The Stereochemistry of Carbenoid Cyclopropanation Reactions**

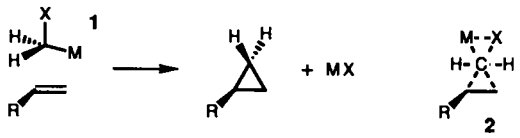
Hans Christian Stiasny and Reinhard W. Hoffmann*

Abstract: The stereochemical course of the intramolecular carbenoid cyclopropanation reaction has been studied for the epimeric carbenoids **12a** and **12b**. In these reactions the *tert*-butyldimethylsilyloxy substituent serves as an internal stereochemical reference point. It was found that **12b** cyclizes rapidly at −110 °C in a complexation-assisted concerted process to give the bicyclo[3.1.0]hexane **16**. The diastereomer **12a** cyclizes more slowly at −100 °C to give both **16** and **17**; the former is probably formed by a complexation-assisted carbolithiation pathway.

Keywords
alkenes · carbenoids · carbolithiations · cyclopropanations · mechanistic studies

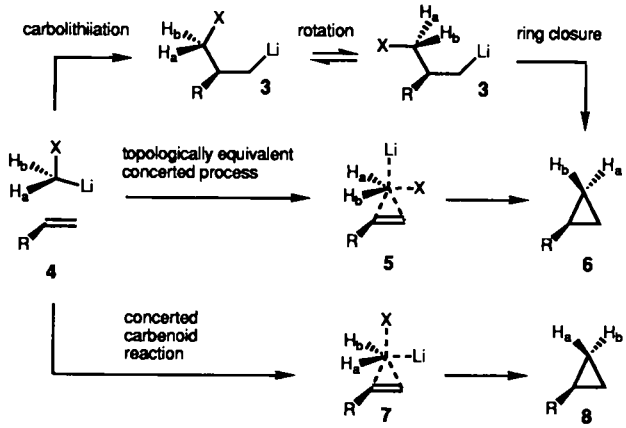
Introduction

The cyclopropanation of alkenes by α-halogenated alkylmetal compounds **1** (Scheme 1) is a synthetically important transformation.[2] Two types of reagents have mainly been used—the α-halogenoalkyllithium compounds and the Simmons–Smith reagents where zinc is the key metal.[3] It has been demonstrated in several instances[4, 5] that the cyclopropanation reaction proceeds directly from the organometallic compound and does not involve formation of a free carbene. Compounds such as **1** have hence been designated as carbenoids.[5]



Scheme 1.

Two mechanisms have been advanced for the formation of cyclopropanes from an α-haloalkylmetal compound **1** and an alkene: a concerted process via a transition state initially depicted as **2** (Scheme 1)[6] and a two-step process involving carbometalation of the alkene to give **3** followed by intramolecular nucleophilic substitution to furnish the cyclopropane (Scheme 2).[7] The two-step mechanism has been rigorously ruled out for the addition of chloromethyllithium to alkenes,[8] but it might operate in other instances.[7] The alternative would be a concerted mechanism. Theoretical considerations[9] describe the transition state as being governed by $\pi_{alkene}/\sigma^*_{C-X}$ and $\sigma_{C-M}/\pi^*_{alkene}$ interactions. This implies that the distinct arrangement **7** for the transition state should also be possible. The transition state topology could be identified if 1) the reacting carbenoid carbon is a stereogenic center of known configuration, as indicated in **4** by labeling H_a and H_b and if 2) the reacting enantioface of the double bond is identified. This can most easily be achieved by linking the prochiral alkene to the carbenoid center, that is, by a study of the stereochemical course of intramolecular cyclopropanations. In order to reduce the number of possible transition states, the linking chain should be short enough to allow only the formation of a *cis*-fused bicyclo[n.1.0]alkane. This is tantamount to applying the endocyclic restriction test[10] to the hypothetical transition states **5** or **7**. Intramolecular cyclopropanations have been reported,[11] but the issue of stereochemistry has not been adressed.



Scheme 2.

We describe here a study on the stereochemistry of the intramolecular carbenoid cyclopropanation reaction, a study which is based on the stereoselective exchange of diastereotopic bromine atoms in compounds such as **11** by lithium.[12] The substrate **11** was chosen, because the stereocenter bearing the silyloxy group can serve as an internal stereochemical reference point.

[*] R. W. Hoffmann, H. C. Stiasny
Philipps-Universität Marburg, Fachbereich Chemie
D-35032 Marburg (Germany)
Telefax: Int. code + (06421) 28-8917

[**] Chiral Organometallic Reagents, Part XV. For Part XIV, see ref. [1].

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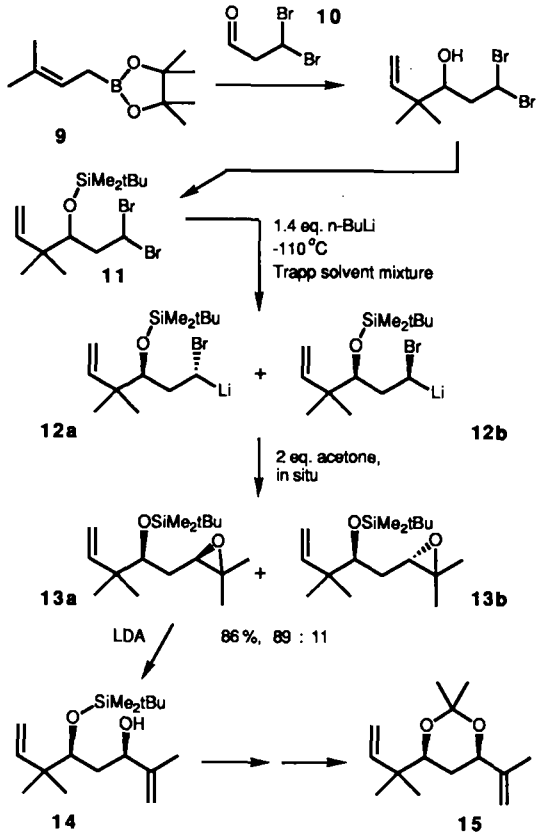
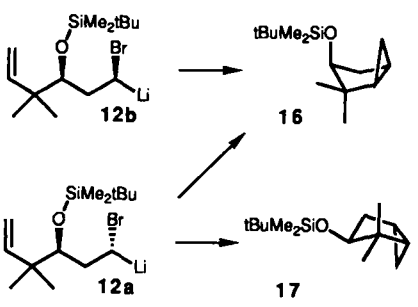


Scheme 3.

Results

The starting material **11** was generated by reaction of aldehyde **10**[13] with the butenylboronate **9**[14] (62%) followed by silylation of the intermediate alcohol (97%) (Scheme 3). Diastereoselective bromine–lithium exchange[12] on **11** and trapping of the carbenoids **12** with acetone in situ gave rise to the two epoxides **13** (86%) in an 89:11 ratio. The relative configurations of the products **13** were established by conversion of the major diastereomer to the acetonide **15**; ^{1}H NMR coupling constants and the ^{13}C NMR criteria described by Rychnovsky[15] and Evans[16] were used to show that **15** is derived from a *syn*-diol.

