl transfer had occurred and necessarily led to the cross-over products *syn*-**15** and *syn*-**16**. *Accordingly, the silyl [1,4] O→C migrations described above result from genuine (= intramolecular) rearrangements.*



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Experimental

All reactions were performed in oven-dried (100 °C) glassware under dry nitrogen. THF was freshly distilled from K/Na and CH_2Cl_2 from CaH_2. Products were purified by flash chromatography[25] on Merck silica gel 60 (particle size 0.040−0.063 mm, 230−240 mesh ASTM; eluents given in brackets). Yields refer to analytically pure samples. Isomer ratios of diastereomeric mixtures were derived from suitable ^{1}H-NMR integrals. − ^{1}H- and {^{1}H}-decoupled ^{13}C NMR (tetramethylsilane or $CHCl_3$ as internal standard in $CDCl_3$): Bruker AC 200, AC 250, WH 400; integrals (^{1}H NMR) and DEPT spectra (^{13}C NMR) in accord with assignments; coupling constants in Hz; AB spectra: H_B refers to low- and H_A to high-field resonance. − IR (film): Perkin-Elmer 1600. − MTB: *tert*-Butyl methyl ether.

2-Methyl-5-hexen-3-ol (**3a**)[34]: To a stirred solution of isobutyraldehyde (8.35 g, 0.12 mol), allyl bromide (14.7 ml, 21.0 g, 0.17 mol, 1.50 equiv.) in THF (150 ml), and satd. aqueous NH_4Cl solution zinc dust (15.1 g, 0.23 mmol, 2.00 equiv.) was added within 45 min. After 1 h of stirring at room temp., the reaction mixture was diluted with MTB (300 ml) and the aqueous layer extracted with MTB (2 × 200 ml). Distillation of the residue obtained by evaporation of the solvents from the combined extracts furnished **3a** (9.78 g, 74%, b.p. 130−133 °C).

2,2-Dimethyl-5-hexen-1-ol (**3b**)[35]: Prepared as described for **3a** from pivalaldehyde (6.30 ml, 5.00 g, 58.0 mmol), allyl bromide (6.40 ml, 9.13 g, 75.5 mmol, 1.30 equiv.), and zinc dust (5.31 g, 81.3 mmol, 1.40 equiv.); distillation yielded **3b** (4.32 g, 58%, b.p. 143−145 °C).

4-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]-5-methyl-1-hexene (**4a**): At 0 °C **3a** (1.06 g, 9.28 mmol) in THF (5 ml) was added dropwise to a suspension of KH (0.67 g, 16.7 mmol, 1.80 equiv.) in THF (10 ml). After 30 min, chlorodimethyl(1,1,2-trimethylpropyl)silane (1.92 ml, 9.77 mmol, 1.05 equiv.) was added, and the solution was stirred for 12 h at room temp. The reaction was quenched with satd. aqueous NH_4Cl solution (5 ml)/H_2O (10 ml) and the resulting mixture extracted with MTB (3 × 100 ml). Kugelrohr distillation (180 °C/1−2 Torr) of the residue obtained by evaporation of the solvent from the combined extracts furnished **4a** (1.90 g, 77%). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.06 and 0.08 [2 s, $Si(CH_3)_2$], 0.80−0.93 (m, 5-CH_3, 6-H_3, 2 × 1′-CH_3, 2′-CH_3, 3′-H_3), 1.51−1.80 (m, 5-H, 2′-H), 2.19 (ddm$_c$, $J_{3,2}$ = 7.1, $J_{3,4}$ = 5.9, 3-H_2), 3.48 (td, $J_{4,3}$ = 6.0, $J_{4,5}$ = 4.3, 4-H), 5.00 (dm$_c$, $J_{1\text{-}H(cis),2} \approx 9-10$, 1-$H_{cis}$), 5.02 (dm$_c$, $J_{1\text{-}H(trans),2} \approx 17-18$, 1-$H_{trans}$), 5.81 (ddt, $J_{2,1\text{-}H(trans)}$ = 17.2, $J_{2,1\text{-}H(cis)}$ = 10.1, $J_{2,3}$ = 7.2, 2-H). − IR: $\tilde{\nu}$ = 3080 cm^{-1}, 2960, 2870, 1640, 1460, 1485, 1365, 1250, 1055, 995, 910, 830, 775, 665.

$C_{15}H_{32}OSi$ (256.5) Calcd. C 70.24 H 12.57
Found C 70.25 H 12.86

4-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]-5,5-dimethyl-1-hexene (**4b**): Prepared as described for **4a** from **3b** (1.24 g, 9.67 mmol), KH (0.97 g, 24.1 mmol, 2.70 equiv.) and chlorodimethyl(1,1,2-trimethylpropyl)silane (1.90 ml, 1.73 g, 9.67 mmol, 1.00 equiv.); yield 2.22 g (85%). − ^{1}H NMR (250 MHz): δ = 0.06 and 0.08 [2 s, $Si(CH_3)_2$], 0.80−0.94 (m, 2 × 1′-CH_3, 2′-CH_3, 3′-H_3), superimposes 0.87 (s, 2 × 5-CH_3, 6-H_3), 1.66 (qq, $J_{2',2'\text{-}Me} = J_{2',3'}$ = 6.9, 2′-H), 2.09−2.24 (m, 3-H^1), 2.30−2.44 (m, 3-H^2), 3.33 (dd, J = 5.8, J' = 4.6, 4-H), 4.97 (dm$_c$, $J_{1\text{-}H(cis),2} \approx 10$, 1-$H_{cis}$), 5.00 ($J_{1\text{-}H(trans),2} \approx 17$, 1-$H_{trans}$), 5.80−5.97 (m, 2-H). − IR: $\tilde{\nu}$ = 3075 cm^{-1}, 2955, 2865, 1640, 1465, 1395, 1380, 1365, 1250, 1085, 1030, 995, 910, 830, 775, 660. − No correct combustion analysis could be obtained.

