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Diastereoselective Bromine/Lithium Exchange Reactions of 3-Alkoxy-1,1-dibromo-alkanes[*]

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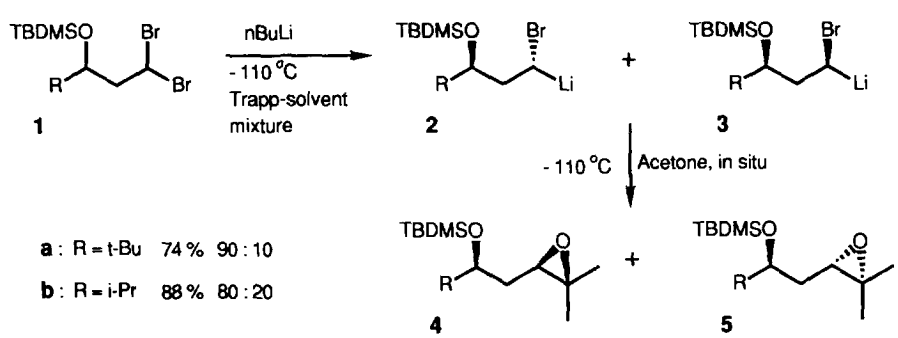
Abstract: *The diastereoselectivity in the bromine/lithium exchange reaction on chiral 3-alkoxy-1,1-dibromo-alkanes has been investigated. The differentiation of the two diastereotopic bromine atoms was found not to depend solely on a conformational preorganisation of the substrate, as surmised previously. It became apparent that steric crowding at the δ-center controls the spatial orientation of a C-3-oxygen substituent at the chiral center, which may be the cause of the asymmetric induction observed.* Copyright © 1996 Elsevier Science Ltd

Introduction

In previous papers of this series[1,2,3] we reported on the diastereoselective bromine/lithium exchange reactions of chiral 1,1-dibromoalkanes, by which ß-hydroxy-epoxides such as **4** or **5**, or a variety of 1,3-diol derivatives[4] may be accessed.

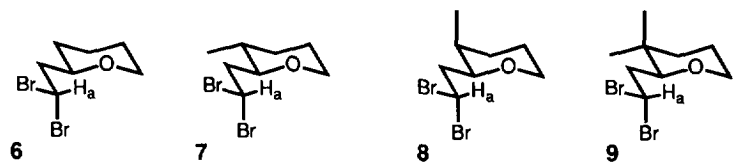


Kinetic control in the bromine/lithium exchange reaction can be realized when the reaction is carried out in the presence of 2 equivalents of acetone by in situ trapping of the carbenoids **2** and **3** initially formed. Substrates **1a** and **1b** exist (especially at low temperatures during the bromine/lithium exchange reaction) in a preferred conformation, and it was suggested that the level of diastereoselectivity could somehow be related to the ground state conformational preferences[3] of the substrates **1**. At that time the access to compounds of type **1** was quite limited; methods meanwhile developed[5,6] in our laboratory make a wider range of com-

pounds **1** available. We report here on a more general study on the diastereoselectivity of the bromine/lithium-exchange reaction.

Conformational Preorganization and Diastereoselectivity?

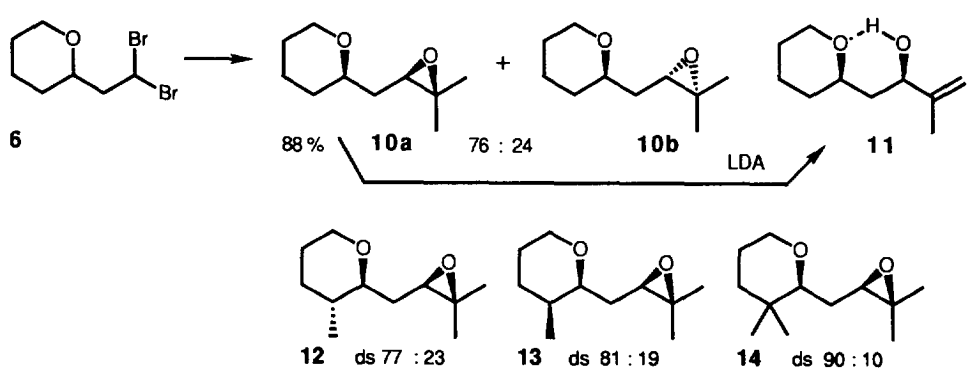
MM2-calculations had shown[3] that the methoxy compound corresponding to **1b** populates a single backbone conformation to ca. 94% at -110°C, the temperature of the bromine/lithium exchange reaction. For the methoxy compound corresponding to **1a** this holds to >99%. In order to find out, whether this is related to the diastereoselectivity of the bromine/lithium exchange reaction, we prepared and studied the tetrahydropyran derivatives **6-9**, for which MM2-calculations suggested also very high conformational preferences at -110°C.



