Chiral Organometallic Reagents, III[1)]

On the Configurational Stability of α-Bromoalkyllithium Compounds

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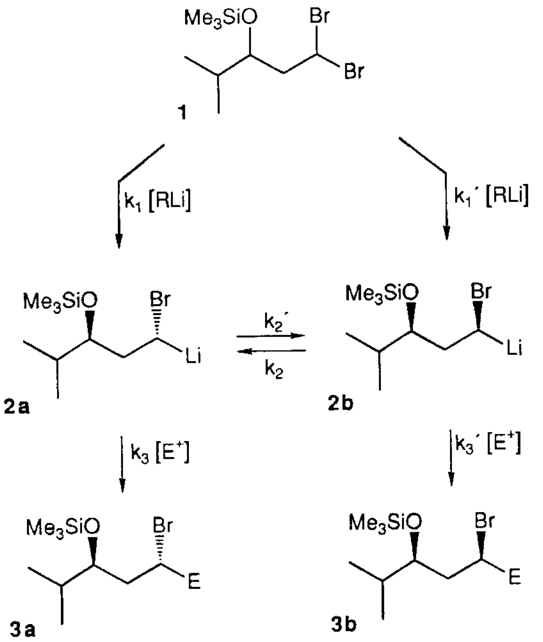
The carbenoids 2 undergo at −110°C a bromine/lithium exchange reaction with 1,1-dibromo alkanes. This leads to partial equilibration of the carbenoids 2 during their generation from the 1,1-dibromo compound 1. In the absence of the precursor 1, the carbenoids 2 have been found to be configurationally stable at −110°C.

Diastereoselectivity in the formation of the products **3** from the dibromo compound **1** via the diastereomeric carbenoids **2**[2)] depends on the relative magnitude of the various rate constants for (a) the kinetic diastereoselectivity in the exchange of the diastereotopic bromine atoms in **1** (= k_1), (b) the epimerisation of the carbenoids **2** (= k_2) and (c) the trapping of the carbenoids **2** by electrophiles (= k_3). We report here on investigations to gain a better understanding of the mechanistic aspects of this reaction.

Scheme 1

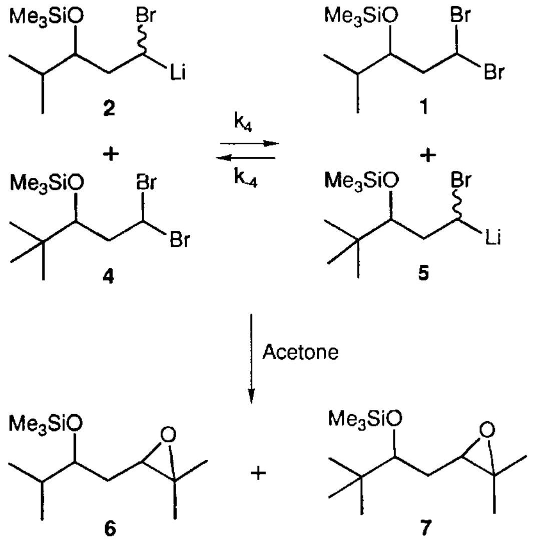


E^+ = Electrophile

Equilibration of the Carbenoids 2 Mediated by the Dibromo Compound 1

Seyferth has shown many years ago[3)] that α-bromocyclopropyllithium compounds undergo bromine/lithium exchange with their precursor, the 1,1-dibromocyclopropanes. This results in an equilibration of the diastereomeric α-bromo*cyclopropyl*lithium compounds during their generation[1,4)]. An analogous equilibration of the α-bromo*alkyl*lithium compounds **2** during their generation from the dibromo compound **1** may be one of the factors that affect the diastereomer ratio of the products **3**. In order to prove or disprove the occurrence of such an exchange reaction we have treated the carbenoids **2** with one equivalent of the dibromo compound **4** at −100°C in a Trapp solvent mixture[5)].

Scheme 2



The mixture is quenched after 10 min by addition of acetone to give both epoxides **6** and **7**, the latter predominating slightly. Thus, the bromine exchange between the carbenoids **2** and the dibromo compound **4** has occurred to a substantial extent already during 10 min at −100°C. Therefore, partial equilibration of the carbenoids **2** should have occurred during their generation from the dibromo compound

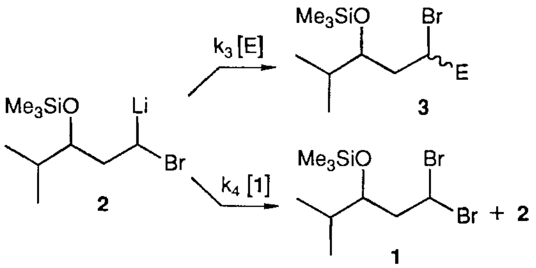
1. The product ratios of **3** (68:32 to 73:27) obtained by reaction of pregenerated carbenoids **2** with electrophiles (methods A and D in ref.[2]) may therefore not represent the kinetic diastereoselectivity in the exchange of the diastereotopic bromine atoms in **1**. Higher butyllithium concentrations or a more rapid addition of butyllithium should give rise to less equlilbrateted mixtures of the carbenoids. The variations in the diastereomer ratios of all the experiments carried out by method A[2] 68:32 to 74:26 (cf. p. 1245) therefore reflect the reproducibility of the experiments, i.e. variations in the extent to which equilibration of **2** has occurred during the generation of the carbenoids[2].