3-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]-4-methylpentanal (**5a**): Compound **4a** (7.76 g, 30.3 mmol) in CH_2Cl_2 (60 ml) was ozonolyzed at −78 °C until the solution turned blue (60 min). Triphenylphosphane (7.94 g, 30.3 mmol, 1.00 equiv.) was added and the solution stirred for 1 h at room temp. Ph_3PO was removed by diluting the crude product with petroleum ether/ether (100:1, 200 ml). Flash chromatography [petroleum ether/ether (100:1)] of the residue obtained by evaporation of the solvents yielded **5a** (4.64 g, 60%). − ^{1}H NMR (250 MHz): δ = 0.08 and 0.10 [2 s, $Si(CH_3)_2$], 0.79−0.93 (m, 4-CH_3, 5-H_3, 2 × 1′-CH_3, 2′-CH_3, 3′-H_3), 1.62 (qq, $J_{2',2'\text{-}Me} = J_{2',3'}$ = 6.9, 2′-H), 1.80 (qqd, $J_{4,4\text{-}Me} = J_{4,5}$ = 6.8, $J_{4,3}$ = 4.5, 4-H), AB signal (δ_A = 2.43, δ_B = 2.51, $J_{A,B}$ = 15.6, in addition split by $J_{A,3}$ = 4.8, $J_{A,1}$ = 2.1, $J_{B,3}$ = 6.8, $J_{B,1}$ = 3.0, 2-H_2), 4.03 (ddd, $J_{3,2\text{-}H(B)}$ = 6.8, $J_{3,2\text{-}H(A)} = J_{3,4}$ = 4.6, 3-H), 9.82 (dd, $J_{1,2\text{-}H(B)}$ = 3.0, $J_{1,2\text{-}H(A)}$ = 2.1, 1-H). − IR: $\tilde{\nu}$ = 2960 cm^{-1}, 2870, 2720, 1730, 1465, 1390, 1250, 1090, 1050, 830, 775.

$C_{14}H_{30}O_2Si$ (258.5) Calcd. C 65.06 H 11.70
Found C 65.23 H 11.82

3-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]-4,4-dimethylpentanal (**5b**): Prepared as described for **5a**. **4b** (2.53 g, 9.35 mmol) in CH_2Cl_2 (60 ml), −78 °C, 50 min; Ph_3P (2.73 g, 9.34 mmol, 1.00 equiv.) yielded a slightly contaminated sample of **5b** (1.89 g, 74%) by Kugelrohr distillation (70 °C/0.2−0.4 Torr). − ^{1}H NMR (250

MHz): δ = 0.07 and 0.11 [2 s, Si(CH$_3$)$_2$], 0.88 (s, 2 × 4-CH$_3$, 5-H$_3$), superimposed by 0.80−0.95 (m, 2 × 1′-CH$_3$, 2′-CH$_3$, 3′-H$_3$), 1.64 (qq, $J_{2',2'\text{-Me}} = J_{2',3'} = 6.9$, 2′-H), AB signal ($\delta_A = 2.51$, $\delta_B = 2.62$, $J_{A,B} = 16.7$, in addition split by $J_{A,3} = 5.1$, $J_{A,1} = 2.9$, $J_{B,3} = 5.1$, $J_{B,1} = 1.7$, 2-H$_2$), 3.89 (dd, $J_{3,2\text{-H(B)}} = J_{3,2\text{-H(A)}} = 5.1$, 3-H), 9.85 (dd, $J_{1,2\text{-H(A)}} = 2.8$, $J_{1,2\text{-H(B)}} = 1.8$, 1-H). − IR: $\tilde{\nu}$ = 2960 cm^{-1}, 2870, 2725, 1725, 1470, 1395, 1380, 1365, 1255, 1095, 1025.

$C_{15}H_{32}O_2Si$ (272.5) Calcd. C 66.11 H 11.84
Found C 66.70 H 12.23

(1S,3S*)- and (1R*,3S*)-3-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]-1-methoxy-4-methyl-1-(tributylstannyl)pentane* (*syn-* and *anti-***6a**): A solution of **7a** (0.80 g, 2.63 mmol) in CH$_2$Cl$_2$ (1.5 ml)/AcCl (1.5 ml) was stirred at room temp. for 3 h. Evaporation of the solvents yielded a pale yellow oil which was dissolved in THF (2.0 ml). At −78 °C this solution was added to a freshly prepared (Bu$_6$Sn$_2$ in THF, *n*BuLi, 0 °C, 30 min in THF) solution of Bu$_3$SnLi (1.30 equiv.) in THF (1 ml). The mixture was stirred at −78 °C for 1 h, quenched with satd. aqueous NaHCO$_3$ solution (2 ml)/H$_2$O (10 ml), and extracted with MTB (3 × 30 ml). Flash chromatography [petroleum ether → petroleum ether/ether (100:1)] of the residue obtained by evaporation of the solvents gave **6a** (0.89 g, 60%) as a 1:1 mixture of diastereomers. Pure samples of *syn-* and *anti-***6a** were obtained subsequently by repeated chromatographies of the early and late fractions, respectively. − IR: $\tilde{\nu}$ = 2955 cm^{-1}, 2925, 2870, 2810, 1465, 1375, 1250, 1110, 1045, 860, 830, 775, 660.

$C_{27}H_{60}O_2SiSn$ (563.5) Calcd. C 57.55 H 10.73
Found C 57.82 H 11.01

*syn-***6a**: ^{1}H NMR (400 MHz): δ = 0.06 and 0.09 [2 s, Si(CH$_3$)$_2$], 0.77−0.98 (m, 4-CH$_3$, 5-H$_3$, 2 × 1′-CH$_3$, 2′-CH$_3$, 3′-H$_3$, 3 × 1″-H$_2$, 3 × 4″-H$_3$), 1.32 (tq, $J_{3'',2''} = J_{3'',4''} = 7.2$, 3 × 3″-H$_2$), 1.41−1.59 (m, 3 × 2″-H$_2$), 1.64 (qq, $J_{2',2'\text{-Me}} = J_{2',3'} = 6.9$, 2′-H), AB signal ($\delta_A = 1.70$, $\delta_B = 2.07$, $J_{A,B} = 14.4$, in addition split by $J_{A,3} = 8.4$, $J_{A,1} = 4.0$, $J_{B,1} = 11.3$, $J_{B,3} = 4.8$, 2-H$_2$), 1.80 (qqd, $J_{4,4\text{-Me}} = J_{4,5} = 6.8$, $J_{4,3} = 2.6$, 4-H), 3.24 (s, OMe), 3.69 (ddd, $J_{3,2\text{-H(A)}} = 8.3$, $J_{3,2\text{-H(B)}} = 4.8$, $J_{3,4} = 2.6$, 3-H), 3.77 (dd, $J_{1,2\text{-H(B)}} = 11.3$, $J_{1,2\text{-H(A)}} = 4.0$, 1-H). − ^{13}C NMR: δ = −2.56 and −2.11 [Si(CH$_3$)$_2$], 9.31 (including 2 d due to $^1J_{1'',Sn} = 294$, $^1J'_{1'',Sn} = 281$, 3 × C-1″), 13.66 (3 × C-4″), 15.41, 18.68, 19.93, 20.42, 20.53, 27.00 and 30.63 (4-CH$_3$, C-5, 2 × 1′-CH$_3$, 2′-CH$_3$, C-2′, C-3′), 25.02 (C-1′), 27.54 (including d due to $^2J_{2'',Sn} = 52$, 3 × C-2″), 29.30 (including d due to $^3J_{3'',Sn} = 20$, 3 × C-3″), 34.30 (C-4), 39.79 (C-2), 58.80 (OMe), 74.11 and 76.07 (C-1, C-3).