	6	**7**	**8**	**9**
H_a: ^3J =	10.7 ; 3.2	11.3 ; 2.5	10.7 ; 3.1 Hz	
Conformer population at - 110 °C (MM2)	99 %	97 %	95 %	> 99 %

The large alteration in the coupling constants found for H_a of **6** to **8** demonstrates the predominance of a single conformation in solution. This is the one shown as established for **6** by NOE-experiments.[7] The coupling constants show a temperature dependence when cooling from 35°C to -60°C. From this dependence the population of the conformer shown for **6** may be extrapolated to 99.8% at -110°C. Thus, at this low temperature the compounds **6** to **8** should be essentially monoconformational, and, if this dictates the diastereoselectivity in the bromine/lithium exchange reaction, they should display very high diastereo-selectivity.

The dibromo-compound **6** was treated with n-butyllithium at -110°C in a Trapp solvent mixture in the presence of 2 equivalents of acetone. The attendant kinetically controlled diastereoselectivity was determined from the ratio of the resulting epoxides **10**.

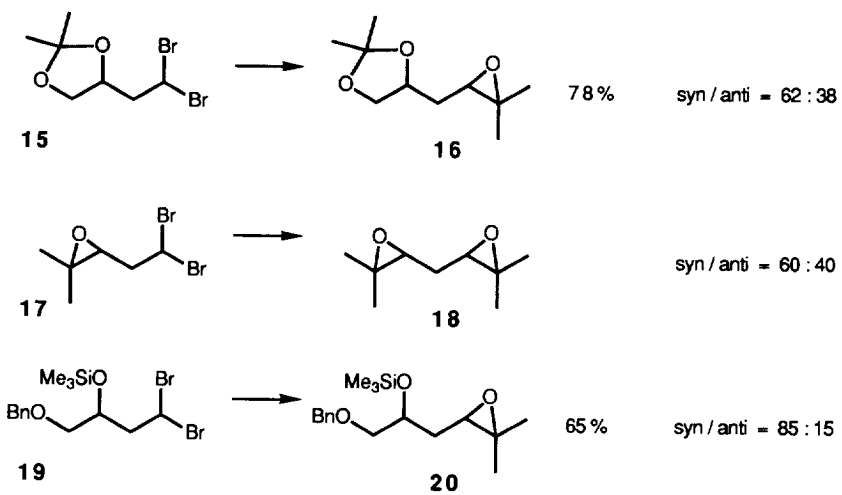


The major diastereomer **10a** of the epoxides was converted to the alcohol **11**. Analysis of the ^{1}H-NMR-coupling constants of **11** showed it to be the 1,3-*syn*-derivative. Hence, the sense of diastereoselectivity on

treatment of **6** with n-butyllithium was the same as observed for **1**,[2] but the level of diastereoselectivity was lower than expected. Similar results were obtained on reaction of the dibromo compounds **7** and **8** to give the epoxides **12** and **13**. Only with the dimethylated derivative **9** did the diastereoselectivity reach 90%. The relative configuration of the epoxides **12** - **14** is assigned in analogy to that of **10**. Obviously, the results demonstrate that the ground state conformation of the dibromides **6** to **9** and therefore also of **1** cannot be the sole factor in determining the diastereoselectivity.

Size of the Oxa-heterocycles and Diastereoselectivity?

On comparing the diastereoselectivities of the compounds **6** and e.g. **1b**, it was not clear at that point, whether constraint of the oxygen substituent in a heterocycle is one of the factors which control the level of diastereoselectivity in the bromine/lithium exchange reaction. For this reason, the dibromo-compounds **15** and **17** were prepared. The dibromocompound **19** was included for comparison. Reaction with n-butyllithium in the presence of acetone led to epoxides **16**, **18**, and **20** respectively.

