Chiral Organometallic Reagents, I

Stereoselective Exchange of Diastereotopic Bromine Atoms by Lithium in 1,1-Dibromo-3-(trimethylsilyloxy)alkanes

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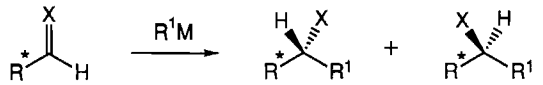
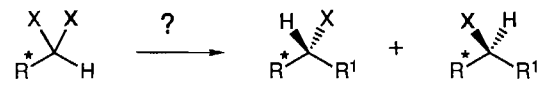
Bromine-lithium exchange in 1,1-dibromo-3-(trimethylsilyloxy)alkanes **4** and **6** affords the carbenoids **8** and **14**, which have been added to ketones, aldehydes, arylboronates, and silylating agents. Diastereoselectivity in the generation and trapping of the carbenoids ranged between 70–90% for **8** and >90% for **14**.

Stereoselective synthesis involves conversion of a prochiral group into a chiral one. The selective formation of a stereogenic center with a particular configuration requires asymmetric induction which can originate either from a chiral reagent or from chiral centers within the substrate molecule. In the latter case, commonly two *diastereotopic faces* of a planar prochiral group are differentiated by an achiral reagent. While this approach is used abundantly[1] in stereoselective synthesis, a planar prochiral group is not the only type of prochiral situation available.



R*chiral residue
X = O, NR, CR_2

Chiral molecules may contain *diastereotopic groups*, a fact that has become widely recognized after NMR spectroscopy has developed into the major analytical tool in organic chemistry[2]. In fact, nature uses the different reactivity of diastereotopic groups in stereoselective biotransformations[3]. It is thus even more surprising that differentiation of diastereotopic groups has been little explored as a route in stereoselective synthesis.



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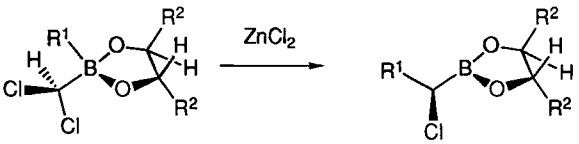
Some reactions in which diastereotopic C–H bonds are differentiated have been recently reported[4,5]. Selective transformation of diastereotopic heteroatoms in chiral compounds are even more scarce[6,7]. A notable example is given by the stereoselective transformations of chiral dichloromethaneboronates, introduced by Matteson[8], demonstrating the preparative potential of diastereotopic groups in stereoselective synthesis.

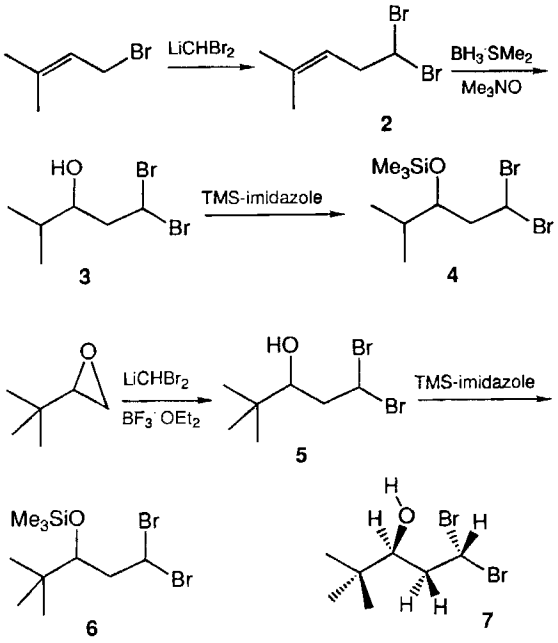


$R^2 = CH_3$, $(CH_3)_2CH$, c-C_6H_{11}

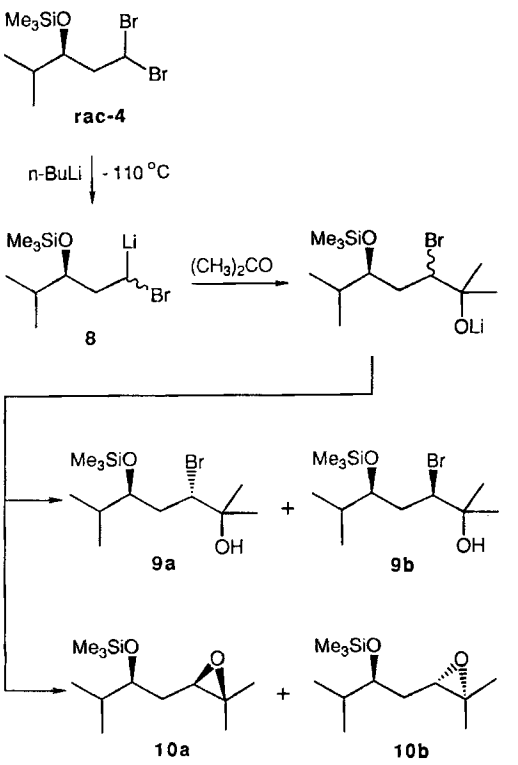
To make use of this potential a chiral substrate **1** is needed, which contains a geminal dihetero substituent, and a reaction by which just one of those heteroatoms is replaced by a different residue. Reactions which allow such transformations on geminal dibromoalkanes have been developed by Villieras[9], i.e. selective exchange in **1** (X = Br) of one bromine by lithium, followed by reaction of the carbenoid intermediate with an electrophile. This was preceded by the seminal studies of Köbrich[10] on the differentiation of diastereotopic halogens on cyclic geminal dihalo compounds such as dihalo norcaranes. This chemistry has since been widely exploited by other groups[11]. Surprisingly, it has not been extended to open-chain compounds containing diastereotopic bromine substituents. First experiments[12] towards this aim have been encouraging. Here we give a detailed account of the preparative results obtained. The following paper[13] deals with the mechanistic implications of these reactions and in consequence the conditions that lead to high diastereoselectivities.

Substrates Containing Diastereotopic Bromine Groups

We have started our investigations with the racemic 1,1-dibromoalkanes **4** and **6**, having a center of chirality at a 1,3-distance to the dibromoalkyl group. We have envisaged that 1,3-asymmetric induction may be facilitated by placing a hydrogen, a bulky alkyl group, and an oxygen substituent at the chiral center.



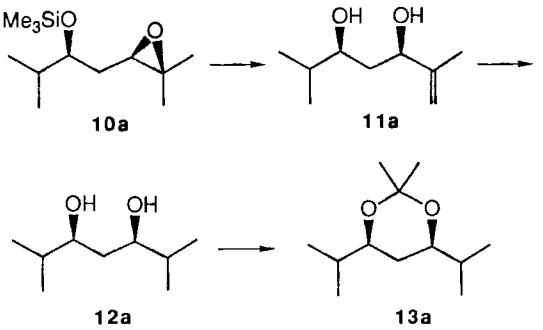
Thus, prenyl bromide is homologated[14] with dibromomethyllithium to give **2**. Hydroboration, oxidation to the alcohol **3**, and silylation proceed readily. In order to generate the alcohol **5**, ring opening of *tert*-butyloxirane[15] by dibromomethyllithium at $-95\,^{\circ}C$ requires the presence of BF_3-OEt_2. Even then, the reaction affords the alcohol **5** with unsatisfactory yields of 30–50%. The yield is limited by a concurrent decomposition of the carbenoid. The lithium bromide thus liberated opens the *tert*-butyloxirane to the bromohydrin which forms the major side product. The ^{1}H-NMR spectrum of alcohol **5** displays clear-cut coupling patterns, from which it can be derived that the alcohol populates predominantly the conformation **7**.



Stereoselective Transformations of the Geminal Dibromides 4, 6

The aim of this study is to selectively exchange one of the two diastereotopic bromine atoms in **4** by lithium, and to trap the resulting carbenoids **8**, e. g. by acetone, to give either the diastereomeric bromohydrins **9** or the epoxides **10**.