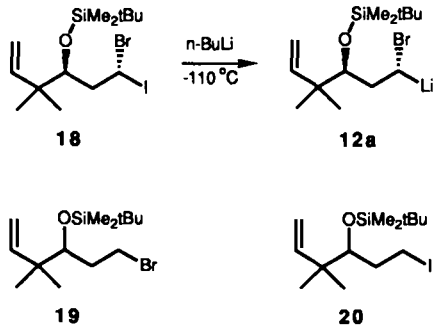
In an alternative procedure, the carbenoids **12** were generated at −110 °C and acetone was only added after 15 min. The epoxide **13a** was produced diastereomerically pure in 45% yield. In addition, a bicyclic product **16** (39%) (Scheme 4) was obtained with high diastereoselectivity (up to 97:3). The *cis* disposition of the silyloxy group and the cyclopropane ring followed from the ^{1}H NMR coupling constants. Apparently, the carbenoid **12b** cyclized rapidly to the bicyclohexane **16**, while **12a** was stable



Scheme 4.

under these conditions. When the mixture of the carbenoids **12** was allowed to warm up to −90 °C without addition of acetone, a mixture of two bicyclohexanes—the previously obtained **16** and the isomer **17**—resulted (79%) in a ratio of approximately 2:1. In order to investigate the course of bicyclization for the individual diastereomers **12a** and **12b**, we attempted to generate each carbenoid separately from diastereomerically pure bromoiodo compounds **18** and **27**, relying on a selective iodine–lithium exchange reaction.[17]

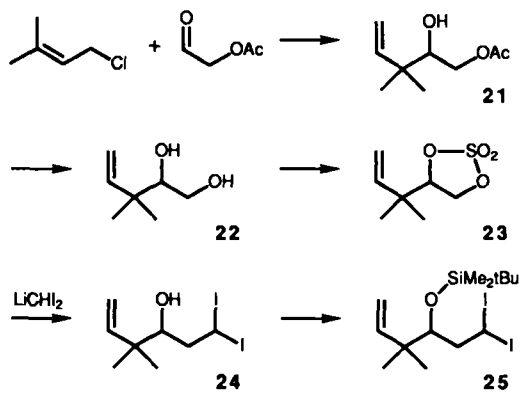
To this end a mixture of the carbenoids **12** was generated as above and maintained for 30 minutes at −120 °C in order to allow the cyclization of **12b** to **16** to proceed to completion. Then, an excess of 1,2-diiodoethane was added, which quenched the residual carbenoid **12a** to furnish the bromoiodo compound **18** (Scheme 5) as a single diastereomer in 45% yield. When **18** was treated with *n*-butyllithium at −110 °C in the presence of acetone, the epoxide **13a** was formed exclusively (32%) alongside 66% of the monobromo compound **19**.[18]



Scheme 5.

The diastereomerically pure carbenoid **12a** was thus generated from **18** (Scheme 5). When the mixture was allowed to stand at −100 °C for one hour before acetone was added (at −110 °C), cyclization of the carbenoid **12a** ensued to give the two bicyclohexanes **16** and **17** (Scheme 4)in a 1.1:1 ratio in 61% yield, as well as 22% of the diastereomerically pure epoxide **13a** and 14% of the monobromo compound **19**. This shows that two cyclization pathways are available to **12a**.

The method used for generating the epimeric carbenoid **12b** selectively was less direct. α-Acetoxyacetaldehyde was prenylated[19] and hydrolyzed to give the diol **22** (69%) (Scheme 6).[20] The latter was converted to the cyclic sulfate **23** in 68% yield. Sharpless[21] and more recently Hoye[22] have shown that cyclic sulfates can readily be opened by nucleophiles. Reaction of **23** with diiodomethyllithium[23] at between −105 and −95 °C for



Scheme 6.

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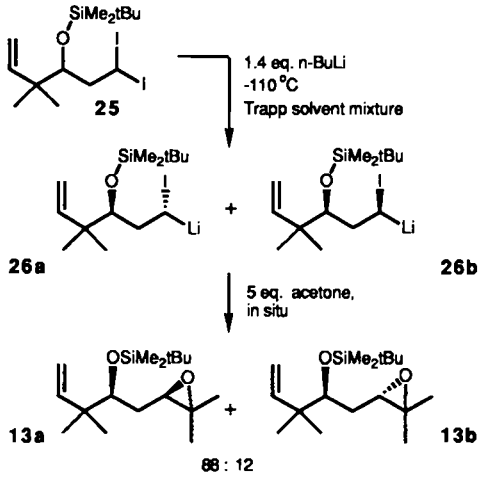
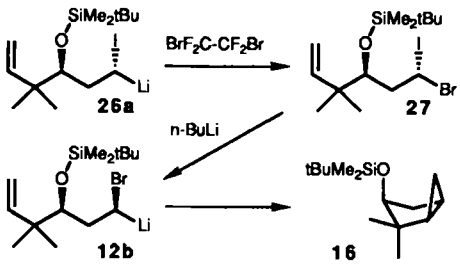


Scheme 7.

9 h furnished the diiodo compound **24** in 65% yield. This route has since been used by us to prepare **11** as well as other 1,1-dibromo-3-hydroxyalkanes. Silylation of **24** finally gave the diiodo compound **25**, corresponding to the dibromo analogue **11**.

Reaction of **25** with *n*-butyllithium in the presence of acetone as described above generated the carbenoids **26** in an 88:12 ratio (Scheme 7), as evidenced by the formation of the epoxides **13** in 24% yield (again the protonation was the dominant reaction, and **20** was formed in 66% yield; Scheme 5). When **26** was generated and acetone added after 30 min, **13a** (28%) was obtained as the only epoxide. The other products were bicyclohexane **16** (36%) and the protonation product **20** (34%). Thus, the behavior of **25** and of the iodocarbenoids **26** mirrors that of the bromo compound **11** and the carbenoids **12**. We hoped to utilize the iodocarbenoid **26a** to access the epimer of **18**, compound **27**. To this end, the diiodo compound **25** was treated with butyllithium as above. The carbenoids **26** were allowed to stand for 15 min at −110 °C, during which time **26b** cyclized to **16**. Then, 1,2-dibromotetrafluoroethane was added, which converted the residual **26a** into the bromoiodo compound **27** (42%) (Scheme 8). The diastereomeric purity of **27** was ascertained by comparison of the ^{13}C NMR spectra of **27** and **18**. Treatment with *n*-butyllithium resulted in selective iodine/lithium exchange generating the carbenoid diastereomer **12b**, which cyclized predominantly to the bicyclohexane **16** (**16**:**17** = 97:3) upon standing at −110 °C (83%).