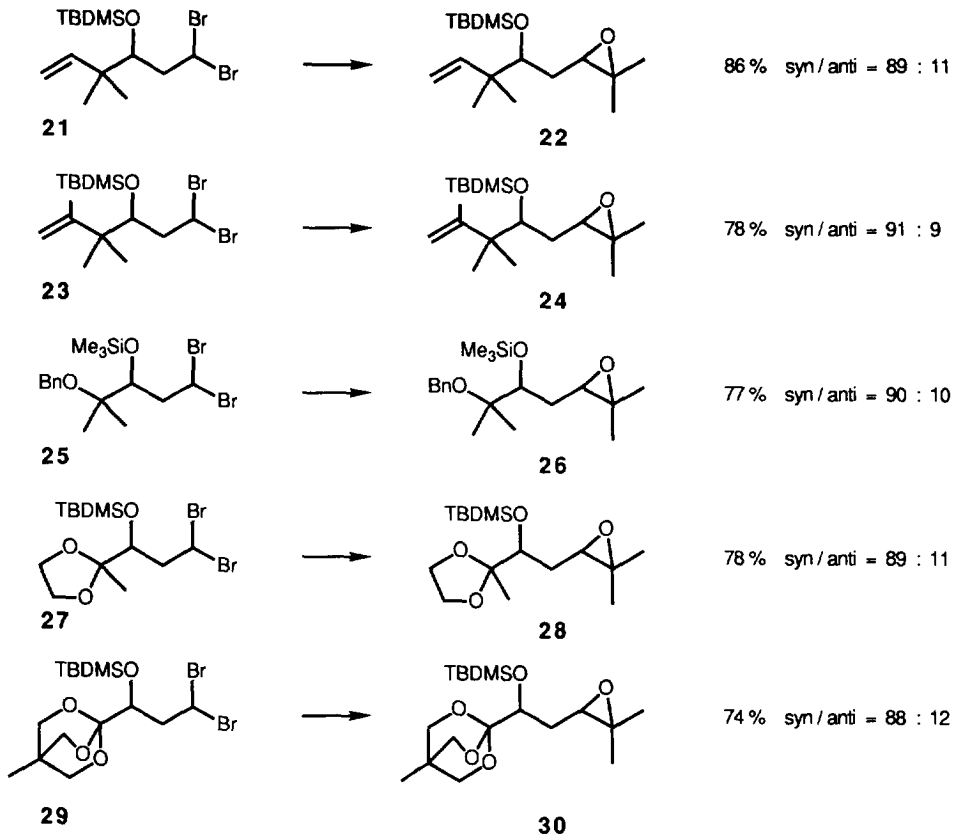


In fact, the diastereoselectivities observed in the formation of the epoxides **16** and **18** were lower than the ones found e.g. for the epoxides **10** above. This suggests that the increased steric freedom of the dibromomethyl group in the compounds **15** and **17** relative to **6**, or for that matter in **19**, leads to a distinctly lower diastereoselectivity in the bromine/lithium exchange reaction.

Is Steric Hindrance the Key to High Diastereoselectivity?

A comparison of the diastereoselecitivity trends in going from **1b** to **1a**, or in going from **17** to **15** and to **6**, or finally in going from **6** to **13** and to **14** suggests that the steric accessibility of the dibromomethyl moiety is an important factor, i.e. higher lateral accessibility of the dibromomethyl group leads to lower diastereoselectivity. We wanted to give this conjecture a further test and wanted to learn, whether further oxygen substituents at C-4 of the 1,1-dibromoalkanes would have a beneficial or detrimental effect on diastereoselectivity. We therefore prepared and studied the series of 1,1-dibromoalkanes **21**, **23**, **25**, **27**, and **29**.

The highest diastereoselectivities attained so far in the bromine/lithium exchange reaction are with substrates in which C-4 is a quaternary center, i.e. **1a**,[2] **9** and **21**,[5,4] This lead is apparently reliable, as with the dibromo-compound **23** where again high diastereoselectivity in the bromine/lithium exchange could be realized.

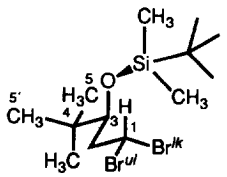


Apparently a quaternary center at C-4 is conductive to high diastereoselectivity, a quaternary center which may carry other than carbon substituents: The oxygenated compounds **25**, **27** and **29** all led to diastereoselectivities which are close to the maximum value of 90:10, so far reached. A quaternary center at C-4 alone is, however, not sufficient for high diastereoselectivity as is seen in the case of the epoxide **17**.

Conclusion

The results reported here have more clearly revealed the structural trends that lead to high diastereoselectivity in the bromine/lithium exchange on 1,1-dibromoalkanes. Tieing back the oxygen substituent at C-3 leads to decreased diastereoselectivity. In turn a quaternary center at C-4 leads to higher diastereoselectivity and these two factors may be related: A quaternary center at C-4 will as a consequence of the t-butyl effect[8] increase the population of the conformers in which the protective group on oxygen, e.g. silyl group of **1a**, points towards the dibromomethyl group, cf. **31**. The silyl group in **31** may be oriented in the direction of C-1, C-5 or C-5'. Each of these orientations results in a syn-pentane interaction, thus, these three conformations have qualitatively the same energy. If C-5' is replaced by a hydrogen atom as in **1b**, the silyl group will orient in this direction, because this is the only conformation free of syn-pentane interactions,[9] and therefore will not interfere with the attack of butyllithium at one of the bromine atoms.