One other variable is the order of the addition of the reagents. Generation of the carbenoids **2** by inverse addition of the dibromo compound **1** to butyllithium followed by trapping with acetone or cyclohexanone (method D) gives the adducts **3** in the same ratio as method A (cyclohexanone) or a slightly increased ratio (acetone). In fact, the chances for partial equilibration of the carbenoids **2** by reaction with the dibromo compound **1** should to a first approximation not depend on the order of addition of the reagents.

If the product ratios of **3** represent *fully* equilibrated carbenoids, the product ratios of all experiments carried out by method A[2] should be the same, provided that the carbenoids **2a** are configurationally stable in the absence of their precursor **1**. That the latter condition is indeed fulfilled will be shown below.

Product mixtures approaching the kinetic diastereoselectivity in the exchange of diastereotopic bromine atoms may be obtained by in situ trapping of the carbenoids with electrophiles as has been found in a different study[1]. The data on p. 1245 show that indeed higher product ratios (ca. 84:16) result for the in situ trapping (method B[2]) of **2** by acetone or cyclohexanone[6]. The extent of partial equilibration of the carbenoids **2** during their generation is essentially limited by the competitive situation outlined in Scheme 3.

Scheme 3



Provided that $k_3[E]/k_4[\mathbf{1}] \geq 10$ throughout the major part of the reaction the diastereomer ratio of **3** would represent the kinetic diastereoselectivity of the reaction of the dibromo compound **1** with butyllithium. The ultimate way to render $k_3[E] \gg k_4[\mathbf{1}]$ would be to use a reversed in situ technique, i.e. to add a mixture of **1** and the ketone (electrophile) to *n*-butyllithium (method C, ref.[2]). The product ratios reported on p. 1245 show that method C affords essentially the same results (ca. 82:18) for trapping of **2** by acetone or cyclohexanone as by means of method B. The fact that both in situ and reverse in situ trapping of **2** by the ketones give the same diastereomer ratio of ca. 82:18 suggests that the condition $k_3[E] > k_4[\mathbf{1}]$ is fulfilled and that this value reflects the true kinetic diastereoselection in the exchange of the diastereotopic bromine atoms of **1**.

If $k_3[E]$ becomes smaller than $k_4[\mathbf{1}]$ the differences in the product ratios between the in situ trapping and the sequential trapping should vanish as the electophile is no longer reactive enough to suppress the equilibration of the carbenoids during their generation. This appears to hold for the trapping of **2** by TMS-imidazole, for which methods A–C lead to identical product ratios of 73:27[2]. This situation may also apply to the trapping by the isopropylboronate (**26**, p. 1245[2]) but it is doubtful whether this also holds for the trapping by the aldehydes (cf. ref.[2]). In fact, aldehydes should have a higher k_3 than ketones. However, it is not the value of a single rate constant, but rather the term $k_3[E]/k_4[\mathbf{1}]$, which controls the level of carbenoid equilibration. It is likely that the aldehyde is so reactive, that it already intercepts part of the butyllithium in the in situ experiments. This does not only lead to a decrease of the concentration of the aldehyde [E], but also to a decrease of that of the butyllithium to the effect that the carbenoids **2** are more slowly generated. As a consequence, the concentration of the dibromo compound **1** decreases more slowly and may not even go to zero in the in situ experiments. All of this may render the term $k_3[E]/k_4[\mathbf{1}]$ smaller than 10 or even smaller than 1 as the reaction progresses. This may account for the at first sight puzzling phenomenon, that in situ trapping of the carbenoids **2** by isobutyraldehyde does not lead to the "expected" 82:18 product ratio.

Kinetic Selectivity in the Exchange of the Diastereotopic Bromine Atoms of 1

The selectivity in the exchange of the diastereotopic bromine atoms of **1** should depend on the nature of the organolithium compound RLi. Once it has been established that in situ trapping of the carbenoids **2** by acetone essentially suppresses equilibration of **2** by bromine/lithium exchange with **1**, it is possible to test various organolithium compounds with respect to their ability to discriminate the bromine atoms of **1**.

Scheme 4

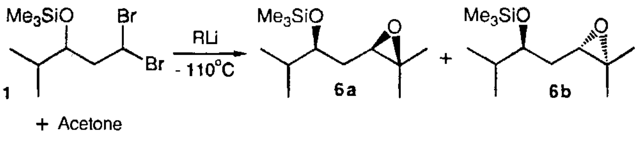


Table 1 records the ratio of the epoxides **6a** and **6b** obtained by in situ trapping of the carbenoids **2**, generated by various organolithium compounds. The more reactive *tert*-butyllithium has been found to be the least selective. In terms of preparative aspects, *n*-butyllithium turns out to be the most efficient reagent.