Scheme 8.

Discussion

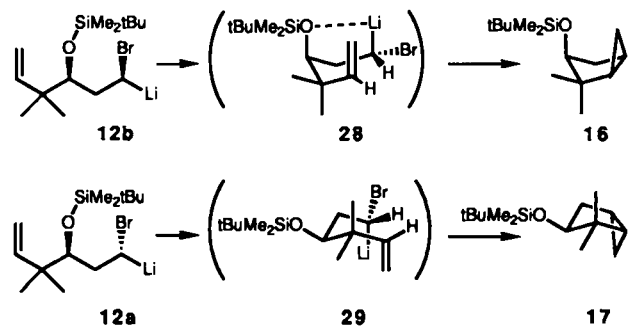
The fact that the carbenoid **12b** cyclizes to a single bicyclohexane **16**, whereas the diastereomeric carbenoid **12a** gives a mixture of two bicyclohexanes **16** and **17** (Scheme 4) rules out a free carbene as intermediate in the cyclization of **12b**. The formation of a free carbene is also unlikely in the cyclization of **12a**, because cyclization occurs in a temperature range in which α-bromoalkyllithium compounds are both chemically and configurationally stable.[24] Hence, epimerization of **12a** to **12b** prior to bicyclization is also unlikely. The formation of the bicyclohexanes **16** and **17** from the carbenoids **12a** and **12b** must therefore follow distinct stereochemical pathways.

The cyclization of **12b** to **16** occurs at temperatures as low as −110 °C with a half life of less than 5 min. Knowledge of the relative configuration of **12b** as well as of **16** yields valuable information regarding the course of this reaction (Scheme 9). The reactive conformer **28** corresponds to the topology **7** (Scheme 2), that is, to a nucleophilic attack of the double bond at the carbenoid center. The same type of reactive conformation can be pictured for the transformation of the diastereomeric carbenoid **12a** to the bicyclohexane **17** (Scheme 9), and yet the cyclization proceeds at noticeably higher temperatures than that of **12b**. The difference between the reactive conformers **28** and **29** is that **28** is set up for internal coordination of the lithium by the silyloxy group, which could facilitate the breaking of the carbon–lithium bond in the transition state. The Lewis base assisted, concerted cyclopropanation is thus the most facile pathway as demonstrated by the conversion of **12b** to **16** at −110 °C.

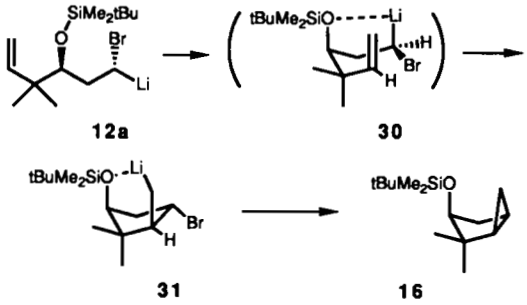
The diastereomeric carbenoid **12a** cyclizes to **17** at −100 °C in a concerted pathway without assistance from a Lewis base. In addition, it cyclizes with equal facility to the diastereomeric bicyclohexane **16**. This cyclization corresponds to topology **5** (Scheme 2), or it could involve a carbolithiation process via **3**. Huisgen had shown that carbolithiation is not involved in the cyclopropanation of alkenes by α-chloromethyllithium.[8] This is in line with the finding that carbolithiations of simple alkenes—even when intramolecular—only proceed at temperatures above −20 °C.[25] However, carbolithiation reactions can occur at substantially lower temperatures when assisted by an internal Lewis base.[26] It therefore seems possible that assistance by the oxygen substitutent as internal Lewis base could facilitate the intramolecular carbolithiation of **12a** via **30** to give **31** (Scheme 10) to such an extent that it becomes competitive with the concerted pathway **12a** → **17**, which is not assisted by a Lewis base.

Our results therefore suggest that, of the various carbenoid cyclopropanation mechanisms, the Lewis base assisted, concerted cyclopropanation (Scheme 9) proceeds with the lowest activation energy. The concerted cyclopropanation via reactive conformation **29** requires temperatures that are at least 10 °C higher. Lewis-base assistance may render the carbolithiation (Scheme 10) competitive with the concerted reactions discussed.

An interesting reaction, which should be discussed in this context, is the formation of spiropentanes **35** from the dibromo compounds **32**.[11] This cyclization cannot proceed through carbolithiation of carbenoids **33**. With a concerted cyclization, di-



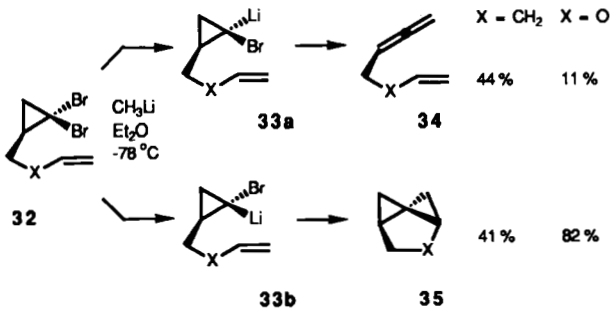
Scheme 9.



Scheme 10.

rectly from the carbenoids **33**, only one of the diastereomers could cyclize, namely, **33b** via topology **7** (Scheme 2).

Spiropentane formation from **32** has been reported to compete with allene formation.[27, 28] In view of our results described above, it could be argued that diastereomer **33b** of the carbenoids **33** cyclizes rapidly at low temperatures to the spiropentane **35**, whereas the diastereomer **33a** eventually generates, at higher temperatures, the allene **34**. If this hypothesis is correct, the spiropentane/allene ratio would reflect the diastereoselectivity in the exchange of the diastereotopic bromine atoms in **32**. The difference in the product ratios observed on going from $X = CH_2$ to $X = O$ (Scheme 11) gives credence to this interpretation, as the ether oxygen should direct the bromine/lithium exchange to the proximal bromine atom,[11, 27, 29] that is, the carbenoid **33b** ($X = O$) would be expected to be the major product. The higher proportion of the spiropentane formed in the oxygenated series suggests that **33b** is the diastereomer that undergoes the spirocyclization. This would have to proceed via a transition state of type **7**, in line with our findings discussed above.



Scheme 11.

Experimental Procedure

All temperatures quoted are not corrected. Temperatures around −100 °C were determined with a GTH 215 precision digital thermometer of Fa. Greisinger, Regenstauf, Germany. ^{1}H NMR, ^{13}C NMR: Bruker AC-300. Boiling range of petroleum ether: 40–60 °C. pH 7 buffer: 56.2 g $NaH_2PO_4 \cdot 2H_2O$ + 213.2 g $Na_2HPO_4 \cdot 2H_2O$ in 1.0 L of water. Flash chromatography: Silica gel Si 60 E. Merck AG, Darmstadt, 40–63 μm. MPLC: 30 cm × 2.5 cm column with Lichroprep Si 60, E. Merck AG, Darmstadt, 15–25 μm, 8 bar. Analytical gas chromatography: Siemens Sichromat 3 with a 30 m × 0.3 mm quartz capillary column with Se 52, 1 bar He, temperature program: 5 min at 100 °C, increase at a rate of 10 °C min^{-1} to 230 °C.