*anti-***6a**: ^{1}H NMR (400 MHz): δ = 0.08 and 0.10 [2 s, Si(CH$_3$)$_2$], 0.82−0.93 (m, 4-CH$_3$, 5-H$_3$, 2 × 1′-CH$_3$, 2′-CH$_3$, 3′-H$_3$, 3 × 1″-H$_2$, 3 × 4″-H$_3$), 1.31 (tq, $J_{3'',2''} = J_{3'',4''} = 7.3$, 3 × 3″-H$_2$), 1.45−1.55 [m, 2-H(1), 3 × 2″-H$_2$], 1.64 (qq, $J_{2'\text{-H},2'\text{-Me}} = J_{2',3'} = 6.9$, 2′-H), 1.74 (qqd, $J_{4,4\text{-Me}} = J_{4,5} = 6.9$, $J_{4,3} = 3.3$, 4-H), 1.92 [ddd, $J_{gem} = 14.4$, $J_{2\text{-H(2)},1} = 12.2$, $J_{2\text{-H(2)},3} = 2.5$, 2-H(2)], 3.27 (s, OMe), 3.74 (ddd, $J_{3,2\text{-H(1)}} = 9.4$, $J_{3,2\text{-H(2)}} = J_{3,4} = 2.9$, 3-H), 3.98 (dd, including $^{117/119}$Sn isotope satellite as d with $^2J_{H,Sn} = 11.9$, $J_{1,2\text{-H(2)}} = 12.2$, $J_{1,2\text{-H(1)}} = 2.3$, 1-H). − ^{13}C NMR: δ = −2.65 and −2.02 [Si(CH$_3$)$_2$], 9.31 (including 2 d due to $^1J_{1'',Sn} = 292$, $^1J'_{1'',Sn} = 278$, 3 × C-1″), 13.65 (3 × C-4″), 16.83, 17.71, 18.65, 20.50, 20.58, 33.81 and 34.29 (4-CH$_3$, C-5, 2 × 1′-CH$_3$, C-3′, 2′-CH$_3$, C-4), 25.04 (C-1′), 27.50 (including d due to $^2J_{2'',Sn} = 53$, 3 × C-2″), 29.26 (including d due to $^3J_{3'',Sn} = 20$, 3 × C-3″), 37.62 (C-2), 58.58 (OMe), 73.26 and 74.87 (C-1, C-3); the signal of C-2′ could not be identified.

(1S,3S*)- and (1R*,3S*)-3-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]-1-methoxy-4,4-dimethyl-1-(tributylstannyl)pentane* (*syn-* and *anti-***6b**): Prepared as described for **6a**. **7b** (0.61 g, 1.93 mmol) in CH$_2$Cl$_2$ (0.8 ml) with AcCl (0.8 ml), 2 h at room temp.; Bu$_3$SnLi (1.30 equiv.) in THF (3.5 ml), −78 °C, 30 min; one flash chromatography [petroleum ether/ether (250:1 → 100:1)] provided *syn-***6b** (0.36 g, 32%) in the early fractions, *syn-***6b**/*anti-***6b** (0.023 g, 2%), and *anti-***6b** (0.36 g, 32%) in the late fractions, together 0.74 g (66%).

$C_{28}H_{62}O_2SiSn$ (577.6) Calcd. C 58.23 H 10.82
Found C 58.18 H 11.01

*syn-***6b**: ^{1}H NMR (400 MHz): δ = 0.07 and 0.14 [2 s, Si(CH$_3$)$_2$], 0.86 (s, 2 × 4-CH$_3$, 5-H$_3$), superimposes 0.81−0.93 (m, 2 × 1′-CH$_3$, 2′-CH$_3$, 3′-H$_3$, 3 × 1″-H$_2$, 3 × 4″-H$_3$), 1.32 (tq, $J_{3'',2''} = J_{3'',4''} = 7.3$, 3 × 3″-H$_2$), 1.47−1.57 (m, 3 × 2″-H$_2$), 1.66 (qq, $J_{2',2'\text{-Me}} = J_{2',3'} = 6.9$, 2′-H), 1.86−2.02 (m, 2-H$_2$), 3.28 (s, OMe), 3.40 (dd, $J_{3,2\text{-H(1)}} = 5.8$, $J_{3,2\text{-H(2)}} = 3.6$, 3-H), 3.62 (dd including $^{117/119}$Sn isotope satellite as d with $^2J_{H,Sn} = 12.4$, $J = 10.6$, $J' = 5.4$, 1-H). − ^{13}C NMR: δ = −1.80 and −1.44 [Si(CH$_3$)$_2$], 9.36 (including 2 d due to $^1J_{1'',Sn} = 291$, $^1J'_{1'',Sn} = 278$, 3 × C-1″), 13.68 (3 × C-4″), 18.62, 20.83 and 20.73 (2 × 1′-CH$_3$, 2′-CH$_3$, C-3′), 25.40 (C-1′), 26.54 (2 × 4-CH$_3$, C-5), 27.54 (including d due to $^2J_{2'',Sn} = 53$, 3 × C-2″), 29.28 (including d due to $^3J_{3'',Sn} = 20$, 3 × C-3″), 34.18 (C-2′), 35.42 (C-4), 38.71 (C-2), 58.35 (OMe), 74.95 and 77.36 (C-1, C-3).