Thus, the dibromo compound **4** admixed with 2.0 equivalents of acetone is treated at $-110\,^{\circ}C$ in a Trapp solvent mixture[16] with *n*-butyllithium. After 3 h, the reaction mixture is quenched at $-95\,^{\circ}C$[9,17] to give 60% of the bromohydrins **9** as a 81:19 diastereomer mixture. Quenching of the reaction mixture after reaching room temperature[9,17] leads directly to the epoxides **10** (71%). The ratio of diastereomers ranges between 74:26 and 84:16 over several runs. In order to assign the relative configuration to the obtained diastereomers, an 85:15 mixture of the epoxides **10** is opened with lithium diisopropylamide to the allylic alcohols **11**, hydrogenation of which furnishes the diols **12**. The diastereomeric diols are separated by chromatography. The minor product is identified by its m. p. and its ^{13}C-NMR spectrum[18] as the C_2-symmetric *anti*-diol. The mixture of the diols **12** is moreover converted to that of the acetonides **13**. The ^{1}H-NMR spectrum shows the major diastereomer **13a** to have σ-symmetry.



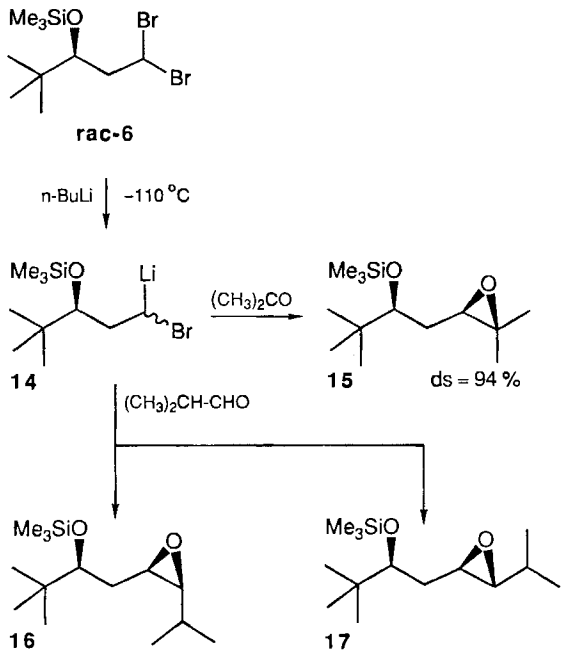
Thus, the transformation of the dibromo compound **4** gives predominantly the stereoisomer **9a** of the bromohydrins and **10a** of the epoxides. The diastereoselectivity depends, if at all, only to a small extent on the reaction temperature. It varies from 80:20 at $-120\,^{\circ}C$ to 70:30 at $-90\,^{\circ}C$. The diastereoselectivity depends, however, on the sequence by which the reactands are combined (cf. Table 1). In the one described above the carbenoids **8** are generated in the presence of acetone as electrophile (in situ method, B). The carbenoids **8** may also be generated in the absence of the electrophile, which is subsequently added after 10 min at $-110\,^{\circ}C$ (successive method, A). Finally, a mixture of the dibromo compound **4** and of acetone is added to *n*-butyllithium at $-110\,^{\circ}C$ (reverse in situ method, C). In one case **4** is added to *n*-butyllithium and the electrophile is subsequently added after 10 min (reverse successive method, D). An interpretation of the differences obtained between these methods will be given in a subsequent paper[19].

Table 1. Products obtained from the reaction of **4**, **6** (carbenoids **8**, **14**) with various ketones and aldehydes as well as from the reaction of **4** with *n*BuLi/boronates **26**, **27**. For methods A–D see text

Electrophile	Method	Products	Yield (%)	Diastereomer Ratio	Determined by [a] gc [b] ^{1}H NMR [c] ^{13}C NMR
Acetone	A	**10a**, **10b**	64	68:32	a)
	B	**10a**, **10b**	62–71	74:26 to 84:16	a)
	B	**9a**, **9b**	59	81:19	b)
	C	**10a**, **10b**	80	84:16	a)
	D	**10a**, **10b**	70	78:22	a)
Cyclohexanone	A	**19a**, **19b**	74	73:27	a)
	B	**19a**, **19b**	85–91	82:18	a)
	B	**18a**, **18b**	90	82:18	b)
	C	**19a**, **19b**	74	81:19	a)
	D	**19a**, **19b**	90	73:27	a)
Cyclopentanone	A	**21a**, **21b**	45	73:27	a)
	B	**21a**, **21b**	30–51	88:12	a)
	B	**20a**, **20b**	45	91:9	c)
	C	**21a**, **21b**	35	88:12	a)
Isobutyraldehyde	A	**23a**, **23b**, **23c**, **23d**	65	55:14:25:6	a)
	B	**23a**, **23b**, **23c**, **23d**	78	53:17:23:6	b)
			57	49:18:25:8	a)
	B	**22a**, **22b**, **22c**, **22d**	61	57:15:28:Trace	c)
	C	**23a**, **23b**, **23c**, **23d**	78	54:17:23:6	a)
n-Butyraldehyde	B	**24a**, **24b**, **24c**, **24d**[d]	86	48:18:26:8	c)
TMS-Triflate	A	**25a**, **25b**	85	74:26	c)
TMS-Imidazole	A	**25a**, **25b**	46	76:24	a)
	B	**25a**, **25b**	65	70:30	a)
	C	**25a**, **25b**	55	71:29	a)
26	B[e]	**28a**, **28b**	60	71:29	b)
27	A[e]	**29a**, **29b**	74–80	73:27 to 83:17	a)
	B[e]	**29a**, **29b**	38	92:8	a)
	C[e]	**29a**, **29b**	45	79:21	a)

[d] No structural assignment possible. — [e] With 1 equiv. of **26**, **27**.

The diastereoselectivity also depends on the structure of the substrate: With **6**, having a *tert*-butyl group on the inducing stereocenter, a higher diastereoselectivity is attained by the addition of the carbenoids **14** to acetone (94:6).

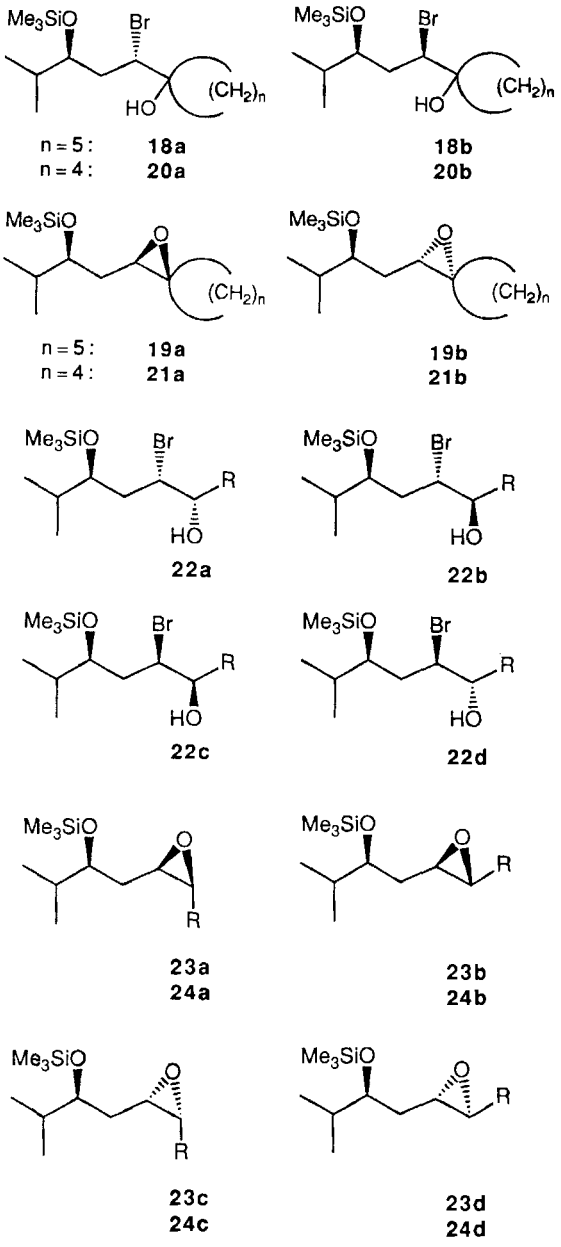


The relative configuration of the epoxide **15** is assigned in analogy to that of **10a**. Likewise, trapping of **14** by isobutyraldehyde leads to only two epoxides. Since these have been identified as a 3:1 *cis/trans* epoxide mixture, the 1,3-induction on transformation of the dibromo compound **6** to the expoxides **16**, **17** must be > 90%. Thus, **6** is a substrate on which high diastereoselectivity in the reaction of the diastereotopic bromine atoms can be realized.

In order to learn more about the scope of the diastereoselection in the reaction of the dibromo compound **4**, the carbenoids **8** are added to a series of ketones and aldehydes using the methods A–D. The results are compiled in Table 1.