1. 1,1-Dibromo-4,4-dimethyl-5-hexen-3-ol: To a solution of 3,3-dibromopropanal (**10**) [13] (3.39 g, 15.7 mmol) in petroleum ether (50 mL) was added 2-(3-methyl-2-butenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**9**) [14] (2.92 g, 14.9 mmol) at 0 °C. After stirring for 3 h the mixture was kept for 2 h at room temperature. Buffer (pH = 7, 20 mL) was added, and the mixture extracted with petroleum ether (3 × 20 mL). The combined organic phases were washed with brine (20 mL) and concentrated in vacuo. The residue was purified by flash chromatography with ethyl acetate/petroleum ether (1:5). Medium-pressure liquid chromatography with the same solvent furnished 0.21 g (7%) of (*E*)-1-bromo-4,4-dimethylhexa-1,5-diene-3-ol, 0.05 g (2%) of the corresponding (*Z*) isomer, and 2.62 g (62%) of the desired alcohol as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.02$ (s, 3H), 1.03 (s, 3H), 1.66 (dd, $J = 4.8$, 1.5 Hz, 1H), 2.38 (ddd, $J = 14.6$, 10.2, 2.9 Hz, 1H), 2.50 (dddd, $J = 14.6$, 10.7, 2.1, <2 Hz, 1H), 3.51 (ddd, $J = 10.3$, 4.8, 2.1 Hz, 1H), 5.08 (dd, $J = 17.5$, 1.2 Hz, 1H), 5.14 (dd, $J = 10.9$, 1.2 Hz, 1H), 5.78 (dd, $J = 17.5$, 10.8 Hz, 1H), 5.86 (dd, $J = 10.7$, 2.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.9$, 23.0, 41.1, 44.4, 47.5, 76.1, 114.5, 144.1. $C_8H_{14}Br_2O$ (286.0): calcd. C 33.59, H 4.93; found C 33.78, H 4.95.

(*E*)-1-Bromo-4,4-dimethylhexa-1,5-diene-3-ol: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.99$ (s, 3H), 1.01 (s, 3H), 1.71 (brs, 1H), 3.80 (d, $J = 6.0$ Hz, 1H), 5.09 (dd, $J = 17.4$, 1.1 Hz, 1H), 5.13 (dd, $J = 10.8$, 1.2 Hz, 1H), 5.80 (dd, $J = 17.4$, 10.9 Hz, 1H), 6.23 (dd, $J = 13.5$, 6.2 Hz, 1H), 6.30 (d, $J = 14.5$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.7$, 23.4, 41.6, 78.8, 108.2, 114.5, 136.7, 144.0.

(*Z*)-1-Bromo-4,4-dimethylhexa-1,5-diene-3-ol: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.02$ (s, 3H), 1.07 (s, 3H), 1.70 (brs, 1H), 4.32 (d, $J = 8.8$ Hz, 1H), 5.09 (dd, $J = 17.4$, 1.1 Hz, 1H), 5.13 (dd, $J = 10.8$, 1.2 Hz, 1H), 5.88 (dd, $J = 17.4$, 10.9 Hz, 1H), 6.10 (dd, $J = 8.8$, 7.3 Hz, 1H), 6.35 (d, $J = 7.4$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.5$, 23.7, 41.8, 75.6, 110.6, 114.5, 134.0, 144.1.

2. 1,1-Dibromo-3-(*tert*-butyldimethylsilyloxy)-4,4-dimethyl-5-hexene (11): Into a solution of 1,1-dibromo-4,4-dimethyl-5-hexen-3-ol (1.89 g, 6.6 mmol) and 2,6-lutidine (1.50 mL, 12.9 mmol) in CH_2Cl_2 (10 mL) was added *tert*-butyldimethylsilyl triflate (1.80 mL, 7.9 mmol) at 20 °C. After 2 h of stirring, methanol (0.5 mL) was added and the mixture stirred for 0.5 h. The solvents were removed in vacuo and the residue extracted with petroleum ether (3 × 10 mL). The combined organic phases were washed with 5% aqueous hydrochloric acid (10 mL) and brine (10 mL). The solvents were removed in vacuo and the residue purified by flash chromatography with *tert*-butyl methyl ether/petroleum ether (1:10) to give 2.58 g (97%) of **11** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.09$ (s, 3H), 0.15 (s, 3H), 0.90 (s, 9H), 0.99 (s, 6H), 2.40 (ddd, $J = 14.9$, 8.2, 3.2 Hz, 1H), 2.59 (ddd, $J = 14.9$, 10.5, 2.3 Hz, 1H), 3.52 (dd, $J = 8.2$, 2.3 Hz, 1H), 5.01 (dd, $J = 16.9$, 1.2 Hz, 1H), 5.10 (dd, $J = 11.5$, 1.2 Hz, 1H), 5.66 (dd, $J = 10.4$, 3.2 Hz, 1H), 5.82 (dd, $J = 16.6$, 11.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -3.8$, −3.6, 18.5, 21.9, 24.9, 26.2, 41.9, 44.7, 50.5, 77.9, 112.7, 145.0. $C_{14}H_{28}Br_2OSi$ (400.3): calcd. C 42.01 H 7.05; found C 42.17 H 7.04.

3. 5-(*tert*-Butyldimethylsilyloxy)-2,3-epoxy-2,6,6-trimethyl-7-octene (13): For this and related experiments, a two-chamber low-temperature reaction vessel was used (Fig. 1) (this apparatus was developed by the glass blower G. Bösherz in our department and is now available from NORMAG GmbH, Hofheim/Germany). The apparatus was cooled in a cooling bath to −110 °C, and the bottom valve closed. Then a solution of the dibromo compound **11** (256 mg, 0.64 mmol) and acetone (0.15 mL, 2.0 mmol) in a Trapp solvent mixture (7 mL) [30] was placed in the lower compartment (A). A solution of *n*-butyllithium in hexane (1.59 M, 0.60 mL, 0.95 mmol) was placed in the top compartment (B). When the internal temperature had reached −110 °C, the butyllithium solution was allowed to drop into the stirred lower compartment.

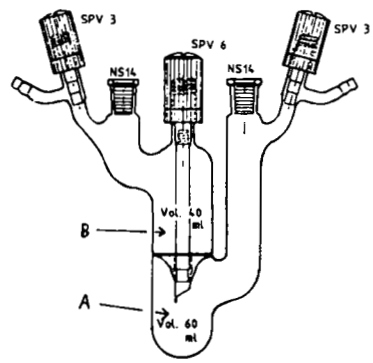


Fig. 1. Low-temperature two-chamber reaction vessel.