*anti-***6b**: ^{1}H NMR (400 MHz): δ = 0.09 and 0.13 [2 s, Si(CH$_3$)$_2$], 0.83 (s, 2 × 4-CH$_3$, 5-H$_3$), superimposes 0.82−0.93 (m, 2 × 1′-CH$_3$, 2′-CH$_3$, 3′-H$_3$, 3 × 1″-H$_2$, 3 × 4″-H$_3$), 1.32 (tq, $J_{3'',2''} = J_{3'',4''} = 7.2$, 3 × 3″-H$_2$), 1.44 [ddd, $J_{gem} = 14.8$, $J_{2\text{-H(1)},3} = 8.7$, $J_{2\text{-H(1)},1} = 1.6$, 2-H(1)], 1.45−1.55 (m, 3 × 2″-H$_2$), 1.66 (qq, $J_{2',2'\text{-Me}} = J_{2',3'} = 6.9$, 2′-H), 2.14 [ddd including $^{117/119}$Sn isotope satellite as d with $^2J_{H,Sn} \approx 17$, $J_{gem} \approx J_{2\text{-H(2)},1} \approx 14$, $J_{2\text{-H(2)},3} \approx 1$, 2-H(2)], 3.27 (s, OMe), 3.52 (dd, $J_{3,2\text{-H(1)}} = 8.7$, $J_{3,2\text{-H(2)}} = 0.9$, 3-H), 4.07 (dd including $^{117/119}$Sn isotope satellite as d with $^2J_{H,Sn} = 12.2$, $J_{1,2\text{-H(2)}} = 13.2$, $J_{1,2\text{-H(1)}} = 1.6$, 1-H). − ^{13}C NMR: δ = −2.68 and −1.72 [Si(CH$_3$)$_2$], 9.27 (including 2 d due to $^1J_{1'',Sn} = 292$, $^1J'_{1'',Sn} = 279$, 3 × C-1″), 13.68 (3 × C-4″), 18.50, 18.74, 20.35, 20.75 (2 × 1′-CH$_3$, 2′-CH$_3$, C-3′), 25.11 (C-1′), 26.31 (2 × 4-CH$_3$, C-5), 27.55 (including d due to $^2J_{2'',Sn} = 53$, 3 × C-2″), 29.33 (including d due to $^3J_{3'',Sn} = 19$, 3 × C-3″), 34.17 (C-2′), 36.21 (C-4), 40.53 (C-2), 59.06 (OMe), 77.67 and 78.36 (C-1, C-3).

3-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]-1,1-dimethoxy-4-methylpentan (**7a**): A solution of **5a** (2.89 g, 11.2 mmol), 2,2-dimethoxypropane (2.70 ml, 22.4 mmol, 2.00 equiv.), and camphersulfonic acid (ca. 30 mg) in MeOH (50 ml) was heated under reflux for 1.5 h. After cooling to room temp., satd. aqueous NaHCO$_3$ solution (100 ml) was added. The mixture was extracted with MTB (2 × 200 ml) and dried with MgSO$_4$. Flash chromatography [petroleum ether/ether (40:1)] of the residue obtained by evaporation of the combined extracts yielded **7a** (2.22 g, 65%). − ^{1}H NMR (250 MHz): δ = 0.08 and 0.09 [2 s, Si(CH$_3$)$_2$], 0.81−0.92 (m, 4-CH$_3$, 5-H$_3$, 2 × 1′-CH$_3$, 2′-CH$_3$, 3′-H$_3$), 1.52−1.82 (m, 2-H$_2$, 4-H, 2′-H), 3.31 (s, 2 × OMe), 3.64 (dt, $J = 8.3$, $J' = 3.9$, 3-H), 4.50 (dd, $J_{1,2\text{-H(1)}} = 7.4$, $J_{1,2\text{-H(2)}} = 4.2$, 1-H). − IR: $\tilde{\nu}$ = 2960 cm^{-1}, 2875, 2830, 1465, 1385, 1250, 1190, 1125, 1095, 1055, 965, 930, 830, 775, 665.

$C_{16}H_{36}O_3Si$ (304.5) Calcd. C 63.10 H 11.91
Found C 63.07 H 12.30

3-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]-1,1-dimethoxy-4,4-dimethylpentan (**7b**): **5b** (1.23 g, 4.53 mmol) was dissolved in 2,2-dimethoxypropane (15 ml)/MeOH (0.5 ml). Camphersulfonic acid (ca. 30 mg) was added and the mixture heated under reflux for 80 min. Addition of satd. aqueous NaHCO$_3$ solution (30 ml), extraction of the aqueous layer with MTB (3 × 30 ml), and flash chromatography [petroleum ether/ether (120:1 → 50:1)] furnished **7b** (1.11 g, 77%). − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.09 and 0.12 [2 s, Si(CH$_3$)$_2$], 0.87 (s, 2 × 4-CH$_3$, 5-H$_3$), superimposed by 0.82−0.93 (m, 2 × 1′-CH$_3$, 2′-CH$_3$, 3′-H$_3$), AB signal ($\delta_A = 1.55$, $\delta_B = 1.89$, $J_{A,B} = 14.3$, in addition split by $J_{A,3} = 8.2$, $J_{A,1} = 3.4$, $J_{B,1} = 8.5$, $J_{B,3} = 2.3$, 2-H$_2$), 1.66 (qq, $J_{2',2'\text{-Me}} = J_{2',3'} = 6.9$, 2′-H), 3.29 and 3.33 (2 s, 2 × OMe), 3.39 (dd, $J_{3,2\text{-H(A)}} = 8.2$, $J_{3,2\text{-H(B)}} = 2.3$, 3-H), 4.55 (dd, $J_{1,2\text{-H(B)}} = 8.5$, $J_{1,2\text{-H(A)}} = 3.4$, 1-H). – IR: $\tilde{\nu} = 2960$ cm^{-1}, 2875, 2830, 1465, 1380, 1250, 1190, 1125, 1095, 1055, 965, 930, 830, 775, 665.

$C_{17}H_{38}O_3Si$ (318.6) Calcd. C 64.09 H 12.02
Found C 63.83 H 11.78

1-Methoxy-4-methyl-1-(tributylstannyl)-3-pentanol (**8**, *syn/anti* mixture): IR: $\tilde{\nu} = 3475$ cm^{-1}, 2955, 2925, 2870, 2815, 1465, 1420, 1375, 1340, 1290, 1180, 1070, 960, 875, 805, 690, 665.