Table 1. Kinetic selectivity in the exchange of the diastereotopic bromine atoms of **1** by in situ trapping of **2** with acetone

RLi	Product ratio **6a**:**6b**
McLi	81:19
*n*BuLi	80:20
PhLi	73:27
*s*BuLi	72:28
*t*BuLi	60:40

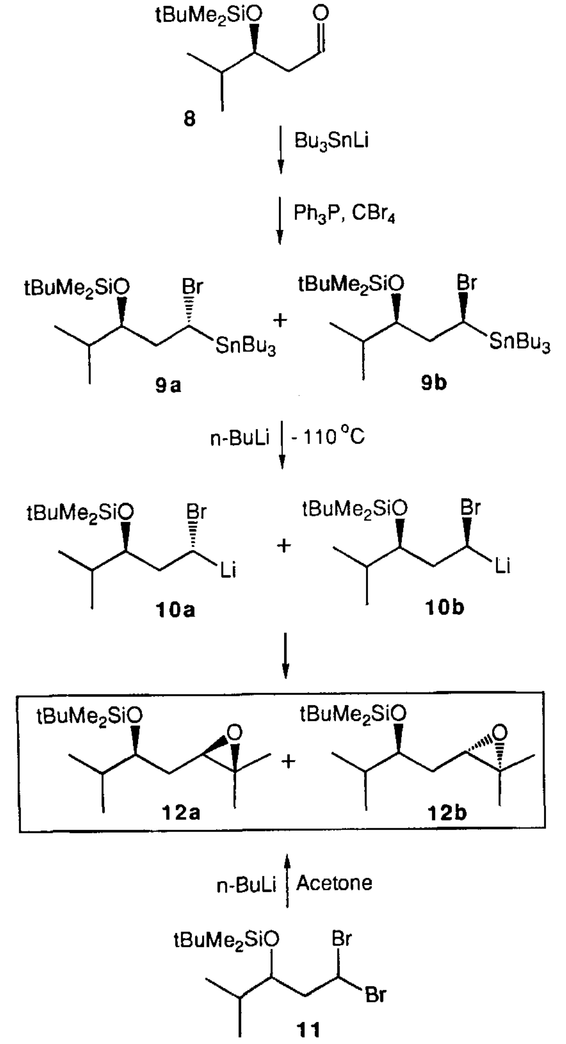
Configurational Stability of the α-Bromoalkyllithium Compounds 2

The statement of configurational stability is always related to a time scale. The interpretation of the data in Table 1 suggests that relative to the rate of being trapped by acetone the carbenoids **2** do not equilibrate to a significant extent (otherwise the product ratios **6a**/**6b** in Table 1 should be constant). Furthermore, it has been shown[7] by a different test that simple α-bromoalkyllithium compounds add to aldehydes at −120°C faster than they undergo enantiomer equilibration. To get information on the configurational stability of **2** on a macroscopic time scale, we have prepared[8] the diastereomeric tin compounds **9**.

By HPLC separation of the 65:35 diastereomer mixture one isomer (**9a**) is available in >97% purity, the other (**9b**) is enriched to about 85%. The isomeric compounds **9** are separatley subjected to a tin/lithium exchange[8] with *n*-butyllithium at −110°C. Addition of acetone after 10 min leads to the epoxides **12**. From the reaction of **9a** 79% of the epoxide **12a** of 99% diastereomeric purity is obtained. In turn, the reaction of the isomer **9b** (containing 15% of **9a**) leads to the epoxides **12**, with **12b** predominating by 75%. The yield is, however, surprisingly low (39%). Perhaps the tributyltin group in **9a** is in a topos which is preferentially attacked by *n*-butyllithium, cf. the reaction of **11** with *n*-butyllithium described below. In **9b**, however, it is the bromine atom which is in that position, where exchange is preferred. Since tin/lithium exchange is only slightly faster than bromine/lithium exchange[8], the latter may be a major side reaction on treatment of **9b** with *n*-butyllithium, accounting for the low yield of **12b**.

The epoxides **12** have also been prepared for reference purposes from the dibromo compound **11**. They are ob-