After stirring for 15 min the mixture was allowed to reach room temperature and stirred for 1 h. An aqueous buffer (pH = 7, 5 mL) was added, the phases were separated, and the aqueous phase was extracted with petroleum ether (3 × 10 mL). The combined organic phases were washed with brine (10 mL) and concentrated in vacuo. The residue was purified by flash chromatography with *tert*-butyl methyl ether/petroleum ether (1:20) to give 164 mg (86%) of the epoxide **13** as a colorless oil. The diastereomer ratio *syn*-(3*R**,5*S**)-**13** (**13a**)/*anti*-(3*R**,5*R**)-**13** (**13b**) was determined from the crude product by GC, ^{1}H NMR, or ^{13}C NMR to be 89:11.

13a: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.05$ (s, 3H), 0.06 (s, 3H), 0.91 (s, 9H), 0.99 (s, 3H), 0.99 (s, 3H), 1.21 (s, 3H), 1.28 (s, 3H), 1.59–1.76 (m, 2H), 2.86 (dd, $J = 6.0$, 6.0 Hz, 1H), 3.51 (dd, $J = 5.6$, 5.1 Hz, 1H), 4.97 (dd, $J = 10.6$, 1.5 Hz, 1H), 4.97 (dd, $J = 17.9$, 1.5 Hz, 1H), 5.85 (dd, $J = 17.9$, 10.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.1$, −3.9, 18.2, 18.8, 22.1, 24.6, 24.9, 26.0, 33.8, 42.4, 58.5, 62.3, 77.6, 112.0, 145.7.

13b: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.07$ (s, 3H), 0.08 (s, 3H), 0.91 (s, 9H), 0.97 (s, 3H), 0.98 (s, 3H), 1.22 (s, 3H), 1.28 (s, 3H), 1.56–1.68 (m, 2H), 2.87 (dd, $J = 6.6$, 5.0 Hz, 1H), 3.59 (dd, $J = 6.9$, 4.1 Hz, 1H), 4.95 (dd, $J = 17.9$, 1.5 Hz, 1H), 4.96 (dd, $J = 10.4$, 1.5 Hz, 1H), 5.86 (dd, $J = 18.1$, 10.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.0$, −3.8, 18.4, 19.1, 22.7, 24.5, 24.9, 26.1, 32.7, 42.2, 59.1, 62.0, 77.2, 111.8, 145.8. $C_{17}H_{34}O_2Si$ (298.6): calcd. C 68.39, H 11.48; **13a** + **13b** found C 68.44, H 11.60.

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4. (3*R,5*S**)-5-(*tert*-Butyldimethylsilyloxy)-2,6,6-trimethyl-1,7-octadiene-3-ol (14)**: To a solution of diisopropylamine (0.14 mL, 1.0 mmol) in ether (1.5 mL) was added a solution of *n*-butyllithium in hexane (1.59 M, 0.50 mL, 0.80 mmol) at 0 °C. After 10 min of stirring, a solution of **13a** (150 mg, 0.50 mmol) in ether (1.5 mL) was added. After 4 h of stirring at 20 °C, a buffer (pH = 7, 5 mL) was added, the phases were separated, and the aqueous phase was extracted with ether (3 × 10 mL). The combined organic phases were washed with brine (10 mL) and concentrated in vacuo. Flash chromatography of the residue with *tert*-butyl methyl ether/petroleum ether (1:10) yielded 97 mg (65%) of **14** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 3H), 0.12 (s, 3H), 0.91 (s, 9H), 0.97 (s, 3H), 0.98 (s, 3H), 1.51 (ddd, J = 14.6, 8.1, 6.5 Hz, 1H), 1.67–1.69 (m, 3H), 1.81 (ddd, J = 14.6, 4.8, 4.8 Hz, 1H), 1.93 (d, J = 2.7 Hz, 1H), 3.52 (dd, J = 6.4, 4.6 Hz, 1H), 4.12–4.16 (m, 1H), 4.80 (dq, J = 1.6, 1.6 Hz, 1H), 4.93 (dd, J = 1.7, 0.7 Hz, 1H), 4.98 (dd, J = 17.9, 1.5 Hz, 1H), 4.98 (dd, J = 10.5, 1.5 Hz, 1H), 5.86 (dd, J = 18.0, 10.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.0, −3.4, 17.4, 18.4, 22.3, 24.5, 26.2, 39.8, 42.6, 74.2, 77.3, 111.2, 112.0, 145.8, 147.5. $C_{17}H_{34}O_2Si$ (298.6): calcd. C 68.39, H 11.48; found C 68.42, H 11.24.

5. (3*R,5*S**)-2,6,6-Trimethyl-1,7-octadiene-3,5-diol**: To a solution of the silyl ether **14** (41 mg, 0.14 mmol) in THF (1 mL) was added a 1 M solution of tetrabutylammonium fluoride in THF (0.17 mL, 0.17 mmol). After 2 h of stirring, the solvents were removed in vacuo, and the residue separated by flash chromatography with ether/petroleum ether (1:1) to give 20 mg (78%) of the diol as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 (s, 6H), 1.48 (ddd, J = 14.4, 10.4, 9.7 Hz, 1H), 1.70 (ddd, J = 14.3, 2.9, 1.8 Hz, 1H), 1.72 (s, 3H), 2.84 (s, 1H), 3.22 (s, 1H), 3.52 (brd, J = 10.5 Hz, 1H), 4.24 (dd, J = 9.6, 2.6 Hz, 1H), 4.81 (dq, J = 1.5, 1.5 Hz, 1H), 4.98 (dd, J = 1.7, 0.9 Hz, 1H), 5.04 (dd, J = 17.5, 1.4 Hz, 1H), 5.08 (dd, J = 10.8, 1.4 Hz, 1H), 5.80 (dd, J = 17.5, 10.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.8, 22.1, 22.7, 36.1, 41.5, 76.8, 78.9, 110.8, 113.4, 145.1, 147.4. $C_{11}H_{20}O_2$ (184.3): calcd. C 71.70, H 10.94; found C 71.72, H 10.97.

6. (4*R,6*S**)-2,2-Dimethyl-4-(1,1-dimethyl-2-propenyl)-6-(1-methylethenyl)-1,3-dioxane (15)**: A solution of the diol (19 mg, 0.10 mmol), obtained as described above in experiment 5, and *p*-toluenesulfonic acid (0.5 mg) in 2,2-dimethoxypropane (1 mL) was stirred for 1 h. Two drops of triethylamine were added, and the solvents removed in vacuo. Flash chromatography of the residue with *tert*-butyl methyl ether/petroleum ether (1:10) furnished 20 mg (89%) of **15** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (s, 3H), 0.99 (s, 3H), 1.27 (ddd, all J = 12 Hz, 1H), 1.40 (s, 3H), 1.42 (s, 3H), 1.43 (ddd, J = 12.7, 2.6, 2.6 Hz, 1H), 1.72 (s, 3H), 3.54 (dd, J = 11.6, 2.4 Hz, 1H), 4.19 (dd, J = 11.4, 2.3 Hz, 1H), 4.82 (brs, 1H), 4.97 (dd, J = 16.9, 1.5 Hz, 1H), 4.98 (brs, 1H), 4.98 (dd, J = 11.5, 1.5 Hz, 1H), 5.88 (dd, J = 16.9, 11.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.4, 19.6, 22.5, 23.1, 30.2, 30.4, 40.0, 72.6, 75.5, 98.5, 110.7, 111.9, 145.1, 145.7. $C_{14}H_{24}O_2$ (224.3): calcd. C 74.95, H 10.78; found C 74.93, H 10.71.