$C_{19}H_{42}O_2Sn$ (421.3) Calcd. C 54.17 H 10.05
Found C 54.20 H 10.23

(1S,3S*)-1-Methoxy-4-methyl-1-(tributylstannyl)-3-pentanol* (*syn*-**8**): Prepared as described for *anti*-**8**. *syn*-**6a** (143 mg, 0.25 mmol), Bu_4NF (1 M in THF, 2.00 ml); 60°C, 4.5 h; yield 86.5 mg (81%). – ^{1}H NMR (400 MHz): δ = 0.81–1.00 (m, 4-CH_3, 5-H_3, 3 × 1′-H_2, 3 × 4′-H_3), 1.32 (tq, $J_{3',2'} = J_{3',4'} = 7.3$, 3 × 3′-$H_2$), 1.40–1.57 (m, 3 × 2′-$H_2$), 1.59–1.76 (m, 4-H), in part superimposed by AB signal ($\delta_A = 1.71$, $\delta_B = 1.94$, $J_{A,B} = 14.7$, in addition split by $J_{A,1} = J_{A,3} = 2.4$, $J_{B,1} = 11.8$, $J_{B,3} = 9.7$, 2-H_2), 3.32 (s, OMe), 3.53 (m_c, 3-H), 3.68 (d, $J_{OH,3} = 1.0$, OH), 3.97 (dd including $^{117/119}$Sn isotope satellite as d with $^2J_{H,Sn} = 12.8$, $J_{1,2\text{-H(B)}} = 11.9$, $J_{1,2\text{-H(A)}} = 2.8$, 1-H). – ^{13}C NMR: δ = 9.41 (including 2 d due to $^1J_{1',Sn} = 299$ and $^1J'_{1',Sn} = 286$, 3 × C-1′), 13.63 (3 × C-4′), 17.59 and 18.48 (4-CH_3, C-5), 27.46 (including d due to $^2J_{2',Sn} = 54$, 3 × C-2′), 29.18 (including d due to $^3J_{3',Sn} = 20$, 3 × C-3′), 33.70 (C-4), 38.34 (C-2), 59.03 (OMe), 80.30 and 81.02 (C-1, C-3).

(1R,3S*)-1-Methoxy-4-methyl-1-(tributylstannyl)-3-pentanol* (*anti*-**8**): A solution of *anti*-**6a** (0.36 g, 0.64 mmol) in Bu_4NF (1 M in THF, 3.00 ml) was heated at 60°C for 4.5 h. The mixture was diluted with MTB (100 ml) and H_2O (10 ml) and the aqueous layer was extracted with MTB (3 × 30 ml). Flash chromatography [petroleum ether/ether (30:1)] of the residue obtained from evaporation of the solvents yielded *anti*-**8** (0.23 g, 85%). – ^{1}H NMR (400 MHz): δ = 0.83–1.01 (m, 4-CH_3, 5-H_3, 3 × 1′-H_2, 3 × 4′-H_3), 1.32 (tq, $J_{3',2'} = J_{3',4'} = 7.3$, 3 × 3′-$H_2$), 1.41–1.57 (m, 3 × 2′-$H_2$), 1.67 (dqq, $J_{4,3} = J_{4,4\text{-Me}} = J_{4,5} = 6.7$, 4-H), AB signal ($\delta_A = 1.80$, $\delta_B = 2.02$, $J_{A,B} = 14.8$, in addition split by $J_{A,1} = 6.6$, $J_{A,3} = 2.0$, $J_{B,3} = 9.5$, $J_{B,1} = 3.7$, 2-H_2), 3.27 (d, $J_{OH,3} = 2.7$, OH), 3.32 (s, OMe), 3.44–3.51 (m, 3-H), 4.05 (dd, $J_{1,2\text{-H(A)}} = 6.6$, $J_{1,2\text{-H(B)}} = 3.7$, 1-H). – ^{13}C NMR (no DEPT spectrum measured): δ = 9.50 (including 2 d due to $^1J_{1',Sn} = 302$ and $^1J'_{1',Sn} = 289$, 3 × C-1′), 13.63 (3 × C-4′), 18.12 and 18.62 (4-CH_3, C-5), 27.44 (including d due to $^2J_{2',Sn} = 54$, 3 × C-2′), 29.18 (including d due to $^3J_{3',Sn} = 20$, 3 × C-3′), 33.80 and 36.85 (C-2, C-4), 59.00 (OMe), 77.66 [or 78.94(!?)] and 78.94 (C-1, C-3).

1-Methoxy-4-methyl-1-(tributylstannyl)-3-(trimethylsilyloxy)-pentane (**9**, *syn/anti* mixture): IR: $\tilde{\nu} = 2960$ cm^{-1}, 2925, 2870, 2810, 1465, 1375, 1250, 1180, 1110, 1075, 1055, 935, 875, 840, 750, 685.

$C_{22}H_{50}O_2SiSn$ (493.4) Calcd. C 53.55 H 10.21
Found C 53.48 H 10.30

(1S,3S*)-1-Methoxy-4-methyl-1-(tributylstannyl)-3-(trimethylsilyloxy)pentane* (*syn*-**9**): Prepared as described for *anti*-**9**. *syn*-**8** (221 mg, 0.52 mmol) and 2,6-lutidine (0.18 ml, 1.30 mmol, 2.50 equiv.) in CH_2Cl_2 (2.0 ml), trimethylsilyl triflate (0.15 ml, 0.78 mmol, 1.50 equiv.); filtration through silica gel (desactivated with 7% aqueous NH_3); yield 232 mg (90%). – ^{1}H NMR (400 MHz): δ = 0.13 (s, $SiMe_3$), 0.80–0.98 (m, 4-CH_3, 5-H_3, 3 × 1′-H_2, 3 × 4′-H_3), 1.32 (tq, $J_{3',2'} = J_{3',4'} = 7.3$, 3 × 3′-$H_2$), 1.41–1.59 [m, 2-H(1), 3 × 2′-H_2], 1.65 (qqd, $J_{4,4\text{-Me}} = J_{4,5} = 6.8$, $J_{4,3} = 4.3$, 4-H), 1.96 [ddd, $J_{gem} = 14.4$, $J_{2\text{-H(2)},1} = 12.6$, $J_{2\text{-H(2)},3} = 2.2$, 2-H(2)], 3.28 (s, OMe), 3.75 (ddd, $J_{3,2\text{-H(1)}} = 9.7$, $J_{3,4} = 4.3$, $J_{3,2\text{-H(2)}} = 2.2$, 3-H), 3.97 (dd including $^{117/119}$Sn isotope satellite as d with $^2J_{H,Sn} = 13.8$, $J_{1,2\text{-H(2)}} = 12.6$, $J_{1,2\text{-H(1)}} = 2.2$, 1-H).