Addition to cyclohexanone results in the highest yield of the adducts **18** or **19**, respectively, wereas on addition to cyclopentanone yields are low, due to a competing enolization of the ketone[20]; in one case cyclopentylidenecyclopentanone is isolated in 30–40% yield. The major isomers **20a**, or **21a**, are assumed to have the same relative configuration as the acetone adducts **9a** and **10a**. On addition of the carbenoids **8** to various aldehydes all four diastereomeric epoxides **23** are obtained as a mixture. Based on their characteristic signals in the ^{13}C-NMR spectra the *cis*- and *trans*-oxiranes of **23** can be discerned. Thus, a tentative structural assignment for all the diastereomeric products has been made. In the case of the *n*-butyraldehyde adducts **24** the

spectra of the mixture are too complex to allow an assignment.

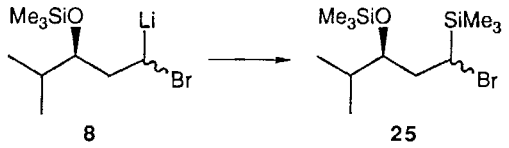


22, **23**, R = i-Pr; **24**, R = n-Pr

In the reaction of the dibromo compound **4** via the carbenoids **8** with the aldehydes the 1,3-asymmetric induction (**23a** + **23b**): (**23c** + **23d**) has been found to be on the lower side (ca. 70:30) of the range in diastereoselectivities found for the ketone additions (79:30 to 88:12). Moreover, in the addition of the carbenoids **8** to aldehydes an additional stereocenter is created due to the prochiral nature of the aldehyde group. The attendant simple diastereoselection is reflected in the *cis*/*trans* structure of the epoxides **23**, **24**. For both epoxide pairs **23a**/**23b** and **23c**/**23d** simple diastereoselection is ca. 3–4:1, the *cis*-isomers being favored. This means that in the precursor bromohydrins **22** the *syn*-diastereomers **22a** and **22c** predominate (cf. ref.[21]).

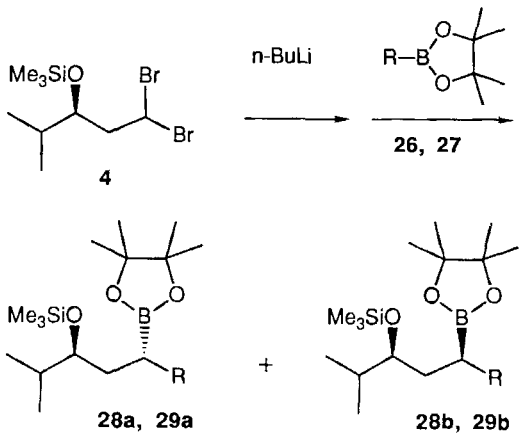
Reaction of the Carbenoids 8 and 14 with other Electrophiles

Carbenoids have been trapped by *silylation* previously[14,22]. Treatment of **8** with TMS chloride has remained unsuccessful. However, silylation is cleanly effected with TMS triflate using the preformed carbenoids **8** (method A). Likewise, silylation can be realized with TMS-imidazole in lower yields.



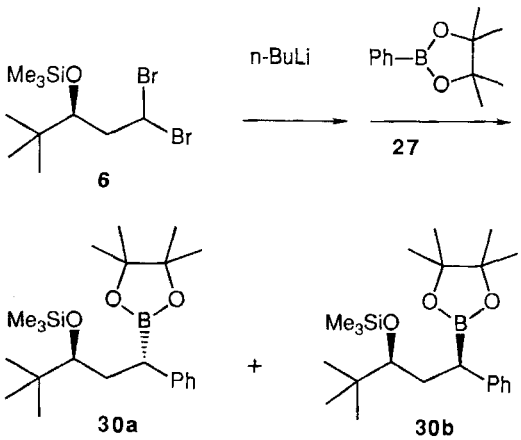
8 **25**

Next, we have examined the *borylation* of the carbenoids **8** and **14**, a well-known reaction for such species. Reaction of **8** with the isopropylboronate **26** gives 60% of the homologated boronates **28** as a 71:29 mixture. Similar results are obtained with the phenylboronate **27**.



26, **28**, R = i-Pr 60% 71 : 29

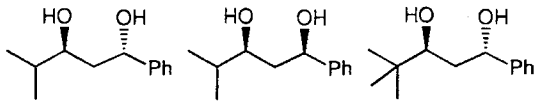
27, **29**, R = Ph 80% 73 : 27



70% 93 : 7

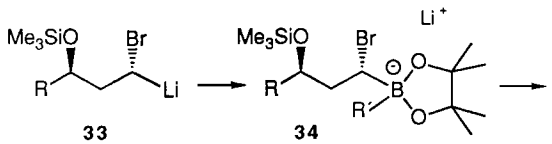
The structure of the diastereomeric boronates **29** as well as of the boronate **30** obtained from **6** and **27** is secured by conversion to the corresponding diols **31** and **32** by oxida-

tion with alkaline hydrogen peroxide followed by fluorodesilylation. The diols **31** and **32** have been identified[23] with reference to their characteristic[24] ^{13}C-NMR spectra.

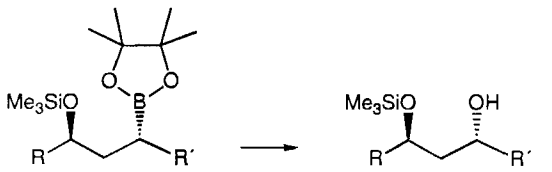


31a **31b** **32**

The identification of the major diol components as **31a** and **32**, respectively, confirms the sense of asymmetric induction in the replacement of one of the two diastereotopic bromine atoms in **4** (and **6**): Working backwards, oxidation of the carbon-boron bond in **35** to **36** is known to occur with retention of configuration[25].



33 **34**



35 **36**

Rearrangement of the ate complex **34** to the alkylboronates **35** should occur with inversion of configuration[26]. Thus, the major diastereomer of the ate complex should have structure **34**, derived from the carbenoid **33**. This is the same diastereomer of the carbenoid that is assumed to give rise to the major diastereomer **9a** of the bromohydrins and epoxides **10a** and **15** mentioned above. The consistent stereochemical picture rests however on the tacit assumption that the carbenoids **8** and **14** are configurationally stable under the conditions applied. Evidence for this being true has been provided elsewhere[19].

In summary, we have delineated in this study reaction pathways by which stereoselective carbon-carbon bond formation is effected utilizing diastereotopic bromine atoms with selectivities of up to 93% using the dibromo compound **6** and with up to 80–85% using the dibromo compound **4**.

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Experimental

All temperatures quoted are not corrected. – ^{1}H and ^{13}C NMR: Bruker AC-300. – Analytical gas chromatography: Siemens Sichromat 3, 30 m capillary column with SE 52. – Column chromatography: Kieselgel 60 (0.063–0.200 mm), Merck. – Flash chromatography: Kieselgel 60 (0.040–0.063 mm), Merck.

1. *5,5-Dibromo-2-methyl-2-pentene* (**2**): Lithium diisopropylamide was generated from 35.8 ml (0.25 mol) of diisopropylamine in 125 ml of anhydrous ether and 125 ml of anhydrous THF by addition of 167 ml (0.25 mol) of a 1.5 M solution of *n*-butyllithium in *n*-hexane at −10°C over 30 min. The mixture was cooled to −95°C, and a solution of 17.5 ml (0.25 mol) of dibromomethane in 80 ml of anhydrous THF was added dropwise over 60 min. After stirring for 30 min at −95°C a solution of 37.3 g (0.25 mol) of 1-bromo-3-methyl-2-butene in 30 ml of anhydrous THF was added dropwise. The mixture was allowed to reach −50°C over 2.5 h. Then 100 ml of 5 N hydrochloric acid was added with stirring. After reaching room temperature the phases were separated and the aqueous phase was extracted 5 times with 100 ml each of ether. The combined organic phases were washed with 50 ml of brine, dried with Na_2SO_4, and concentrated. The resulting 56 g of a dark brown liquid was bulb-to-bulb distilled at 10^{-2} Torr from a bath of 50°C: 53 g (87%) of **2**, as a colorless liquid. For analysis 0.5 g of **2** was purified by flash chromatography over a 22-cm column with silica gel using petroleum ether (40–60°C) as eluent. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.64 (s, 3H), 1.73 (s, 3H), 3.09 (t, *J* = 6.6 Hz, 2H), 5.15 (m, 1H), 5.56 (td, *J* = 6.2 and 0.8 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.4, 25.8, 43.9, 45.7, 119.3, 137.0.