7. 2,2-Dimethyl-3-*endo*-(*tert*-butyldimethylsilyloxy)bicyclo[3.1.0]hexane (16): A solution of the dibromo compound **11** (294 mg, 0.73 mmol) in a Trapp solvent mixture (8 mL) [30] was placed into the lower chamber (A) of the two-chamber apparatus. A 1.59 M solution of *n*-butyllithium in hexane (0.65 mL, 1.03 mmol) and Trapp solvent mixture (1 mL) were placed in the top chamber (B). After the apparatus had been cooled to −110 °C, the *n*-butyllithium solution was allowed to drop into the lower chamber with stirring. After 15 min a solution of acetone (0.20 mL, 2.7 mmol) in the Trapp solvent mixture (2 mL) was precooled in the top chamber and added to the lower chamber. After 15 min of stirring, the mixture was allowed to reach room temperature and stirred for 1 h. An aqueous buffer (pH = 7, 5 mL) was added, the phases separated, and the aqueous phase extracted with petroleum ether (3 × 10 mL). The combined organic phases were washed with brine (10 mL) and concentrated in vacuo. GC analysis of the crude product indicated a ratio of **13a**:**16**:**17**:**19** of 49:38:5:8; **13b** could not be detected. The residue was separated by flash chromatography (petroleum ether/*tert*-butyl methyl ether = 1:0 to 10:1) to give 98 mg (45%) of **13a** and 96 mg (52%) of **16**, **17**, and **19** as colorless liquids. **16**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.01 (s, 3H), 0.00 (s, 3H), 0.23 (dddd, J = 8.1, 8.1, 4.3, 1.2 Hz, 1H), 0.77 (ddd, all J = 4.0 Hz, 1H), 0.87 (s, 9H), 0.96 (s, 3H), 1.01 (s, 3H), 1.16–1.22 (m, 1H), 1.24–1.34 (m, 1H), 1.66 (d, J = 13.7 Hz, 1H), 2.17 (dddd, J = 13.7, 5.9, 4.8, 1.2 Hz, 1H), 3.55 (d, J = 6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.2, −4.7, 8.5, 15.2, 18.0, 21.4, 25.8, 29.1, 29.2, 37.2, 44.3, 79.9. $C_{14}H_{28}OSi$ (240.5): calcd. C 69.93, H 11.74; found C 70.09, H 11.67.

8. 2,2-Dimethyl-3-*exo*-(*tert*-butyldimethylsilyloxy)bicyclo[3.1.0]hexane (17): The dibromo compound **11** (185 mg, 0.46 mmol) in Trapp solvent mixture (5 mL) [30] was allowed to react with a 1.56 M solution of *n*-butyllithium in hexane (0.40 mL, 0.62 mmol) as described above in experiment 7. Before the addition of acetone (0.10 mL, 1.4 mmol) in a Trapp solvent mixture (2 mL), the mixture was stirred for 1 h at −90 °C and recooled to −110 °C. Workup as described in experiment 7 provided a crude product, which contained **16** and **17** in a 2:1 ratio, and no **13** (by GC analysis). Flash chromatography with petroleum ether furnished 87 mg (79%) of **16** and **17**. $C_{14}H_{28}OSi$ (240.5): calcd. C 69.93, H 11.74; found C 70.05, H 11.84. Both diastereomers were obtained in pure form by repeated flash chromatography. **17**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.04 (s, 3H), −0.03 (s, 3H), 0.10–0.16 (m, 1H), 0.21 (ddd, J = 7.9, 7.9, 5.6 Hz, 1H), 0.86 (s, 9H), 0.89 (s, 3H), 0.98 (s, 3H), 1.05–1.13 (m, 1H), 1.32–1.42 (m, 1H), 1.66 (ddd, J = 12.2, 9.0, 3.8 Hz, 1H), 1.90 (dd, J = 12.2, 7.1 Hz, 1H), 3.30 (dd, J = 9.1, 7.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.2, −4.5, 6.8, 12.4, 18.0, 22.6, 24.5, 25.8, 27.0, 34.8, 40.4, 77.1. Approximately 4% of 1-bromo-3-(*tert*-butyldimethylsilyloxy)-4,4-dimethyl-5-hexene (**19**) was obtained as a by-product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 3H), 0.13 (s, 3H), 0.93 (s, 9H), 1.00 (s, 3H), 1.01 (s, 3H), 1.91 (dddd, J = 14.6, 7.3, 7.3, 5.0 Hz, 1H), 2.06 (dddd, J = 14.6, 8.1, 8.1, 3.1 Hz, 1H), 3.39 (ddd, J = 9.8, 8.3, 7.5 Hz, 1H), 3.53 (dd, J = 7.4, 3.3 Hz, 1H), 3.49–3.57 (m, 1H), 5.00 (dd, J = 10.5, 1.4 Hz, 1H), 5.00 (dd, J = 17.8, 1.4 Hz, 1H), 5.88 (dd, J = 17.8, 10.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −3.9, −3.6, 18.4, 22.7, 24.7, 26.2, 31.7, 37.3, 42.1, 77.7, 112.0, 145.6. $C_{14}H_{29}BrOSi$ (321.4): calcd. C 52.32, H 9.10; found C 52.43, H 9.23.