(1R,3S*)-1-Methoxy-4-methyl-1-(tributylstannyl)-3-(trimethylsilyloxy)pentane* (*anti*-**9**): At 0°C trimethylsilyl triflate (0.06 ml, 0.30 mmol, 1.60 equiv.) was added dropwise to *anti*-**8** (80.3 mg, 0.19 mmol) and 2,6-lutidine (0.06 ml, 0.50 mmol, 2.70 equiv.) in CH_2Cl_2 (1.2 ml). The mixture was stirred at 0°C for 1 h and quenched with Et_3N (0.5 ml). Satd. aqueous $NaHCO_3$ solution (10 ml) was added, and the aqueous layer was extracted with MTB (3 × 30 ml). Filtration through silica gel (desactivated with 7% aqueous NH_3) of the residue obtained by evaporation of the solvents yielded *anti*-**9** (89.0 mg, 95%). – ^{1}H NMR (400 MHz): δ = 0.11 (s, $SiMe_3$), 0.79 (d, $J_{4\text{-Me},4} = J_{5,4} = 8.3$, 4-$CH_3$, 5-$H_3$), 0.90 (t, $J_{4',3'} = 7.3$, 3 × 4′-H_3), superimposes ca. 0.83–0.98 (m, 3 × 1′-H_2), 1.32 (tq, $J_{3',2'} = J_{3',4'} = 7.3$, 3 × 3′-$H_2$), 1.40–1.59 (m, 3 × 2′-$H_2$), 1.69–1.83 [m, 2-H(1), 4-H], 2.07 [ddd, $J_{gem} = 15.7$, $J_{2\text{-H(2)},1} = 10.7$, $J_{2\text{-H(2)},3} = 5.1$, 2-H(2)], 3.26 (s, OMe), 3.65 (ddd, $J_a = 7.6$, $J_{3,2\text{-H(2)}} = 5.1$, $J_b = 3.4$, 3-H), 3.76 (dd, $J_{1,2\text{-H(2)}} = 10.6$, $J_{1,2\text{-H(1)}} = 4.5$, 1-H).

1-Methoxy-4-methyl-1-(trimethylsilyl)-3-pentanol (**11**, *syn/anti* mixture): IR: $\tilde{\nu} = 3470$ cm^{-1}, 2960, 2900, 2800, 1465, 1410, 1365, 1250, 1180, 1085, 1030, 1005, 840, 750, 700, 615.

$C_{10}H_{24}O_2Si$ (204.4) Calcd. C 58.77 H 11.83
Found C 58.54 H 11.74

(1S,3S*)-1-Methoxy-4-methyl-1-(trimethylsilyl)-3-pentanol* (*syn*-**11**): Prepared as described for *anti*-**11**. *syn*-**9** (110 mg, 0.22 mmol) in THF (2.50 ml), *n*BuLi (1.37 M in hexane, 0.17 ml, 0.23 mmol, 1.10 equiv.), –78°C, 15 min; flash chromatography [petroleum ether/ether (5:1)]; yield 37.1 mg (82%). – ^{1}H NMR (400 MHz): δ = 0.08 (s, Me_3Si), 0.917 and 0.921 (2 d, $J_{4\text{-Me},4} = J_{5,4} = 6.8$, 4-$CH_3$, 5-$H_3$), AB signal ($\delta_A = 1.54$, $\delta_B = 1.62$, $J_{A,B} = 14.8$, in addition split by $J_{A,1} = 3.4$, $J_{A,3} = 2.4$, $J_{B,1} = 11.2$, $J_{B,3} = 9.2$, 2-H_2), superimposed by 1.59–1.72 (m, 4-H), 3.18 (dd, $J_{1,2\text{-H(B)}} = 11.2$, $J_{1,2\text{-H(A)}} = 3.6$, 1-H), 3.40 (s, OMe), 3.55–3.61 (m, 3-H), 3.73 (d, $J_{OH,3} = 1.0$, OH). – ^{13}C NMR: δ = –2.90 ($SiMe_3$), 17.33 and 18.50 (4-CH_3, C-5), 33.85 (C-4), 34.37 (C-2), 59.61 (OMe), 78.61 and 79.12 (C-1, C-3).

(1R,3S*)-1-Methoxy-4-methyl-1-(trimethylsilyl)-3-pentanol* (*anti*-**11**): At –78°C *n*BuLi (1.37 M in hexane, 0.13 ml, 0.18 mmol, 1.10 equiv.) was added dropwise to a solution of *anti*-**9** (79.5 mg, 0.16 mmol) in THF (1.5 ml). After 15 min, the reaction was quenched with satd. aqueous NH_4Cl solution (1 ml)/H_2O (10 ml), and the aqueous layer was extracted with MTB (3 × 30 ml). Flash chromatography [petroleum ether/ether (5:1)] of the residue obtained by evaporation of the solvents yielded *anti*-**11** (25.6 mg, 78%). – ^{1}H NMR (400 MHz): δ = 0.09 (s, $SiMe_3$), 0.90 and 0.95 (2 d, $J_{4\text{-Me},4} = J_{5,4} = 6.8$, 4-$CH_3$, 5-$H_3$), AB signal ($\delta_A = 1.63$, $\delta_B = 1.75$, $J_{A,B} = 14.9$, in addition split by $J_{A,1} = 7.4$, $J_{A,3} = 2.2$, $J_{B,3} = 10.0$, $J_{B,1} = 3.7$, 2-H_2), superimposed in part by 1.64 (dqq, $J_{4,3} = J_{4,4\text{-Me}} = J_{4,5} = 6.8$, 4-H), 3.00 (br. s, OH), 3.22 (dd, $J_{1,2\text{-H(A)}} = 7.4$, $J_{1,2\text{-H(B)}} = 3.7$, 1-H), 3.40 (s, OMe), 3.56–3.62 (m, 3-H). – ^{13}C NMR: δ = –2.81 ($SiMe_3$), 17.93 and 18.54 (4-CH_3, C-5), 33.31 (C-2), 34.06 (C-4), 59.85 (OMe), 75.27 and 75.33 (C-1, C-3).