Scheme 5



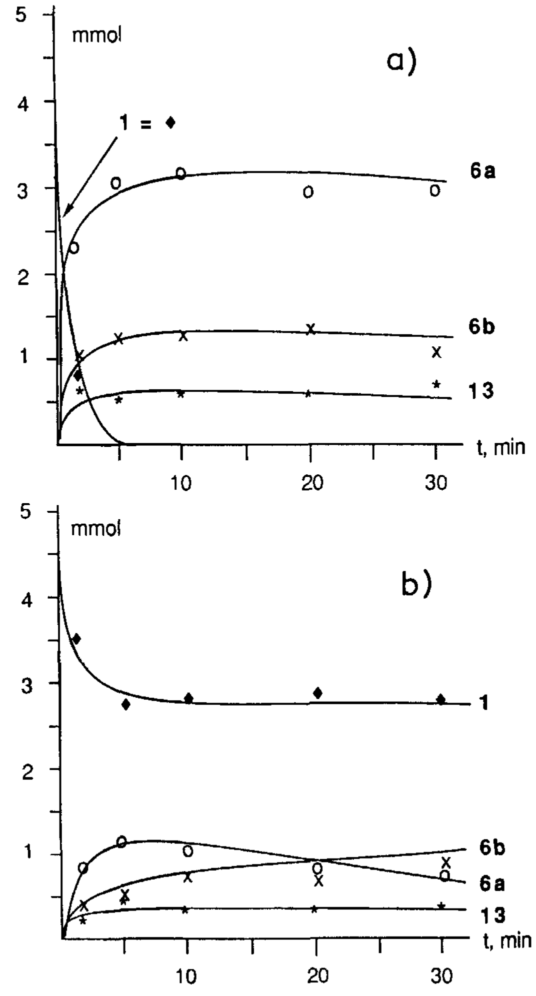
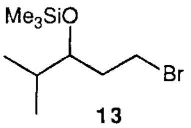


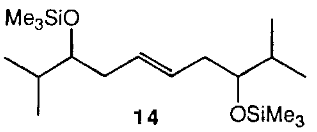
Figure 1. Time dependence of the products on the reaction of **1** with a) 1.5 equivalents of *n*BuLi and b) with 0.6 equivalents of *n*BuLi

tained in 88% yield in an 80:20 ratio by situ trapping of the carbenoids with acetone. The structures of the diastereomers of **12** are assigned by desilylation to the epoxy alcohols, which are independently generated from the silylated epoxy alcohols **6** obtained from **1**[2]. The structural assignment of the isomeric tin compounds **9** is based on that of the epoxides **12**, taking into account that tin/lithium exchange has been shown to occur with retention of configuration[9].

These experiments demonstrate that the α-bromoalkyllithium compound **10a** is configurationally stable for at least 10 min at −110°C, and indicate that the same may hold for its epimer **10b**. These results have encouraged us to perform a direct test of the configurational stability of a mixture of carbenoids **2**. To this end a solution of **1** in a Trapp solvent mixture[5] is converted to the carbenoids **2** by reaction with 1.5 equivalents of *n*-butyllithium. Aliquots containing an internal standard are ejected at representative time intervals into precooled (−110°C) acetone/THF. The products, in particular the diastereomer composition of the epoxides **6** are analysed by gas chromatography.



13



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Quenching after 0 and 2 min reveals the presence of residual dibromo compound **1**. After 5 min, the bromine/lithium exchange is complete. The bromo compound **13** is found in all the samples to ca. 10%, be it formed by adventitious moisture in the acetone or by deprotonation of the acetone. Traces (< 3%) of the dimer **14** have also been found, which is formed as the major product upon warming of solutions of **2** to −60°C. The amounts of the products are plotted as a function of the time between the generation and trapping of the carbenoids **2** in Figure 1a). The essentially constant ratio of **6a**/**6b** (ca. 71:29) corresponds to that found by method A in ref.[2] and indicates the configurational stability of the carbenoids **2** over the period investigated, provided the ratio does not respresent the equilibrium value. In order to test this, a second, otherwise identical experiment has been carried out using only 0.6 equivalents of *n*-butyllithium. Apart from remaining **1**, the time dependence of the products recorded in Figure 1b) revealed the ongoing equilibration of the carbenoids via the dibromo compound **1**. Actually, the **6a**/**6b** ratio reaches a maximum of 74:26 after 2 min and decreases constantly, inverting after 20 min in an approach to an equilibrium, in which **2b** is favored over **2a**.

In summary, we have shown that the carbenoids **2** equilibrate within 20−30 min at −110°C in the presence of their precursor dibromo compound **1**. In the absence of the latter they are configurationally stable.

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Experimental

All temperatures quoted are not corrected. — ^{1}H, ^{13}C NMR: Bruker AC 300. — Analytical gas chromatography: Siemens Sichromat 3 with a 30-m capillary column, SE 52. — Preparative gas chromatography: Wilkens Aerograph A-90-P3, 1.5 m × 0.63 cm column with 5% apiezon on Chromosorb G, AW-DMCS 60−80 mesh. — Column chromatography: Silica gel 60 (0.063−0.200 mm, Merck). — Flash chromatography: silica gel 60 (0.040−0.063 mm, Merck). — Preparative HPLC: Merck-Hitachi; Lichrosorb RP-18-10.

1. *Bromine/lithium Exchange between the Carbenoid* **2** *and 1,1-Dibromo-4,4-dimethyl-3-(trimethylsilyloxy)pentane* (**4**): To a solution of 166 mg (0.5 mmol) of 1,1-dibromo-4-methyl-3-(trimethylsilyloxy)pentane (**1**) in 5 ml of a Trapp solvent mixture[5] was added at −100°C 0.41 ml (0.6 mmol) of a 1.46 M solution of *n*-butyllithium in hexane. After stirring for 10 min, a solution of 173 mg (0.5 mmol) of 1,1-dibromo-4,4-dimethyl-3-trimethylsilyloxypentane (**4**) in 5 ml of a Trapp solvent mixture was added dropwise. After stirring for 10 min, 58 mg (1.0 mmol) of acetone was added. The mixture was stirred for 1 h at −100°C. After reaching room temp., the mixture was poured onto 50 ml of a saturated aqueous NH_4Cl solution. The phases were separated, and the aqueous phase was extracted twice with 20 ml each of ether. The combined organic phases were washed with 50 ml of brine, dried with $MgSO_4$ and concentrated in vacuo. The crude product was analysed by gas chromatography (120−180°C) which showed the presence of both diastereomers of **6** as well as of both diastereomers of **7**.