9. (1*R,3*S**)-1-Bromo-3-(*tert*-butyldimethylsilyloxy)-1-iodo-4,4-dimethyl-5-hexene (18)**: A solution of the dibromo compound **11** (738 mg, 1.84 mmol) in a Trapp solvent mixture (20 mL) [30] and a 1.56 M solution of *n*-butylllithium in hexane (1.30 mL, 2.07 mmol) were allowed to react at −120 °C as described above in experiment 3. The mixture was stirred for 30 min. A solution of 1,2-diiodoethane (743 mg, 2.6 mmol) in Trapp mixture (20 mL) was precooled and added. This resulted in an intense yellow color. The mixture was stirred for 15 min at −120 °C, allowed to reach −100 °C, and stirred for 1 h. By the end of this sequence, the mixture was colorless. After the mixture had reached room temperature, an aqueous buffer (pH = 7, 20 mL) was added, the phases were separated, and the aqueous phase extracted with petroleum ether (3 × 20 mL). The combined organic phases were washed with brine (20 mL) and concentrated in vacuo. Flash chromatography of the residue with petroleum ether furnished 367 mg (45%) of the diastereomerically pure **18** as a colorless oil. The product was stored in a refrigerator. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.10 (s, 3H), 0.14 (s, 3H), 0.89 (s, 9H), 0.98 (s, 6H), 2.56 (ddd, J = 15.0, 8.0, 3.8 Hz, 1H), 2.64 (ddd, J = 15.0, 10.6, 2.4 Hz, 1H), 3.46 (dd, J = 7.8, 2.5 Hz, 1H), 5.01 (dd, J = 16.9, 1.3 Hz, 1H), 5.02 (dd, J = 11.5, 1.3 Hz, 1H), 5.50 (dd, J = 10.5, 3.9 Hz, 1H), 5.81 (dd, J = 16.7, 11.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −3.8, −3.7, 9.2, 18.5, 22.0, 24.9, 26.2, 41.7, 52.7, 78.7, 112.6, 145.0. $C_{14}H_{28}BrIOSi$ (447.3): calcd. C 37.60, H 6.31; found C 37.89, H 6.47.

10. (3*R,5*S**)-13 (13a)** from **18**: A solution of the bromoiodo compound **18** (69 mg, 0.15 mmol) and acetone (0.03 mL, 0.4 mmol) in a Trapp solvent mixture (2.5 mL) [30] were allowed to react with a 1.56 M solution of *n*-butyllithium in hexane (0.16 mL, 0.25 mmol), as described above in experiment 3, to furnish 46 mg of a product mixture. GC analysis showed the absence of **13b**, and the presence of **13a** and **19** in a 1:2 ratio.

11. Bicyclo[3.1.0]hexanes 16 and 17 from 18: A solution of the bromoiodo compound **18** (126 mg, 0.28 mmol) in a Trapp solvent mixture (3 mL) [30] was allowed to react with a 1.45 M solution of *n*-butyllithium in hexane (0.27 mL, 0.42 mmol) and Trapp solvent mixture (1 mL) [30], as described in experiment 8. After 1 h of stirring at −100 °C, the mixture was cooled back to −110 °C, and a precooled solution of acetone (0.10 mL, 1.4 mmol) in Trapp solvent mixture (1 mL) added. After 15 min of stirring, the mixture was allowed to reach room temperature. Workup as described in experiment 8 furnished 73 mg of a crude product. GC analysis showed the presence of **16**, **17**, **13a**, and **19** in a 33:30:23:14 ratio.

12. 3,3-Dimethyl-4-pentene-1,2-diol (22): Tin(II) chloride dihydrate (64.1 g, 284 mmol) was added to a solution of acetoxyacetaldehyde (19.4 g, 189 mmol) [31] and 1-chloro-3-methyl-2-butene (21.8 g, 208 mmol) in DMF (380 mL). The mixture was cooled to 0 °C, and sodium iodide (42.6 g, 284 mmol) added. After 12 h of stirring at 20 °C, 30% aqueous NH_4F solution (380 mL, 3.1 mol) and *tert*-butyl methyl ether (400 mL) were added. After 1 h of stirring, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 100 mL). The combined organic phases were washed with brine (2 × 100 mL), dried with $MgSO_4$, and concentrated in vacuo to give 27.5 g (ca. 80%) of crude **21**. The product contained some DMF and ca. 20% of 2-acetoxy-3,3-dimethyl-4-hexen-1-ol. **21**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (s, 3H), 1.06 (s, 3H), 2.07 (s, 3H), 3.56 (ddd, J = 8.9, 3.6, 2.4 Hz, 1H), 3.93 (dd, J = 11.5, 8.9 Hz, 1H), 4.23 (dd, J = 11.5, 2.4 Hz, 1H), 5.06 (dd, J = 17.4, 1.1 Hz, 1H), 5.08 (dd, J = 10.9, 1.1 Hz, 1H), 5.84 (dd, J = 17.4, 10.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9, 22.7, 23.1, 40.3, 66.4, 76.2, 113.6, 144.0, 171.3.
The crude acetates obtained were dissolved in (285 mL) a 1.0 M solution of KOH in methanol. After stirring 12 h the mixture was concentrated and the residue was partitioned between water (30 mL) and *tert*-butyl methyl ether (30 mL). The phases were separated, and the aqueous phase saturated with potassium carbonate and extracted with *tert*-butyl methyl ether (5 × 30 mL). The combined organic phases were washed with brine (2 × 30 mL), dried with Na_2SO_4, and concentrated in vacuo. Distillation of the residue at 60–72 °C/0.05 Torr furnished 16.9 g (69%) of the diol **22** as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (s, 3H), 1.04 (s, 3H), 3.41–3.50 (m, 2H), 3.63–3.74 (m, 1H), 5.05 (dd, J = 17.5, 1.3 Hz, 1H), 5.08 (dd, J = 10.8, 1.3 Hz, 1H), 5.84 (dd, J = 17.5, 10.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7, 23.1, 40.0, 63.1, 78.2, 113.5, 144.5. These data are consistent with those reported in ref. [20].

13. 3-(1′,1′-Dimethyl-2′-propenyl)-1,3,2-dioxathiolan-2,2-dioxide (23): A solution of SO_2Cl_2 (3.67 g, 27.2 mmol) in CH_2Cl_2 (20 mL) was added at −90 °C over 1 h to a solution of the diol **22** (3.20 g, 24.6 mmol) and triethylamine (12.0 mL, 86 mmol) in

CH_2Cl_2 (150 mL). The mixture was allowed to reach room temperature over 12 h and was stirred for further 3 h. Aqueous buffer (pH = 7, 50 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic phases were washed with brine (20 mL) and concentrated in vacuo. Flash chromatography of the residue with *tert*-butyl methyl ether/petroleum ether (1:3) furnished 3.23 g (68%) of the cyclic sulfate **23** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 3H), 1.17 (s, 3H), 4.40 (dd, J = 8.7, 8.7 Hz, 1H), 4.54 (dd, J = 8.5, 6.5 Hz, 1H), 4.72 (dd, J = 8.8, 6.4 Hz, 1H), 5.17 (dd, J = 17.5, 0.5 Hz, 1H), 5.24 (dd, J = 10.7, 0.5 Hz, 1H), 5.78 (dd, J = 17.5, 10.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7, 22.7, 39.2, 69.4, 87.2, 116.4, 139.6. $C_7H_{12}O_4S$ (192.2): calcd. C 43.74, H 6.29; found C 43.74, H 6.36.