$C_6H_{10}Br_2$ (241.9) Calcd. C 29.79 H 4.17
Found C 29.94 H 4.17

2. *1,1-Dibromo-4-methyl-3-pentanol* (**3**): To a solution of 53 g (0.21 mol) of **2** in 250 ml of anhydrous THF was added at 0°C dropwise 23.4 ml (0.23 mol) of a 10 M solution of borane in dimethyl sulfide. After stirring for ca. 15 h the mixture was recooled to 0°C, and 31.9 g (0.43 mol) of anhydrous trimethylamine oxide was added in portions. The mixture was slowly warmed to room temp. and eventually heated to reflux for 1 d. After cooling, 10 ml of 1,2-dihydroxyethane and 90 ml of water were added, and the mixture was stirred for 6 h. The phases were separated, and the aqueous phase was extracted three times with 100 ml each of ether. The combined organic phases were washed with 50 ml of brine, dried with Na_2SO_4, and concentrated to ca. 80 ml. The resulting solution was fractionated to give 33.2 g (60%) of **3** as a colorless oil at b.p. 63–65°C/10^{-2} Torr. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 6.8 Hz, 6H), 0.95 (d, sept, *J* = 6.8 and 1.3 Hz, 1H), 1.57 (s, 1H), 2.43–2.54 (m, 2H), 3.6–3.7 (m, 1H), 5.88–5.93 (m, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.3, 18.4, 33.6, 44.1, 49.7, 74.8.

$C_6H_{12}Br_2O$ (260.0) Calcd. C 27.72 H 4.65
Found C 27.97 H 4.78

3. *1,1-Dibromo-4-methyl-3-(trimethylsilyloxy)pentane* (**4**): To a solution of 17.25 g (66 mmol) of **3** in 150 ml of anhydrous petroleum ether (40–60°C) was added 11.22 g (80 mmol) of 1-(trimethylsilyl)-imidazole. Imidazole precipitated, and the reaction was complete after 2 d at room temperature. 700 ml of saturated aqueous NH_4Cl solution was added until the mixture was no longer alkaline, the phases were separated, and the aqueous phase was extracted three times with 100 ml each of ether. The combined organic phases were washed with 50 ml of brine, dried with $MgSO_4$, and concentrated to give 15.2 g of a colorless liquid. Distillation at 32–35°C/10^{-2} Torr yielded 13.45 g (67%) of **4**. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.15 (s, 9H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 1.69–1.77 (m, 1H), 2.33–2.50 (AB part of an ABXY system, J_{AB} = 14, J_{AX} = 10.3, J_{AY} = 9.2, J_{BX} = 3.5, J_{BY} = 3.0 Hz, 2H), 3.70 (ddd, *J* = 9.2, 4.6, and 3.0 Hz, 1H), 5.68 (dd, *J* = 10.3 and 3.5 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 17.2, 17.9, 33.5, 44.6, 48.7, 75.5.

$C_9H_{20}Br_2OSi$ (332.2) Calcd. C 32.54 H 6.07
Found C 32.64 H 6.18

4. *1,1-Dibromo-4,4-dimethyl-3-pentanol* (**5**): 33 ml (50 mmol) of a 1.5 M solution of *n*-butyllithium in *n*-hexane was added at −90°C under nitrogen over 30 min to a solution of 3.2 ml (50 mmol) of anhydrous dichloromethane in 60 ml of anhydrous THF and 60 ml of anhydrous ether. After stirring for 30 min a solution of 3.5 ml (50 mmol) of dibromomethane in 20 ml of anhydrous THF was added dropwise. After stirring for 30 min a solution of 5.00 g (50 mmol) of *tert*-butyl oxirane in 20 ml of anhydrous THF was added over 30 min. After stirring for 10 min at −95°C, 6.25 ml of BF_3-OEt_2 was added, and the mixture was kept for 4 h between −85 and −110°C. The yellowish color disappeared while warming to −40°C over 2 h. 20 ml of saturated aqueous $NaHCO_3$ solution was added. The phases were separated at room temperature and the aqueous phase was extracted four times with 50 ml each of ether. The combined organic phases were washed with 50 ml of brine, dried with Na_2SO_4, and concentrated to give 12.8 g of a yellowish oil which was chromatographed over 100 g of silica gel with CH_2Cl_2: 10.2 g of a colorless oil which contained according to the ^{1}H-NMR spectrum 1-bromo-3,3-dimethyl-2-butanol. Therefore, the oil was dissolved in 50 ml of methanol, and solid $NaOCH_3$ was added until the violet color of a phenolphthalein indicator persisted. To the mixture were added 50 ml of water and 50 ml of ether, the phases were separated, and the aqueous phase was extracted three times with 50 ml each of ether. The combined organic extracts were washed with 50 ml of brine, dried with Na_2SO_4, and concentrated to give 6.0 g of an oil which was chromatographed over 60 g of silica gel with CH_2Cl_2: 4.5 g (32%) of **5**. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (s, 9H), 1.75 (dd, *J* = 5.2 and 1.0 Hz, 1H), 2.36 to 2.54 (AB part of an ABXY system, J_{AB} = 14.6, J_{AX} = 10.6, J_{BY} = 10.1, J_{BX} = 2.8, J_{AY} = 2.1, $J_{B/OH}$ = 1.0 Hz, 2H), 3.45 (dd, *J* = 10.1 and 5.2 Hz, 1H), 5.88 (dd, *J* = 10.6 and 2.8 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 34.6, 44.8, 47.6, 77.8.

$C_7H_{14}Br_2O$ (274.0) Calcd. C 30.68 H 5.15
Found C 30.70 H 5.02

5. *1,1-Dibromo-4,4-dimethyl-3-(trimethylsilyloxy)pentane* (**6**): 4.0 g (15 mmol) of **5** and 2.53 g (18 mmol) of 1-(trimethylsilyl)imidazole were allowed to react for 5 d as described under 3. The crude product was purified by chromatography over 60 g of silica gel with CH_2Cl_2 to give 4.2 g (83%) of **6** as a colorless oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.17 (s, 9H), 0.88 (s, 9H), 2.42–2.56 (m, 2H), 3.49 (m, 1H), 5.65 (m, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 1.0, 26.2, 35.1, 45.2, 48.7, 79.4.

$C_{10}H_{22}Br_2OSi$ (346.2) Calcd. C 34.69 H 6.41
Found C 34.83 H 6.44

6. *2,2-Dimethyl-3-[3-methyl-2-(trimethylsilyloxy)butyl]oxirane* (**10**); *Successive Method, A:* A solution of 332 mg (1.0 mmol) of **4** in 8 ml of anhydrous THF, 4 ml of anhydrous petroleum ether (b.p. 40–60°C), and 4 ml of anhydrous ether (Trapp solvent mixture[16]) was cooled to −110°C. 0.9 ml (1.3 mmol) of a 1.45 M solution of *n*-butyllithium in *n*-hexane was slowly added with a precooled (−78°C) syringe such that the liquid ran down the cold wall of the flask. After stirring for 10 min at this temp. 0.15 ml (2.0 mmol) of anhydrous acetone was added with the help of a precooled (−78°C) syringe. After stirring for 1 h the mixture was allowed to reach 20°C over ca. 2 h. Then 20 ml of saturated aqueous NH_4Cl solution was added. The phases were separated, and the aqueous phase was extracted three times with 20 ml each of ether. The combined organic phases were washed with 20 ml of brine, dried with Na_2SO_4, and concentrated to give 250 mg of an oil, which was purified by flash chromatography with petroleum ether (40–60°C)/ether (20:1) to give 148 mg (64%) of **10** as a colorless oil. The ratio of diastereomers was determined by gas chromatography (100°C) to be **10a**:**10b** = 68:32.

$C_{12}H_{26}O_2Si$ (230.4) Calcd. C 62.55 H 11.37
Found C 62.70 H 11.59

(2′*R**,3*S**)-**10a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.12 (s, 9H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 1.27 (s, 3H), 1.32 (s, 3H), 1.57–1.79 (m, 3H), 2.87 (t, *J* = 6.1 Hz, 1H), 3.58 (dt, br., 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.4, 18.0, 18.4, 18.9, 24.9, 33.2, 33.3, 57.7, 61.8, 75.6.

(2′*R**,3*R**)-**10b**: The following signals could be recorded. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 9H), 2.76 (dd, *J* = 7.1 and 4.9 Hz, 1H), 3.62 (dt, *J* = 8.7 and 4.3 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 17.8, 17.9, 19.1, 25.0, 32.5, 39.9, 58.5, 62.2, 74.9.