2. *Kinetic Diastereoselectivity of in situ Trapping of the Carbenoids* **2** *Generated by Bromine/Lithium Exchange in* **1** *by Different Organolithium Compounds:* To a solution of 166 mg (0.5 mmol) of **1** and of 58 mg (1.0 mmol) of acetone in 5 ml of a Trapp solvent mixture[5] was added at −110°C one equivalent of the organolithium compound in 20 ml of a Trapp solvent mixture. After stirring for 1 h at −110°C, the mixture was allowed to reach room temp. and was processed as described under 1.

3. *4-(tert-Butyldimethylsilyloxy)-5-methyl-1-hexene:* A solution of 1.14 g (10.0 mmol) of 4-hydroxy-5-methyl-1-hexene in 10 ml of anhydrous THF was treated with 1.15 g (10.0 mmol) of a 35% suspension of potassium hydride in white oil. After the hydrogen evolution had ceased, 1.43 g (9.5 mmol) of *tert*-butylchlorodimethylsilane was added. The mixture was allowed to react for ca. 15 h and then hydrolysed by careful addition to 20 ml of saturated aqueous NH_4Cl solution. The phases were separated, and the organic phase was washed with 20 ml of saturated aqueous NH_4Cl solution. The combined aqueous phases were extracted twice with 10 ml each of ether, and the combined organic phases were washed with 30 ml of brine, dried with $MgSO_4$, and concentrated. The residual oil (2.30 g) was purified by chromatography with petroleum ether (40−60°C) on 80 g of silica gel to give 1.22 g (56%) of 4-(*tert*-butyldimethylsilyloxy)-5-methyl-1-hexene. — ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.04 (s, 3H), 0.05 (s, 3H), 0.86 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.93 (s, 9H), 1.69 (sept d, J = 6.8 and 4.6 Hz, 1H), 2.17−2.22 (m, 2H), 3.45−3.50 (m, 1H), 4.90−5.07 (m, 2H), 5.75−5.89 (m, 1H). — ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.6, −4.2, 17.3, 18.2, 18.5, 25.9, 32.6, 38.6, 76.6, 116.3, 135.9.

$C_{13}H_{28}OSi$ (228.5)	Calcd.	C 68.35 H 12.35
	Found	C 68.40 H 12.57

4. *3-(tert-Butyldimethylsilyloxy)-4-methylpentanal* (**8**): Into a solution of 11.42 g (50.0 mmol) of 4-(*tert*-butyldimethylsilyloxy)-5-methyl-1-hexene in 50 ml of anhydrous CH_2Cl_2 was introduced at −78°C a stream of ozone. After the blue color persisted, an excess

of ozone was removed by a stream of nitrogen. 3.90 g (60 mmol) of zinc and 7.7 ml of acetic acid were added. The mixture was allowed to reach room temp. with vigorous stirring, filtered and the filtrate was washed with 100 ml each of saturated aqueous $NaHCO_3$ solution until the aqueous phase was no longer acidic. The combined aqueous phases were washed with 20 ml of CH_2Cl_2. The combined organic phases were washed with 100 ml of saturated aqueous NH_4Cl solution which was back-extracted with 20 ml of CH_2Cl_2. The combined organic phases were washed with 100 ml of brine, dried with $MgSO_4$, and concentrated. The crude product (11.80 g) was chromatographed on 200 g of silica gel with petroleum ether (40 – 60 °C)/ether (4:1) to give 10.37 g (90%) of **8**. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 3H), 0.03 (s, 3H), 0.88 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 7.8 Hz, 3H), 0.88 (s, 9H), 1.74 – 1.82 (m, 1H), 2.39 – 2.57 (ABXY system, J_{AB} = 15.7, J_{AX} = 7.0, J_{BX} = 4.6, J_{AY} = 3.0, J_{BY} = 3.1 Hz, 2H), 4.03 (dt, J = 7.0 and 4.6 Hz, 1H), 4.03 (dd, J = 3.0 and 2.0 Hz, 1H), 9.82 (dd, J = 2.1 and 2.0 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.6, –4.5, 17.2, 18.1, 25.8, 34.0, 47.3, 72.5, 202.7.