14. 1,1-Diiodo-4,4-dimethyl-5-hexen-3-ol (24): To a solution of CH_2Cl_2 (2.0 mL, 31 mmol) in diethyl ether (20 mL) and THF (20 mL) was added a precooled 1.67 M solution of *n*-butyllithium in hexane (12.0 mL, 20.0 mmol) at −100 °C. After 15 min of stirring, a solution of diiodomethane (5.74 g, 21.4 mmol) in THF (5 mL) was added dropwise over 5 min at −110 °C. Stirring was continued for 1 h at this temperature, and a solution of the sulfate **23** (2.43 g, 12.7 mmol) in THF (5 mL) was added dropwise over 5 min. Stirring was continued for 3 h at −105 °C. The mixture was allowed to reach −95 °C over 6 h and finally −70 °C over 12 h. Twelve drops of conc. sulfuric acid were added followed by water (0.20 mL, 11 mmol). The mixture was stirred for 20 h at room temperature. TLC analysis showed complete hydrolysis of the sulfate ester. Aqueous buffer (pH = 7, 20 mL) was added. The phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (20 mL) and concentrated in vacuo. Flash chromatography of the residue with *tert*-butyl methyl ether/petroleum ether (1:7 to 1:3) furnished 0.54 g (12%) of the starting sulfate **23** and 3.12 g (65%) of the diiodo compound **24** as a slightly pink oil. **24** was stored at −20 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (s, 3H), 1.02 (s, 3H), 1.63 (br s, 1H), 2.32 (ddd, J = 14.7, 10.0, 2.9 Hz, 1H), 2.48 (ddd, J = 14.7, 11.6, 2.0 Hz, 1H), 3.27 (dd, J = 9.9, 2.0 Hz, 1H), 5.07 (dd, J = 17.5, 1.2 Hz, 1H), 5.13 (dd, J = 10.8, 1.2 Hz, 1H), 5.18 (dd, J = 11.5, 2.9 Hz, 1H), 5.78 (dd, J = 17.5, 10.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −28.1, 22.2, 23.1, 40.9, 50.4, 78.6, 114.4, 144.3. $C_8H_{14}I_2O$ (380.0): calcd. C 25.29, H 3.71; found C 25.50, H 3.75.

15. 3-(*tert*-Butyldimethylsilyloxy)-1,1-diiodo-4,4-dimethyl-5-hexene (25): The alcohol **24** (630 mg, 1.66 mmol) was silylated with *tert*-butyldimethylsilyl triflate as described in experiment 2. Flash chromatography with petroleum ether yielded 771 mg (94%) of **25** as a pinkish oil. Compound **25** was stored at −20 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 3H), 0.15 (s, 3H), 0.90 (s, 9H), 0.98 (s, 6H), 2.46 (ddd, J = 15.1, 7.7, 4.0 Hz, 1H), 2.63 (ddd, J = 15.1, 10.9, 2.3 Hz, 1H), 3.24 (dd, J = 7.7, 2.2 Hz, 1H), 4.99 (dd, J = 10.9, 3.9 Hz, 1H), 5.01 (dd, J = 16.7, 1.4 Hz, 1H), 5.02 (dd, J = 11.5, 1.4 Hz, 1H), 5.82 (dd, J = 16.5, 11.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −27.4, −3.7, −3.3, 18.5, 22.0, 25.0, 26.2, 41.7, 53.7, 80.3, 112.6, 145.0. $C_{14}H_{28}I_2OSi$ (494.3): calcd. C 34.02, H 5.71; found C 34.28, H 5.70.

16. Epoxide 13 (from the diiodo compound **25**): Compound **25** (191 mg, 0.38 mmol), acetone (0.07 mL, 1.0 mmol), and a 1.56 M solution of *n*-butyllithium in hexane (0.40 mL, 0.62 mmol) were allowed to react as described in experiment 3. GC analysis of the crude reaction product showed the presence of **13a**, **13b**, and 3-(*tert*-butyldimethylsilyloxy)-1-iodo-4,4-dimethyl-5-hexene (**20**) in a ratio of 23.8:3.2:73. Flash chromatography provided 120 mg of a mixture of **13a**, **13b**, and **20** as a colorless oil. By repeated flash chromatography **20** could be separated. **20**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 3H), 0.10 (s, 3H), 0.90 (s, 9H), 0.97 (s, 3H), 0.97 (s, 3H), 1.82–1.94 (m, 1H), 2.01–2.13 (m, 1H), 3.10 (ddd, all J = 8.6 Hz, 1H), 3.28 (ddd, J = 9.1, 9.1, 5.1 Hz, 1H), 3.38 (dd, J = 7.1, 3.1 Hz, 1H), 4.98 (dd, J = 17.9, 1.4 Hz, 1H), 4.98 (dd, J = 10.5, 1.4 Hz, 1H), 5.86 (dd, J = 17.9, 10.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −3.9, −3.5, 4.8, 18.4, 22.8, 24.7, 26.1, 38.4, 42.1, 79.8, 112.0, 145.6. $C_{14}H_{29}IOSi$ (368.4): calcd. C 45.65, H 7.94; found C 45.70, H 7.93.

17. (1*R,3*R**)-1-Bromo-3-(*tert*-butyldimethylsilyloxy)-1-iodo-4,4-dimethyl-5-hexene (27)**: The diiodo compound **25** (512 mg, 1.04 mmol), a 1.67 M solution of *n*-butyllithium in hexane (0.93 mL, 1.55 mmol), and 1,2-dibromotetrafluoroethane (0.30 mL, 2.5 mmol) were allowed to react as described in experiment 9. Flash chromatography with petroleum ether furnished 194 mg (42%) of diastereomerically pure **27** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 3H), 0.16 (s, 3H), 0.90 (s, 9H), 0.99 (s, 6H), 2.31 (ddd, J = 15.1, 7.7, 4.3 Hz, 1H), 2.66 (ddd, J = 15.1, 10.3, 2.6 Hz, 1H), 3.36 (dd, J = 7.6, 2.5 Hz, 1H), 5.02 (dd, J = 16.7, 1.4 Hz, 1H), 5.03 (dd, J = 11.8, 1.4 Hz, 1H), 5.42 (dd, J = 10.3, 4.3 Hz, 1H), 5.86 (dd, J = 16.5, 11.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −3.8, −3.3, 12.2, 18.5, 21.8, 25.0, 26.2, 42.0, 52.5, 79.3, 112.7, 145.0.

18. (3*R,5*R**)-13 (13b)** from **27**: The bromoiodo compound **27** (95 mg, 0.21 mmol), acetone (0.05 mL, 0.7 mmol), and a 1.67 M solution of *n*-butyllithium in hexane (0.25 mL, 0.42 mmol) were allowed to react as described in experiment 3, and 23 mg (37%) of the epoxide **13b** and 29 mg (43%) of the bromo compound **19** were isolated.

19. Bicyclo compound 16 from **27**: The bromoiodo compound **27** (79 mg, 0.18 mmol) and a 1.67 M solution of *n*-butyllithium in hexane (0.21 mL, 0.35 mmol) were allowed to react as described in experiment 7, and 35 mg (83%) of **16** in 94% d.e. was isolated. The presence of **13** could not be detected.

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