In situ Method, B: To 332 mg (1.0 mmol) of **4** and 0.15 ml (2.0 mmol) of acetone in 15 ml of a Trapp solvent mixture[16] was added 1.3 mmol of *n*-butyllithium in *n*-hexane (precooled to −78°C) at −110°C over 15 s as described above. The reaction mixture was processed as above.

Reverse in situ Method, C: 1.3 mmol of *n*-butyllithium in *n*-hexane was dissolved in 10 ml of an anhydrous Trapp solvent mixture[16] and cooled to −110°C. A mixture of 332 mg (1.0 mmol) of **4** and 0.15 ml (2.0 mmol) of anhydrous acetone in 5 ml of a Trapp solvent mixture was added using a precooled (−78°C) syringe as described above. The mixture was processed as before.

Reverse Successive Method, D: A solution of 1.2 mmol of *n*-butyllithium in *n*-hexane in 10 ml of anhydrous Trapp solvent mixture[16] was cooled to −110°C. 332 mg (1.0 mmol) of **4** and after 10 min 0.15 ml (2.0 mmol) of anhydrous acetone were added from a precooled (−78°C) syringe as described above. The mixture was processed as before.

7. *3-Bromo-2,6-dimethyl-5-(trimethylsilyloxy)-2-heptanol* (**9**): 664 mg (2.0 mmol) of **4** was allowed to react with acetone as described under 6. This time the reaction mixture was stirred at −110°C for 3 h and quenched at −90°C by addition of 50 ml of saturated aqueous NH_4Cl solution. After reaching room temp. the mixture was worked up as described under 6. to give 510 mg of a yellowish oil which was purified by flash chromatography with petroleum ether (40–60°C)/ether (9:1) to give 730 mg (60%) of **9** as a colorless oil. The ratio of diastereomers was determined by GC (160°C) to be 91:19.

$C_{12}H_{27}BrO_2Si$ (311.3) Calcd. C 46.29 H 8.74
Found C 46.36 H 9.04

(2*R**,5*R**)-**9a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.17 (s, 9H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H), 1.33 (s, 3H), 1.36 (s, 3H), 1.69–1.84 (m, 3H), 2.14 (s, 1H), 3.77 (ddd, *J* = 8.8, 4.6, and 2.4 Hz, 1H), 4.19 (dd, *J* = 10.7 and 2.6 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.7, 17.6, 18.2, 25.9, 27.1, 34.2, 37.5, 69.5, 72.4, 75.7.

8. *(3R*,5S*)-2,6-Dimethyl-1-heptene-3,5-diol* (**11a**): 5.9 ml of a 1.52 M solution of *n*-butyllithium in *n*-hexane (9.0 mmol) was added at 0°C to a solution of 1.5 ml (11 mmol) of diisopropylamine in 15 ml of anhydrous ether. After stirring at room temperature for 15 min the solution was cooled to 0°C. A solution of 1.4 g (6.1 mmol) of **10** (85:15 diastereomeric mixture) in 10 ml of ether was added using a syringe. The mixture was allowed to reach room temp. and heated for 6 h under reflux. 10 ml of 4.5 N HCl in ether was added carefully. After stirring for 1 h, 30 ml of a saturated aqueous NH_4Cl solution and 5 ml of 2 N HCl were added. The mixture was neutralized with 2 N NaOH, and the organic phase was separated. The aqueous phase was extracted three times with 20 ml each of ether.

The combined organic phases were dried with Na_2SO_4 and concentrated. The residue was purified by flash chromatography with petroleum ether (40–60°C)/ether (1:1) over a column with 16 cm of silica gel. The resultant oil was bulb-to-bulb distilled at 20 Torr from a bath of 145°C to give 800 mg (83%) of **11** as a 83:17 (^{13}C NMR) mixture of diastereomers.

$C_9H_{18}O_2$ (158.2) Calcd. C 68.31 H 11.46
Found C 68.22 H 11.40

(3*R**,5*S**)-**11a**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.8 Hz, 6H), 1.44–1.66 (m, 3H), 1.69 (s, 3H), 3.5 (br. s, 2H), 3.59 (ddd, *J* = 9.9, 5.1, and 2.3 Hz, 1H), 4.22 (dd, *J* = 9.5 and 3.1 Hz, 1H), 4.77 (t, *J* = 1.5 Hz, 1H), 4.93 (t, *J* = 0.7 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.4, 17.6, 18.0, 33.9, 37.6, 76.4, 77.2, 110.5, 147.3.

(3*R**,5*R**)-**11b**: The following signals could be recorded: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.7 Hz, 3H), 4.30 (t, *J* = 5.3 Hz, 1H), 4.84 (br. s, 1H), 5.01 (br. s, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.8, 18.3, 18.6, 33.5, 37.1, 72.6, 73.5, 110.0, 147.1.

9. *(3R*,5S*)-2,6-Dimethyl-3,5-heptanediol* (**12a**): Ca. 10 mg of 5% Rh on alumina was stirred in 5 ml of anhydrous ethanol under hydrogen. 160 mg (1.0 mmol) of **11** was added and the suspension stirred until 24 ml of hydrogen had been absorbed (ca. 15 min). The catalyst was filtered and washed with 20 ml of ether. The combined organic phases were washed with 30 ml of saturated aqueous NH_4Cl solution, and the aqueous phase was back extracted three times with 20 ml each of ether. The combined organic phases were dried with Na_2SO_4 and concentrated. The residue was bulb-to-bulb distilled at 20 Torr from a bath of 140°C. The resulting oil (120 mg, 75%) was a 85:15 mixture of diastereomers. Separation was achieved by flash chromatography with petroleum ether (40–60°C)/ether (1:1) over a column with 16 cm of silica gel.

(3*R**,5*S**)-**12a**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.85 (d, *J* = 6.8 Hz, 12H), 1.27–1.52 (m, 2H), 1.52–1.66 (m, *J* = 6.8 Hz, 2H), 3.36 (br. s, 2H), 3.55 (ddd, *J* = 10.2, 5.1, and 1.8 Hz, 2H); cf. ref.[27,28]. – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.3, 18.3, 34.2, 35.8, 78.1.

$C_9H_{20}O_2$ (160.3) Calcd. C 67.45 H 12.58
Found C 67.37 H 12.81

(3*R**,5*R**)-**12b**: M.p. 74–75°C (cf. 71–72°C[27,29], 79–81°C[18,28]). – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.8 Hz, 6H), 0.95 (d, *J* = 6.7 Hz, 6H), 1.58 (dd, *J* = 6.4 and 5.2 Hz, 2H), 1.70 (m, *J* = 6.7 Hz, 2H), 2.26 (br. s, 2H), 3.63 (m, 2H); cf. ref.[18,27,29]. – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.9, 18.6, 33.7, 36.5, 74.1; cf. ref.[18].

10. *(4R*,6S*)-4,6-Diisopropyl-2,2-dimethyl-1,3-dioxane* (**13a**): To a solution of 3.0 ml (24 mmol) of 2,2-dimethoxypropane in 4.0 ml of anhydrous dimethylformamide were added ca. 10 mg of *p*-toluenesulfonic acid and 320 mg (2.0 mmol) of the above diastereomeric mixture of **12**. After stirring at room temp. for 20 h 20 ml of saturated aqueous $NaHCO_3$ solution was added. The organic phases were separated, and the aqueous phase was extracted three times with 20 ml each of ether. The combined organic phases were dried with Na_2SO_4 and concentrated. The residue was purified by flash chromatography with petroleum ether (40–60°C)/ether (50:1) over a column with 16 cm of silica gel to give 380 mg (95%) of **13a** as a colorless liquid.

$C_{12}H_{24}O_2$ (200.3) Calcd. C 71.95 H 12.08
Found C 72.20 H 12.18

(4*R**,6*S**)-**13a**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.8 Hz, 6H), 0.90 (d, *J* = 6.7 Hz, 6H), 1.07 (q, *J* = 11.8 Hz, 1H), 1.36 (s, 3H), 1.38 (s, 3H), 1.45 (dt, *J* = 12.6 and 2.5 Hz, 1H), 1.59 (m, 2H), 3.44 (ddd, *J* = 11.5, 6.7, and 2.4 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.7, 18.5, 19.8, 30.3, 30.33, 33.2, 74.1, 98.1.