5. *1-Bromo-3-(tert-butyldimethylsilyloxy)-4-methyl-1-(tributylstannyl)pentane* (**9**): Lithium diisopropylamide was generated at 0°C from 2.02 g (20 mmol) of diisopropylamine in 40 ml of anhydrous THF with 13.7 ml (21 mmol) of a 1.53 M solution of *n*-butyllithium in hexane. After cooling to –78 °C, 5.80 g (20 mmol) of tributyltin hydride was added. After 20 min, a solution of 4.61 g (20 mmol) of **8** in 5 ml of anhydrous THF was added dropwise. Stirring was continued at –78 °C for 1 h. Then the mixture was allowed to reach room temperature. It was washed twice with 150 ml each of saturated aqueous NH_4Cl solution. The aqueous phases were back-extracted twice with 50 ml each of ether. The combined organic phases were washed with 200 ml of brine, dried with $MgSO_4$, and concentrated. The residual oil (10.1 g) was dissolved in 150 ml of anhydrous CH_2Cl_2. 6.63 g (20 mmol) of tetrabromomethane and 5.24 g (20 mmol) of triphenylphosphane were added. After stirring for 4 h, the mixture was processed as described above. The crude products were triturated three times with 50 ml each of petroleum ether (40 – 60 °C). The combined organic phases were chromatographed on 250 g of silica gel with petroleum ether (40 – 60 °C) to give 6.15 g (53%) of **9** as a 67:33 diastereomeric mixture.

$C_{24}H_{53}BrOSiSn$ (584.4) Calcd. C 49.33 H 9.14
Found C 49.48 H 9.10

The diastereomers were separated by preparative HPLC using methanol/water (20:1). The faster eluting (1*R**,3*R**)-**9a** was obtained pure. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 3H), 0.08 (s, 3H), 0.70 – 1.05 (m, 30H), 1.20 – 1.36 (m, 6H), 1.38 – 1.58 (m, 6H), 1.64 – 1.95 (m, 3H), 3.68 – 3.84 (m, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = –3.7, –3.9, 9.6, 13.5, 16.4, 17.9, 18.1, 26.0, 27.2, 28.8, 33.6, 36.2, 39.2, 74.0.

The other diastereomer (1*R**,3*S**)-**9b** was enriched to only 85% by HPLC.

6. *Generation of the Individual α-Bromoalkyllithium Compounds* **10** *from the Pentanes* **9**: To 38 mg (65 μmol) of **9a** in 2 ml of a Trapp solvent mixture[5] was added at –110 °C by means of a syringe 127 μl (195 μmol) of a 1.53 M solution of *n*-butyllithium in *n*-hexane. After stirring for 20 min, 11.6 mg (0.2 mmol) of acetone was added, and the mixture was allowed to reach room temperature and was processed as described under 1. The crude oxiranes **12** were purified by flash chromatography with petroleum ether (40 – 60 °C)/ether (95:5) to give 14 mg (ca. 80%) of (2*R**,3*S**)-3-[2-(*tert*-butyldimethylsilyloxy)-3-methylbutyl]-2,2-dimethyloxiranes **12** as a colorless oil. The diastereomer ratio was determined by GC (120 – 160 °C) to be 98.8:1.2.

A mixture of **9b** and **9a** (85:15) was treated exactly as above to give 6 mg (ca. 30%) of a mixture of **12b**/**12a** = 75:25. The products were identified by a comparison with the material described under 8.

7. *1,1-Dibromo-3-(tert-butyldimethylsilyloxy)-4-methylpentane* (**11**): 1.30 g (5.0 mmol) of 1,1-dibromo-4-methyl-3-pentanol[2], 67 mg (10 mmol) of imidazole, 90 mg (6.0 mmol) of *tert*-butylchlorodimethylsilane, and a few mg of 4-(dimethylamino)pyridine were dissolved in 5 ml of DMF. After stirring for 3 d, the solution was diluted with 50 ml of ether. It was washed with 50 ml each of saturated aqueous NH_4Cl solution until the aqueous phase was no longer alkaline. The combined aqueous phases were back-extracted twice with 30 ml of ether. The combined organic phases were washed with 50 ml of brine, dried with $MgSO_4$, and concentrated. The residual oil was chromatographed on 70 g of silica gel with petroleum ether (40 – 60 °C)/ether (9:1) to give 1.64 g of the crude product which contained some 1,3-di-*tert*-butyl-1,1,3,3-tetramethyldisiloxane. The latter contaminant was removed by bulb-to-bulb distillation at 0.05 Torr from a bath of 80 – 120 °C, leaving behind 1.41 g (75%) of **11**. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 3H), 0.11 (s, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H), 0.90 (s, 9H), 1.80 (sept d, J = 6.9 and 3.6 Hz, 1H), 1.32 – 2.52 (ABXY system, J_{AB} = 14.4, J_{AX} = 10.1, J_{BY} = 9.1, J_{BX} = 3.7, J_{AY} = 3.1 Hz, 2H), 3.72 (dt, J = 9.1 and 3.6 Hz, 1H), 5.69 (dd, J = 10.1 and 3.7 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.5, –4.3, 16.2, 17.9, 18.1, 25.9, 33.2, 44.5, 48.0, 74.9.