1-Methoxy-4,4-dimethyl-1-(tributylstannyl)-3-pentanol (**12**, *syn/anti* mixture)

$C_{20}H_{44}O_2Sn$ (435.3) Calcd. C 55.19 H 10.19
Found C 54.79 H 10.26

(1S,3S*)-1-Methoxy-4,4-dimethyl-1-(tributylstannyl)-3-pentanol* (*syn*-**12**): Prepared as described for *anti*-**12**. *syn*-**6b** (86.1 mg, 0.15 mmol), Bu_4NF (1.00 M in THF, 1.50 ml); 60°C, 4.5 h; yield 39.6 mg (61%). – ^{1}H NMR (400 MHz): δ = 0.87–0.94 (m, 3 × 1′-H_2), superimposes 0.896 (s, 2 × 4-CH_3, 5-H_3) and 0.902 (t, $J_{4',3'}$ =

7.3, 3 × 4'-H_3), 1.32 (tq, $J_{3',2'} = J_{3',4'} = 7.3$, 3 × 3'-$H_2$), 1.41 – 1.60 (m, 3 × 2'-H_2), AB signal ($\delta_A = 1.77$, $\delta_B = 1.88$, $J_{A,B} = 14.7$, in addition split by $J_{A,1} = 2.7$, $J_{A,3} = 1.8$, $J_{B,1} = 11.5$, $J_{B,3} = 9.9$, 2-H_2), 3.31 (s, OMe), 3.40 (br. d, $J_{3,2\text{-H(B)}} = 9.9$, 3-H), 3.76 (d, $J_{OH,3} = 1.0$, OH), 3.95 (dd including $^{117/119}Sn$ isotope satellite as d with $^2J_{H,Sn} = 13.4$, $J_{1,2\text{-H(B)}} = 11.4$, $J_{1,2\text{-H(A)}} = 2.9$, 1-H). – ^{13}C NMR: $\delta = 9.39$ (including 2 d due to $^1J_{1',Sn} = 299$, $^1J'_{1',Sn} = 287$, 3 × C-1'), 13.66 (3 × C-4'), 25.67 (2 × 4-CH_3, 5-H_3), 27.46 (including d due to $^2J_{2',Sn} = 53$, 3 × C-2'), 29.18 (including d due to $^3J_{3',Sn} = 20$, 3 × C-3'), 34.64 (C-4), 35.98 (C-2), 59.02 (OMe), 81.40 (C-3), 83.62 (including d due to $^1J_{1,Sn} = 51$, C-1).

(1R,3S*)-1-Methoxy-4,4-dimethyl-1-(tributylstannyl)-3-pentanol* (*anti*-**12**): A solution of *anti*-**6b** (87.8 mg, 0.15 mmol) in Bu_4NF (1.00 M in THF, 1.50 ml) was heated at 60°C for 4.5 h. The mixture was diluted with MTB (100 ml) and H_2O (10 ml). The layer was extracted with MTB (3 × 30 ml) and dried with $MgSO_4$. Flash chromatography [petroleum ether/ether (30:1)] of the residue obtained by evaporation of the solvents yielded *anti*-**12** (56.8 mg, 86%). – ^1H NMR (400 MHz): δ = ca. 0.86 – 0.96 (m, 3 × 1'-H_2), superimposes 0.90 (t, $J_{4',3'} = 7.3$, 3 × 4'-H_3) and 0.91 (s, 2 × 4-CH_3, 5-H_3), 1.32 (tq, $J_{3',2'} = J_{3',4'} = 7.3$, 3 × 3'-$H_2$), 1.41 – 1.62 (m, 3 × 2'-H_2), AB signal ($\delta_A = 1.75$, $\delta_B = 2.01$, $J_{A,B} = 14.7$, in addition split by $J_{A,1} = 5.9$, $J_{A,3} = 1.7$, $J_{B,3} = 10.5$, $J_{B,1} = 3.8$, 2-H_2), 3.27 (d, $J_{OH,3} = 2.0$, OH), 3.32 (s, OMe), 3.40 (ddd, $J_{3,2\text{-H(B)}} = 10.5$, $J_{3,2\text{-H(A)}} = J_{3,OH} = 1.9$, 3-H), 4.04 [dd including $^{117/119}Sn$ isotope satellite as d with $^2J_{H,Sn} = 5.4$(?), $J_{1,2\text{-H(A)}} = 5.9$, $J_{1,2\text{-H(B)}} = 3.8$, 1-H]. – ^{13}C NMR: $\delta = 9.51$ (including 2 d due to $^1J_{1',Sn} = 304$, $^1J'_{1',Sn} = 290$, 3 × C-1'), 13.67 (3 × C-4'), 25.82 (2 × 4-CH_3, 5-H_3), 27.43 (including d due to $^2J_{2',Sn} = 53$, 3 × C-2'), 29.19 (including d due to $^3J_{3',Sn} = 20$, 3 × C-3'), 34.21 (C-2), 34.71 (C-4), 58.96 (OMe), 79.34 (C-3), 80.37 (including d due to $^1J_{1,Sn} = 29$, C-1).

1-[Dimethyl(1,1,2-trimethylpropyl)silyl]-1-methoxy-4,4-dimethyl-3-pentanol (**14**, *syn/anti* mixture): IR: $\tilde{\nu} = 3505\ \text{cm}^{-1}$, 2960, 2870, 1465, 1380, 1365, 1250, 1080, 1015, 835, 815, 765.