(4*R**,6*R**)-**13b**: ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.7, 18.9, 24.4, 33.0, 34.4, 72.0, 100.1.

11. *3-[3-Methyl-2-(trimethylsilyloxy)butyl]-1-oxaspiro[2.5]octane* (**19**): 997 mg (3.0 mmol) of **4** was allowed to react with 0.47 g (4.5 mmol) of cyclohexanone as described under 6. Flash chromatography with petroleum ether (40–60°C)/ether (95:5) gave 750 mg (91%) of **19**. GC (180°C) revealed it to be a 83:17 mixture of diastereomers.

$C_{15}H_{30}O_2Si$ (270.5) Calcd. C 66.61 H 11.18
Found C 66.83 H 11.17

Major diastereomer, presumably (2*R**,2′*S**)-**19a**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.12 (s, 9H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H), 1.47–1.78 (m, 13H), 2.86 (t, *J* = 6.1 Hz, 1H), 3.58 (dt, *J* = 6.8 and 5.0 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 18.0, 18.4, 24.8, 24.9, 25.8, 29.4, 32.5, 33.3, 35.6, 62.0, 62.2, 75.6.

19b: ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 17.7, 18.4, 24.8, 24.9, 25.8, 29.7, 31.8, 33.8, 35.8, 62.0, 62.9, 75.0.

12. *1-[1-Bromo-4-methyl-3-(trimethylsilyloxy)pentyl]cyclohexanol* (**18**): 664 mg (2.0 mmol) of **4** and 209 mg (3.0 mmol) of cyclohexanone were allowed to react as described under 7. Flash chromatography with petroleum ether (40–60°C)/ether (95:5) gave 461 mg (90%) of **18**. GC (180°C) revealed it to be a 82:18 mixture of diastereomers.

$C_{15}H_{31}BrO_2Si$ (351.4) Calcd. C 51.27 H 8.89
Found C 51.48 H 8.92

Presumably (1′*R**,3′*R**)-**18a**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.16 (s, 9H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H), 1.50–1.87 (m, 14H), 3.79 (ddd, *J* = 9.2, 4.5, and 2.3 Hz, 1H), 4.24 (dd, *J* = 10.8 and 2.6 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.7, 17.7, 18.3, 21.9, 22.1, 25.7, 33.6, 34.2, 36.4, 36.7, 70.1, 72.8, 75.8.

18b: ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.4, 15.1, 20.0, 21.9, 21.94, 25.7, 30.0, 33.6, 35.1, 38.3, 67.2, 72.6, 75.4.

13. *2-[3-Methyl-2-(trimethylsilyloxy)butyl]-1-oxaspiro[2.4]heptane* (**21**): 664 mg (2.0 mmol) of **4** and 190 mg (2.2 mmol) of cyclopentanone were allowed to react as described under 6. Flash chromatography with petroleum ether (40–60°C)/ether (92:8) gave 150 mg (30%) of **21** as a colorless oil.

$C_{14}H_{28}O_2Si$ (256.5) Calcd. C 65.57 H 11.00
Found C 65.53 H 11.07

Presumably (2′*R**,2*S**)-**21a**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.12 (s, 9H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 1.57–1.84 (m, 11H), 3.09 (t, *J* = 6.1 Hz, 1H), 3.59 (dt, br., 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.4, 18.0, 18.4, 25.1, 29.3, 33.4, 33.7, 34.7, 59.3, 68.9, 75.5.

14. *1-[1-Bromo-4-methyl-3-(trimethylsilyloxy)pentyl]cyclopentanol* (**20**): 997 mg (3.0 mmol) of **4** and 420 mg (4.5 mmol) of cyclopentanone were allowed to react as described under 7. Flash chromatography with petroleum ether (40–60°C)/ether (9:1) gave 450 mg (45%) of **21** as a colorless oil.

$C_{14}H_{29}BrO_2Si$ (337.4) Calcd. C 49.84 H 8.66
Found C 49.96 H 8.40

Presumably (1′*R**,3′*R**)-**20a**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.14 (s, 9H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 1.58–2.03 (m, 12H), 3.76 (ddd, *J* = 9.9, 5.2, and 1.8 Hz, 1H), 4.21 (dd, *J* = 11.3 and 1.9 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.7, 17.6, 18.3, 23.6, 24.9, 34.2, 36.8, 37.9, 42.3, 68.1, 75.5, 84.7.

15. *2-Isopropyl-3-[3-methyl-2-(trimethylsilyloxy)butyl]oxirane* (**23**): 664 mg (2.0 mmol) of **4** and 158 mg (2.2 mmol) of isobutyr-

aldehyde were allowed to react as described under 6. Flash chromatography with petroleum ether (40–60°C)/ethyl acetate (97:3) resulted in 190 mg (78%) of **23**. The ratio of diastereomers was determined by GC (100°C).

$C_{13}H_{28}O_2Si$ (244.5) Calcd. C 63.87 H 11.55
Found C 63.71 H 11.75

Major diastereomer, presumably (2*R**,3*S**,2′*R**)-**23a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.13 (s, 9H), 0.85–1.11 (m, 12H), 1.3–1.9 (m, 4H), 2.56 (dd, *J* = 9.3 and 4.3 Hz, 1H), 3.05–3.10 (m, 1H), 3.57–3.75 (m, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 18.0, 20.3, 27.2, 32.1, 33.4, 55.2, 62.4, 75.7.

23b: ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 18.0, 30.5, 33.1, 36.7, 55.0, 64.3, 75.4. – **23c**: 0.5, 18.0, 20.3, 27.5, 31.4, 34.0, 55.5, 63.4, 75.0. – **23d**: 0.5, 18.0, 30.5, 33.8, 36.4, 55.0, 64.5, 75.0.

16. *4-Bromo-2,7-dimethyl-6-(trimethylsilyloxy)-3-octanol* (**22**): 664 mg (2.0 mmol) of **4** and 216 mg (3.0 mmol) of isobutyraldehyde were allowed to react as described under 7. Flash chromatography with petroleum ether (40–60°C)/ether (9:1) gave 395 mg (61%) of **22** as a colorless oil. ^{13}C NMR revealed the presence of three diastereomers.

$C_{13}H_{29}BrO_2Si$ (325.4) Calcd. C 48.00 H 8.98
Found C 48.14 H 8.91

17. *2-[3-Methyl-2-(trimethylsilyloxy)butyl]-3-propyloxirane* (**24**): 332 mg (1.0 mmol) of **4** and 79 mg (1.0 mmol) of *n*-butyraldehyde were allowed to react as described under 6. Flash chromatography with petroleum ether (40–60°C)/ether (96:4) gave 210 mg (86%) of **24** as a colorless oil. The ^{13}C-NMR spectrum revealed the presence of four diastereomers.

$C_{13}H_{28}O_2Si$ (244.5) Calcd. C 63.87 H 11.55
Found C 63.67 H 11.56

18. *1-Bromo-4-methyl-1-(trimethylsilyl)-2-(trimethylsilyloxy)-pentane* (**25**): 332 mg (1.0 mmol) of **4** was allowed to react with 334 mg (1.5 mmol) of trimethylsilyl trifluoromethanesulfonate as described under 6. (successive method, A). Flash chromatography with petroleum ether (40–60°C) gave 277 mg (85%) of **25** as a 74:26 mixture of diastereomers (determined by ^{13}C NMR).

$C_{12}H_{29}BrOSi_2$ (325.4) Calcd. C 44.29 H 8.91
Found C 44.46 H 9.02

Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.15 (s, 9H), 0.20 (s, 9H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 1.65–1.75 (m, 3H), 3.43 (dd, *J* = 9.6 and 5.2 Hz, 1H), 3.80–3.87 (dt, *J* = 6.6 and 4.8 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = –2.9, 0.8, 18.2, 18.3, 34.2, 36.7, 42.2, 75.4.

Minor diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.14 (s, 9H), 0.15 (s, 9H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H), 1.76–1.90 (m, 2H), 1.94–2.05 (m, 1H), 3.16 (dd, *J* = 12.6 and 2.8 Hz, 1H), 3.90 (ddd, *J* = 9.0, 4.0, and 2.9 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = –3.1, 0.5, 14.7, 20.3, 29.6, 38.2, 40.5, 75.1.