$C_{12}H_{26}Br_2OSi$ (374.2) Calcd. C 38.51 H 7.00
Found C 38.77 H 6.88

8. *3-[2-(tert-Butyldimethylsilyloxy)-3-methylbutyl]-2,2-dimethyloxiranes* (**12**): A solution of 748 mg (2.0 mmol) of **11** in 20 ml of a Trapp solvent mixture[5] and 290 mg (5.0 mmol) of acetone was treated at –110 °C with 1.25 ml (2.2 mmol) of a 1.75 M solution of *n*-butyllithium in *n*-hexane. The mixture was processed as described under 1. The crude product was purified by flash chromatography with CH_2Cl_2 to give 480 mg (88%) of a 80:20 mixture of **12a** and **12b**.

$C_{15}H_{32}BrO_2Si$ (272.5) Calcd. C 66.11 H 11.84
Found C 66.06 H 11.97

(2′*R**,3*S**)-**12a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 3H), 0.07 (s, 3H), 0.89 (d, J = 6.8 Hz, 3H), 0.90 (s, 9H), 0.92 (d, J = 6.7 Hz, 3H), 1.27 (s, 3H), 1.33 (s, 3H), 1.55 – 1.82 (m, 3H), 2.89 (t, J = 6.1 Hz, 1H), 3.62 (dt, J = 6.2 and 5.0 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.5, 17.8, 18.0, 18.1, 18.9, 24.9, 25.9, 32.7, 33.1, 57.8, 61.7, 75.1.

(2′*R**,3*R**)-**12b**: ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.5, 17.4, 17.6, 18.1, 19.1, 25.0, 25.9, 31.9, 33.6, 57.8, 62.3, 74.6.

9. *3-(2-Hydroxy-3-methylbutyl)-2,2-dimethyloxiranes*[10]: To a solution of 200 mg (0.73 mmol) of the oxiranes **12** in 10 ml of anhydrous THF was added 1.0 ml (1.0 mmol) of a 1 N solution of tetrabutylammonium fluoride in THF. After stirring at room temp. for 1 h, 10 ml of saturated aqueous NH_4Cl solution was added, and the mixture was extracted 5 times with 10 ml each of ether. The combined organic phases were dried with Na_2SO_4 and concentrated. The residue was purified by flash chromatography on a 16 × 2-cm column with petroleum ether (40 – 60 °C)/ether (1:1). The ^{1}H-NMR spectrum showed the diastereomer ratio (75:25) to be the same as that of the starting material **12**.

$C_9H_{18}O_2$ (158.2) Calcd. C 68.31 H 11.46
Found C 68.24 H 11.28

(2′*R**,3*S**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H), 1.28 (s, 3H), 1.32 (s, 3H), 1.48 (ddd, J = 14.4, 9.4, and 8.4 Hz, 1H), 1.71 (m, J = 6.7 Hz, 1H), 1.82 (ddd,

J = 14.4, 4.5, and 2.8 Hz, 1H), 2.29 (s, broad, 1H), 2.94 (dd, J = 8.2 and 4.5 Hz, 1H), 3.64 (m, broad, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.7, 18.5, 19.0, 24.8, 32.5, 33.8, 57.8, 63.3, 76.0.

(2′*R**,3*R**): ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.3, 18.8, 19.1, 24.9, 33.1, 34.0, 58.7, 62.1, 74.7.

A 85:15 mixture of the same diastereomeric epoxy alcohols was obtained by the above described procedure starting from a 85:15 mixture of the epoxides **6**.

10. *1-Bromo-4-methyl-3-(trimethylsilyloxy)pentane* (**13**): To a solution of 664 mg (2.0 mmol) of 1,1-dibromo-4-methyl-3-(trimethylsilyloxy)pentane (**1**) in 20 ml of a Trapp solvent mixture[5] was added at −110°C 1.40 ml (2.2 mmol) of a 1.56 M solution of *n*-butyllithium in hexane. After stirring for 20 min, 50 ml of saturated aqueous NH_4Cl solution was added. The mixture was worked up as described under 1. The crude product was purified by chromatography on 60 g of silica gel with CH_2Cl_2 to give 330 mg (65%) of **13**. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.14 (s, 9H), 0.86 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H), 1.70 (septd, J = 6.8 and 4.8 Hz, 1H), 1.81–2.01 (m, 2H), 3.36–3.55 (m, 2H), 3.60–3.70 (m, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 17.8, 18.1, 31.4, 33.5, 36.1, 75.0.

$C_9H_{21}BrOSi$ (253.3) Calcd. C 42.68 H 8.36
Found C 42.76 H 8.29

11. *2,9-Dimethyl-3,8-bis(trimethylsilyloxy)-5-decene* (**14**): To a solution of 1.66 g (5 mmol) of **1** in 60 ml of a Trapp solvent mixture[5] was added at −110°C 3.6 ml (5.5 mmol) of a 1.55 M solution of *n*-butyllithium in *n*-hexane. The mixture was warmed to −60°C for 4 h. Then the mixture was allowed to reach room temp.; 50 ml of saturated aqueous NH_4Cl solution was added, and the mixture was processed as described under 9. to give 300 mg (35%) of **14** as a diastereomeric mixture. For analysis, a sample was purified by gas chromatography (190°C).