$C_{16}H_{36}O_2Si$ (288.5)	Calcd.	C 66.60	H 12.58
	Found	C 66.33	H 12.88

(1S,3S*)-1-[Dimethyl(1,1,2-trimethylpropyl)silyl]-1-methoxy-4,4-dimethyl-3-pentanol* (*syn*-**14**): Prepared as described for *anti*-**11**. *syn*-**6a** (124 mg, 0.22 mmol) in THF (2.0 ml), *n*BuLi (1.37 M in hexane, 0.17 ml, 0.23 mmol, 1.10 equiv.); –78°C, 30 min; flash chromatography [petroleum ether/ether (5:1)]; yield 57.9 mg (93%). – ^1H NMR (400 MHz): δ = 0.06 and 0.10 [2 s, $Si(CH_3)_2$], 0.85 – 0.92 (m, 2 × 1'-CH_3, 2'-CH_3, 3'-H_3), 0.90 (s, 2 × 4-CH_3, 5-H_3), AB signal ($\delta_A = 1.59$, $\delta_B = 1.70$, $J_{A,B} = 15.0$, in addition split by $J_{A,1} = 10.8$, $J_{A,3} = 10.0$, $J_{B,1} = 3.3$, $J_{B,3} = 1.5$, 2-H_2), in part superimposed by 1.65 (qq, $J_{2',2'\text{-Me}} = J_{2',3'} = 6.9$, 2'-H), 3.27 (dd, $J_{1,2\text{-H(A)}} = 10.9$, $J_{1,2\text{-H(B)}} = 3.3$, 1-H), 3.40 (s, OMe), superimposes 3.41 (dm_c, $J_{3,2\text{-H(A)}} > 8$, 3-H), 3.63 (d, $J_{OH,3} = 0.8$, OH). – ^{13}C NMR: $\delta = -4.86$ [$Si(CH_3)_2$], 18.46, 21.15, 21.24 (2 × 1'-CH_3, 2'-CH_3, C-3'), 23.74 (C-1'), 25.58 (2 × 4-CH_3, C-5), 33.79 (C-2), 34.61 (C-2'), 34.82 (C-4), 59.90 (OMe), 78.45 and 82.46 (C-1, C-3).

(1R,3S*)-1-[Dimethyl(1,1,2-trimethylpropyl)silyl]-1-methoxy-4,4-dimethyl-3-pentanol* (*anti*-**14**): Prepared as described for *anti*-**11**. *anti*-**6b** (121 mg, 0.21 mmol) in THF (2.0 ml), *n*BuLi (1.37 M in hexane, 0.17 ml, 0.23 mmol, 1.10 equiv.), –78°C, 30 min; flash chromatography [petroleum ether/ether (5:1)]; yield 52.0 mg (86%). – ^1H NMR (400 MHz): δ = 0.04 and 0.16 [2 s, $Si(CH_3)_2$], 0.85 – 0.90 (m, 2 × 1'-CH_3, 2'-CH_3, 3'-H_3), 0.91 (s, 2 × 4-CH_3, 5-H_3), AB signal ($\delta_A = 1.58$, $\delta_B = 1.85$, $J_{A,B} = 14.9$, in addition split by $J_{A,1} = 6.1$, $J_{A,3} = 1.8$, $J_{B,3} = 11.0$, $J_{B,1} = 4.0$, 2-H_2), 1.66 (qq, $J_{2',2'\text{-Me}} = J_{2',3'} = 6.9$, 2'-H), 3.13 (d, $J_{OH,3} = 2.3$, OH), 3.39 (s, OMe), 3.41 (dd, $J_{1,2\text{-H(A)}} = 6.1$, $J_{1,2\text{-H(B)}} = 4.0$, 1-H), 3.56 ($dm_c$, $J_{3,2\text{-H(B)}} = 11.0$, 3-H). – ^{13}C NMR: $\delta = -4.80$ and -4.44 [$Si(CH_3)_2$], 18.33, 18.64, 20.70 and 21.10 (2 × 1'-CH_3, 2'-CH_3, C-3'), 23.57 (C-1'), 25.69 (2 × 4-CH_3, C-5), 30.70 (C-2), 34.55 (C-2'), 34.82 (C-4), 59.36 (OMe), 73.95 and 78.15 (C-1, C-3).

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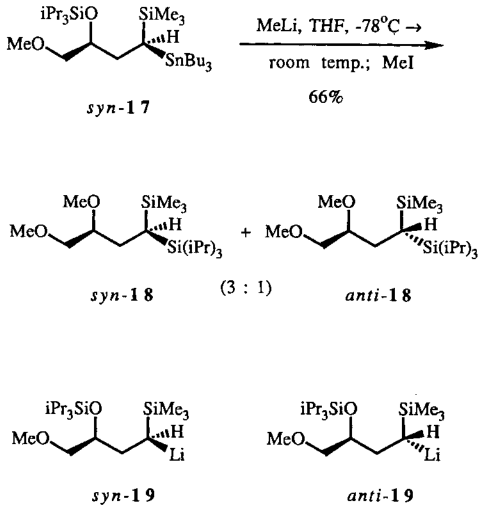
[33] *Note added after acceptance of this manuscript* (June 16, 1992): Very recently, M. Lautens, P. H. M. Delanghe, J. B. Goh, and C. H. Zhang (*J. Org. Chem.* **1992**, *57*, 3270–3272) described retro [1,4]-Brook rearrangements of lithiated alkenes and cyclopropanes which exhibited stereoselectivity and retention of configuration in the C–Li → C–Si bond conversions. However, a mechanistic *necessity* for such a steric course would exist – similar as pointed out in ref.[20] – if these reactions were intramolecular. Lautens et al. studied also the stereochemistry of a retro [1,4]-Brook rearrangement where no such necessity is imposed: MeLi-induced Sn/Li exchange in stannane *syn*-**17**, rearrangement, and *O*-methylation of the resulting alkoxide furnished a 3:1 mixture of compounds *syn*- and *anti*-**18**. Unfortunately, this experiment does not allow to decide which of the alkyllithium precursors *syn*- or *anti*-**19** leads to which of the products. Hence, it remains unknown whether **18** → **19** occurs stereoselectively, and if so, whether with retention or inversion of configuration.



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3a: 32815-70-6 / **3b**: 19550-89-1 / **4a**: 143192-68-1 / **4b**: 143192-69-2 / **5a**: 143192-70-5 / **5b**: 143192-71-6 / *syn*-**6a**: 143192-72-7 / *anti*-**6a**: 143192-73-8 / *syn*-**6b**: 143192-74-9 / *anti*-**6b**: 143192-75-0 / **7a**: 143192-76-1 / **7b**: 143192-77-2 / *syn*-**8**: 143192-78-3 / *anti*-**8**: 143192-79-4 / *syn*-**9**: 143192-80-7 / *anti*-**9**: 143192-81-8 / *syn*-**11**: 143192-82-9 / *anti*-**11**: 143192-83-0 / *syn*-**12**: 143192-84-1 / *anti*-**12**: 143192-85-2 / *syn*-**14**: 143192-86-3 / *anti*-**14**: 143192-87-4 / $(CH_3)_2CHCHO$: 78-84-2 / $(CH_3)_3CCHO$: 630-19-3 / $CH_2{=}CHCH_2Br$: 106-95-6 / $(CH_3)_2CHC(CH_3)_2Si(Me)_2Cl$: 67373-56-2