19. *2-[1-Isopropyl-4-methyl-3-(trimethylsilyloxy)pentyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane* (**28**): To a solution of 1.0 g (3.0 mmol) of **4** and 510 mg (3.0 mmol) of 2-isopropyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**26**) in 15 ml of THF, 9 ml of ether, and 7.5 ml of petroleum ether (40–60°C) was added at –115°C 1.75 ml (3.0 mmol) of a 1.7 M solution of *n*-butyllithium in *n*-hexane over 15 min. After stirring at –115°C for 1 h the mixture was allowed to reach room temp. and then hydrolyzed by the addition of 40 ml of a saturated aqueous NH_4Cl solution. The phases were separated, and the aqueous phase was extracted three times with 30 ml each of ether. The combined organic phases were washed with brine, dried with $MgSO_4$, and concentrated. Chromatography of the residue over silica gel with petroleum ether (40–60°C)/ether (10:1) gave 600 mg (60%) of **28** as a 71:29 mixture of diastereomers (determined by ^{1}H NMR).

$C_{18}H_{39}BO_3Si$ (342.4) Calcd. C 63.14 H 11.48
Found C 63.10 H 11.32

(1′*R**,3′*R**)-**28a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.12 (s, 9H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 1.25 (br. s, 12H), 1.01–1.09 (m, 1H), 1.55–1.71 (m, 3H), 3.35 (ddd, *J* = 9.1, 4.3, and 2.7 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.77, 17.9, 18.1, 21.6, 22.4, 24.8, 25.2, 30.4, 33.0, 34.1, 78.0, 82.8.

The following signals of **28b** could be recorded: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 9H), 0.79 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 3.52 (ddd, *J* = 8.6, 6.1, and 3.0 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 15.1, 19.8, 25.0, 25.04, 29.6, 30.9, 33.8, 75.8, 82.8.

20. *2-[4-Methyl-1-phenyl-3-(trimethylsilyloxy)pentyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane* (**29**): To a solution of 1.0 g (3.0 mmol) of **4** in 10 ml of THF, 6 ml of ether, and 5 ml of petroleum ether (40–60°C) was added at –115°C over 15 min 2.0 ml of a 1.5 M solution of *n*-butyllithium in *n*-hexane. After stirring for 10 min a solution of 0.61 g (3.0 mmol) of 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**27**) in 1.5 ml of THF was added dropwise over 5 min. After stirring at –115°C for 2 h the mixture was allowed to reach –30°C and hydrolyzed by the addition of 30 ml of a saturated aqueous NH_4Cl solution. The mixture was extracted three times with 30 ml each of ether, and the combined organic extracts were washed with brine, dried with $MgSO_4$, and concentrated. The residual 1.16 g of a colorless oil was chromatographed over silica gel with petroleum ether (40–60°C)/ether (10:1) to give 0.91 g (80%) of **29** as a 73:27 mixture of diastereomers (determined by ^{1}H NMR).

$C_{21}H_{37}BO_3Si$ (376.4) Calcd. C 67.01 H 9.91
Found C 67.23 H 9.72

(1*R**,3*R**)-**29a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.10 (s, 9H), 0.77–0.88 (m, 6H), 1.17 (s, 6H), 1.19 (s, 6H), 1.60–1.75 (m, 1H), 2.02 (m, 2H), 2.47 (dd, *J* = 10.0 and 6.0 Hz, 1H), 3.39–3.45 (m, 1H), 7.09–7.25 (m, 5H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.8, 17.6, 18.5, 24.8, 24.9, 33.3, 36.9, 77.6, 83.4, 125.3, 128.0, 143.8.

(1*R**,3*S**)-**29b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 9H), 0.77–0.88 (m, 6H), 1.16 (s, 6H), 1.25 (s, 6H), 1.60–1.75 (m, 1H), 2.02 (m, 2H), 1.84 (dd, *J* = 7.7 and 6.6 Hz, 1H), 3.39–3.45 (m, 1H), 7.09–7.25 (m, 5H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.82, 17.3, 18.2, 24.8, 25.1, 33.1, 34.8, 75.5, 84.0, 125.3, 128.0, 142.9.

21. *4-Methyl-1-phenyl-1,3-pentanediol* (**31**): 2.38 g (6.32 mmol) of **29** was dissolved in 30 ml of THF and treated at 0°C with 1 ml (9 mmol) of a 30% aqueous H_2O_2 solution and 9 ml of a 1 M aqueous sodium hydroxide solution for 3 h. 100 ml of a saturated aqueous NH_4Cl solution, 50 ml of ether, and solid NaCl were added until saturation. The mixture was extracted three times with 50 ml each of ether, the combined organic extracts were washed with brine, dried with $MgSO_4$, and concentrated. Chromatography of the residual 2.2 g of oil over silica gel with petroleum ether (40–60°C)/ether (5:1) gave 0.94 g (56%) of a 3:1 mixture of the 4-methyl-1-phenyl-3-(trimethylsilyloxy)-1-pentanols.

$C_{15}H_{26}O_2Si$ (266.5) Calcd. C 67.62 H 9.83
Found C 67.48 H 9.75

(1*R**,3*R**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.19 (s, 9H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H), 1.72–1.94 (m, 3H), 3.33 (d, *J* = 2.7 Hz, 1H), 3.70–3.77 (m, 1H), 4.99 (m, 1H),

7.23–7.41 (m, 5H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 18.1, 19.2, 33.0, 41.7, 71.2, 76.0, 125.6, 127.2, 128.4, 145.3.

(1*R**,3*S**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.22 (s, 9H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 7.0 Hz, 3H), 1.72–1.94 (m, 3H), 3.33 (d, *J* = 2.7 Hz, 1H), 3.90–3.97 (m, 1H), 4.84 (dd, *J* = 6.4 and 2.9 Hz, 1H), 7.23–7.41 (m, 5H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.6, 18.5, 18.6, 33.9, 39.8, 74.4, 78.2, 125.9, 127.4, 129.6, 144.8.

To a solution of 0.64 g (2.4 mmol) of the above alcohols in 10 ml of THF, was added 3.0 ml (3.0 mmol) of a 1 M solution of tetra-*n*-butylammonium fluoride in THF. After stirring for 2 h, 20 ml of a saturated aqueous NH_4Cl solution was added. The mixture was extracted five times with 15 ml each of ether. The combined organic extracts were washed with 30 ml of brine, dried with $MgSO_4$, and concentrated. The residue was purified by bulb-to-bulb distillation at 10^{-2} Torr from a bath of 180°C; yield: 450 mg (96%) of an oil as a 85:15 (^{13}C NMR) mixture of diastereomers.

$C_{12}H_{18}O_2$ (194.3) Calcd. C 74.19 H 9.34
Found C 74.14 H 9.37

The major diastereomer crystallized from the oil: m. p. 68–70°C. (1*R**,3*R**)-**31a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 1.64–1.91 (m, 3H), 3.62 (q, *J* = 5.8 Hz, 1H), 5.07 (t, *J* = 5.6 Hz, 1H), 7.27–7.40 (m, 5H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.4, 18.2, 33.7, 41.6, 71.8, 73.8, 125.5, 127.3, 128.5, 144.7.

(1*R**,3*S**)-**31b**: ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.7, 18.5, 34.2, 42.0, 75.6, 77.7, 125.7, 127.6, 128.5, 144.7.

22. *3-[3,3-Dimethyl-2-(trimethylsilyloxy)butyl]-2,2-dimethyloxirane* (**15**): 1.04 g (3 mmol) of **6** was allowed to react with 348 mg (6.0 mmol) of acetone as described under 6. (in situ method, **B**). Flash chromatography with petroleum ether (40–60°C)/ether (98:2) gave 660 mg (90%) of **15** as a colorless oil. GC (140°C) revealed it to be a 94:6 mixture of diastereomers.

$C_{13}H_{28}O_2Si$ (244.5) Calcd. C 63.87 H 11.55
Found C 63.90 H 11.55

(3*R**,2′*S**)-**15**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.14 (s, 9H), 0.87 (s, 9H), 1.27 (s, 3H), 1.33 (s, 3H), 1.54–1.84 (ABXY system J_{AB} = 17.6, J_{AX} = 8.9, J_{BY} = 7.2, J_{AY} = 5.3, J_{BX} = 3.0 Hz, 2H), 2.88 (dd, *J* = 7.2 and 5.3 Hz, 1H), 3.42 (dd, *J* = 8.9 and 3.0 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.7, 18.7, 25.0, 26.1, 32.6, 35.5, 57.9, 62.8, 79.3.