$C_{18}H_{40}O_2Si_2$ (344.7) Calcd. C 62.72 H 11.70
Found C 62.88 H 11.77

Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.10 (s, 18H), 0.86 (d, J = 6.6 Hz, 12H), 1.56–1.69 (m, 2H), 2.15–2.20 (m, 4H), 5.43–5.47 (m, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 17.5, 19.0, 32.8, 37.9, 77.6, 129.2.

12. *Direct Evaluation of the Configurational Stability of the Carbenoids* **10**: 1.66 g (5.0 mmol) of **1** and 448 mg (1.67 mmol) of 2,6,10,14-tetramethylpentadecane as internal standard were dissolved in 50 ml of a Trapp solvent mixture[5]. To this mixture was added at −110°C 4.93 ml (7.5 mmol) of a 1.52 M solution of *n*-butyllithium in *n*-hexane (precooled to −78°C). Samples of about 5 ml were ejected by a bridge cooled to −115°C into a solution of 116 mg (2.0 mmol) of acetone in 2 ml of a Trapp solvent mixture at −110°C. To each sample was added 10 ml of saturated aqueous NH_4Cl solution. The phases were separated, and the aqueous phase was extracted twice with 5 ml of ether. The combined organic phases were washed with 20 ml of brine and dried with $MgSO_4$. The amounts of the products formed were determined without concentration of the solution by GC (120–220°C). A set of sample data is given in Table A.

Table A

Time [min]	**1** [mmol]	**13** [mmol]	**6a** [mmol]	**6b** [mmol]	**14** [mmol]
0	5.25	0.0	0.0	0.0	0.0
2	0.85	0.52	2.39	1.05	0.01
5	0.0	0.47	3.09	1.24	0.12
10	0.0	0.49	3.13	1.32	0.07
20	0.0	0.51	2.99	1.38	0.09
30	0.0	0.68	2.99	1.08	0.15

CAS Registry Numbers

1: 132047-52-0 / **2a**: 132047-53-1 / **2b**: 132047-54-2 / **4**: 132047-55-3 / **6a**: 132047-56-4 / **6b**: 132047-57-5 / **7** (isomer 1): 132047-58-6 / **7** (isomer 2): 132047-59-7 / **8**: 132047-61-1 / **10a**: 132079-46-0 / **10b**: 132047-68-8 / **12a**: 132047-62-2 / **12b**: 132047-63-3 / **13**: 132047-66-6 / **14** (isomer 1): 132047-67-7 / **14** (isomer 2): 132047-69-9 / MeLi: 917-54-4 / *n*BuLi: 109-72-8 / PhLi: 591-51-5 / *s*BuLi: 598-20-1 / *t*BuLi: 594-19-4 / 4-hydroxy-5-methyl-1-hexene: 32815-70-6 / 4-(*tert*-butyldimethylsilyloxy)-5-methyl-1-hexene: 132047-60-0 / (2′*R**,3*S**)-3-(2-hydroxy-3-methylbutyl)-2,2-dimethyloxirane: 132047-64-4 / (2′*R**,3*R**)-3-(2-hydroxy-3-methylbutyl)-2,2-dimethyloxirane: 132047-65-5

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[1] For Part II see: A. Schmidt, G. Köbrich, R. W. Hoffmann, *Chem. Ber.* **124** (1991) 1253, preceding paper.

[2] R. W. Hoffmann, M. Bewersdorf, M. Krüger, W. Mikolaiski, R. Stürmer, *Chem. Ber.* **124** (1991) 1243.

[3] D. Seyferth, R. L. Lambert, jr., *J. Organomet. Chem.* **55** (1973) C53.

[4] [4a] K. Kitatani, T. Hiyama, H. Nozaki, *Bull. Chem. Soc. Jpn.* **50** (1977) 3288. – [4b] T. Harada, K. Hattori, T. Katsuhira, A. Oku, *Tetrahedron Lett.* **30** (1989) 6035. – [4c] P. M. Warner, R. D. Herold, *J. Org. Chem.* **48** (1983) 5411. – [4d] A. Weber, R. Galli, G. Sabbioni, U. Stämpfli, S. Walther, M. Neuenschwander, *Helv. Chim. Acta* **72** (1989) 41.

[5] G. Köbrich, H. Trapp, *Chem. Ber.* **99** (1966) 670.

[6] The product ratios obtained on trapping of the carbenoids **2** with cyclopentanone in general and with phenylboronates by methods B and C were considered to be less reliable due to the low yields.

[7] R. W. Hoffmann, T. Ruhland, M. Bewersdorf, *J. Chem. Soc., Chem. Commun.*, in print.

[8] Y. Torisawa, M. Shibasaki, S. Ikegami, *Tetrahedron Lett.* **22** (1981) 2397.

[9] D. S. Matteson, P. B. Tripathy, A. Sarkar, K. M. Sadhu, *J. Am. Chem. Soc.* **111** (1989) 4399.

[10] W. Mikolaiski, *Dissertation*, Univ. Marburg, 1990.

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