23. *2-[3,3-Dimethyl-2-(trimethylsilyloxy)butyl]-3-isopropyloxirane* (**16**/**17**): 346 mg (1.0 mmol) of **6** was allowed to react with 108 mg (1.5 mmol) of isobutyraldehyde as described under 6. (in situ method, **B**). Flash chromatography with petroleum ether (40–60°C)/ether (97:3) gave 160 mg (62%) of a mixture of **16** and **17**.

$C_{14}H_{30}O_2Si$ (258.5) Calcd. C 65.06 H 11.70
Found C 65.01 H 11.66

(2*S**,3*R**,2′R*)-**16**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.14 (s, 9H), 0.87 (s, 9H), 0.95 (d, *J* = 6.7 Hz, 3H), 1.1 (d, *J* = 6.6 Hz, 3H), 1.41–1.71 (m, 3H), 2.58 (dd, *J* = 9.4 and 4.2 Hz, 1H), 3.07 (dt, *J* = 6.0 and 4.2 Hz, 1H), 3.46 (dd, *J* = 8.0 and 3.8 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.8, 19.0, 20.3, 26.2, 27.0, 31.4, 35.5, 56.5, 62.9, 79.3.

(2*R**,3*R**,2′S*)-**17**: ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.8, 18.0, 26.2, 30.3, 35.5, 36.3, 56.5, 64.5, 79.0.

24. *(1′R*,3′R*)-2-[4,4-Dimethyl-1-phenyl-3-(trimethylsilyloxy)-pentyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane* (**30**): To a solution of 1.73 g (5.0 mmol) of **6** and 1.02 g (5.0 mmol) of 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**27**) in 10 ml of THF, 6 ml of ether, and 5 ml of petroleum ether (40–60°C) was added at –115°C over 15 min 3.45 ml (5.0 mmol) of a 1.45 M solution of *n*-butyllithium in *n*-hexane. After stirring for 1 h at –115°C the mixture was allowed to reach room temp. and hydrolysed by addition of 40 ml of a saturated aqueous NH_4Cl solution. The phases were separated, and the aqueous phase was extracted three times with 30 ml each of ether. The combined organic phases were washed with 30 ml of brine, dried with $MgSO_4$, and concentrated. The residual oil (2.08 g) was a 93:7 mixture of diastereomers according to ^{1}H-NMR spectrometry. The diastereomers were separated by chromatography over silica gel with petroleum ether (40–60°C)/ether (20:1).

1.26 g of (1′*R**,3′*R**)-**30a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.18 (s, 9H), 0.87 (s, 9H), 1.17 (s, 6H), 1.21 (s, 6H), 1.47 (ddd, *J* = 13.0, 9.6, and 3.4 Hz, 1H), 2.18 (td, *J* = 12.6 and 1.2 Hz, 1H), 2.54 (dd, *J* = 12.6 and 3.4 Hz, 1H), 3.28 (dd, *J* = 9.6 and 1.2 Hz, 1H), 7.08–7.27 (m, 5H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 1.2, 24.6, 25.0, 26.4, 35.7, 36.8, 81.5, 83.3, 125.2, 128.3, 128.4, 144.1.

$C_{22}H_{39}BO_3Si$ (390.4) Calcd. C 67.68 H 10.07
Found C 67.47 H 10.07

100 mg of (1′*R**,3′*S**)-**30b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 9H), 0.80 (s, 9H), 1.13 (s, 6H), 1.15 (s, 6H), 1.69 (ddd, *J* = 14.5, 9.5, and 3.2 Hz, 1H), 2.07 (ddd, *J* = 14.4, 12.3, and 1.7 Hz, 1H), 2.52 (dd, *J* = 12.2 and 3.2 Hz, 1H), 3.11 (dd, *J* = 9.5 and 1.6 Hz, 1H), 7.07–7.24 (m, 5H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 1.0, 24.4, 26.2, 32.8, 35.2, 79.0, 83.1, 124.9, 128.1, 128.4, 142.2.

25. *(1R*,3R*)-4,4-Dimethyl-1-phenyl-1,3-pentanediol* (**32**): 1.36 g (3.48 mmol) of **30** was oxidized as described under 21. to give 720 mg (74%) of (1*R**,3*R**)-4,4-dimethyl-1-phenyl-3-(trimethylsilyloxy)-1-pentanol. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.20 (s, 9H), 0.88 (s, 9H), 1.61–1.67 (m, 1H), 1.81 (ddd, *J* = 14.2, 10.8, and 2.2 Hz, 1H), 1.92 (d, *J* = 2.3 Hz, 1H), 3.73 (dd, *J* = 9.8, and 2.1 Hz, 1H), 4.84 (td, *J* = 10.8 and 2.6 Hz, 1H), 7.23–7.38 (m, 5H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.90, 26.4, 35.2, 42.2, 71.2, 77.6, 125.5, 127.4, 128.5, 145.9.

$C_{16}H_{28}O_2Si$ (280.5) Calcd. C 68.52 H 10.06
Found C 68.44 H 10.04

640 mg (2.3 mmol) of the above alcohol was desilylated as described under 21. to give 520 mg of crude **32** as a solid. The material was purified by sublimation at 10^{-2} Torr from a bath of 180°C; yield 430 mg (91%) of **32**, m. p. 128–129°C. – ^{1}H NMR (300 MHz, $CDCl_3$ + D_2O): δ = 0.87 (s, 9H), 1.82 (ddd, *J* = 14.4, 10.2, and 3.6 Hz, 1H), 1.91 (ddd, *J* = 14.4, 7.3, and 2.4 Hz, 1H), 3.49 (dd, *J* = 10.3 and 2.4 Hz, 1H), 5.07 (dd, *J* = 7.3 and 3.6 Hz, 1H), 7.25–7.40 (m, 5H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 34.7, 39.4, 71.9, 76.2, 125.5, 127.2, 128.4, 144.8.

$C_{13}H_{20}O_2$ (208.3) Calcd. C 74.96 H 9.68
Found C 74.66 H 9.69

CAS Registry Numbers

2: 132157-15-4 / **3**: 132157-16-5 / **4**: 116212-34-1 / **5**: 132157-17-6 / **6**: 116212-33-0 / **9a**: 132157-18-7 / **9b**: 132157-19-8 / **10a**: 116212-25-0 / **10b**: 116212-26-1 / **11a**: 132157-34-7 / **11b**: 132157-35-8 / **12a**: 65534-62-5 / **12b**: 103668-43-5 / **13a**: 124781-54-0 / **13b**: 132157-36-9 / **15** (*R*,S** isomer): 116212-23-8 / **15** (*R*,R** isomer): 116212-24-9 / **16**: 116212-31-8 / **17**: 116296-84-5 / **18a**: 132157-26-7 / **18b**: 132157-27-8 / **19a**: 132157-20-1 / **19b**: 132157-21-2 / **20a**: 132157-24-5 / **20b**: 132157-25-6 / **21a**: 132157-22-3 / **21b**: 132157-23-4 / **22a**: 132157-28-9 / **22b**: 132203-60-2 / **22c**: 132203-61-3 / **23a**: 116212-32-9 / **23b**: 116296-86-7 / **23c**: 116296-83-4 / **23d**: 116296-87-8 / **24a**: 132157-29-0 / **24b**: 132203-62-4 / **24c**: 132203-63-5 / **24d**: 132203-64-6 / **25** (isomer 1): 132157-30-3 / **25** (isomer 2): 132157-31-4 / **26**: 76347-13-2 / **27**: 24388-23-6 / **28a**:

132157-32-5 / **28b**: 132157-33-6 / **29a**: 116212-30-7 / **29b**: 116212-29-4 / **30a**: 116212-28-3 / **30b**: 116212-27-2 / **31a**: 103668-44-6 / **31b**: 103668-49-1 / **32**: 132157-40-5 / TMS triflate: 27607-77-8 / TMS-imidazole: 18156-74-6 / 1-bromo-3-methyl-2-butene: 870-63-3 / dibromomethane: 74-95-3 / *tert*-butyloxirane: 2245-30-9 / acetone: 67-64-1 / cyclohexanone: 108-94-1 / cyclopentanone: 120-92-3 / isobutyraldehyde: 78-84-2 / *n*-butyraldehyde: 123-72-8 / (1*R**,3*R**)-4-methyl-1-phenyl-3-(trimethylsilyloxy)-1-pentanol: 132157-37-0 / (1*R**,3*S**)-4-methyl-1-phenyl-3-(trimethylsilyloxy)-1-pentanol: 132157-38-1 / (1*R**,3*R**)-4,4-dimethyl-1-phenyl-3-(trimethylsilyloxy)-1-pentanol: 132157-39-2

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