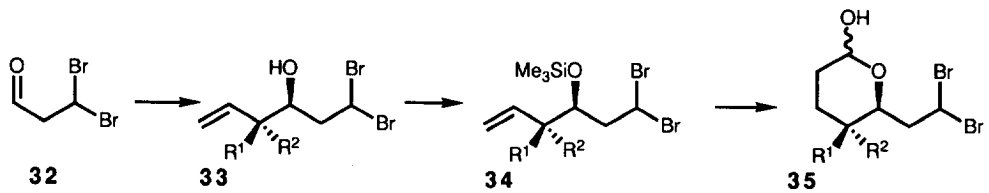
While the preferred conformation of the C-1 to C-4 backbone discussed earlier[3] is a prerequisite to differentiate the diastereotopic bromine atoms, this differentiation may come about by orientation of the C-3-$OSiR_3$ group, which, as outlined above, is controlled to a major extent by the degree of substitution of C-4. An orientation of the silyl residue as shown in **31** hinders a lateral approach of a lithium cation or of butyllithium to the *like*-bromine atom,[16] and therefore allows for selective exchange of the *unlike*-bromine atom[16] in **31**.



31

Preparation of the Starting Materials

The tetrahydropyran derivatives **6** to **9** were prepared starting from the dibromo-aldehyde **32**.[10] Suitable transformations into the homoallylic alcohols **33** were followed by silylation and indirect hydroformylation[11] to give the tetrahydropyranols **35**. The latter were reduced with triethylsilane and trifluoroacetic acid to the desired tetrahydropyrans.

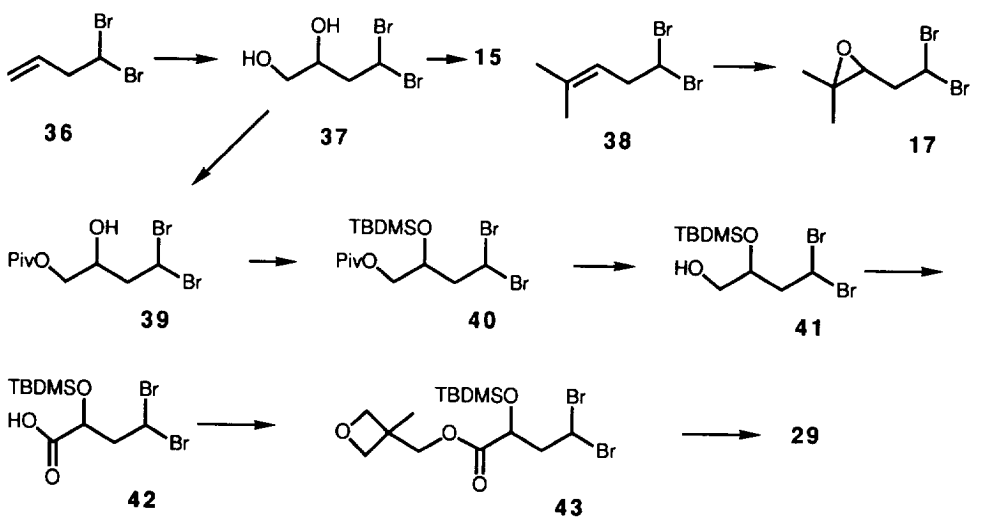


32 33 34 35

a: $R^1 = R^2 = H$ **c**: $R^1 = CH_3$; $R^2 = H$

b: $R^1 = H$; $R^2 = CH_3$ **d**: $R^1 = R^2 = CH_3$

The dioxolane **15** was generated from the corresponding diol **37** derived by bishydroxylation of the alkene **36**.[12] Likewise the alkene **38**[2] was epoxidized to furnish the dibromo-compound **17**.



36 37 38 17

39 40 41

42 43

The compounds **19**, **23**, **25**, and **27** were obtained by silylation of the corresponding alcohols.[6] The route to the OBO-ester **29** started from the diol **37**, which was subject to a protection-deprotection sequence

to furnish the alcohol **41**. Oxidation of the latter gave the acid **42**, which was transformed into the OBO-ester **29** in standard fashion.[13]

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Experimental

All temperatures quoted are not corrected. Temperatures in the -100°C range were determined with a GTH 215 precision digital thermometer of Fa. Greisinger, Regenstauf, Germany. - ^{1}H-NMR, ^{13}C-NMR: Bruker AMX-500; Bruker AC-300; ARX-200. - Boiling range of petroleum ether: 40-60°C. - pH7-buffer: 56.2 g NaH_2PO_4 x $2H_2O$ + 213.2 g Na_2HPO_4 x $2H_2O$ in 1.0 l of water. - Flash chromatography: Silica gel Si 60 E. Merck AG, Darmstadt, 40 - 63 μm. - MPLC: 30 cm x 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 x 0.3 mm quartz capillary column with SE 52, 1 bar He, temperature program 5 min at 100 °C, increase with 10°/min to 230°C.

1. 1,1-Dibromo-5-hexene-3-ol (**33a**): To a solution of 2.06 g (9.8 mmol) of 3,3-dibromo-propionaldehyde (**32**)[10] in 20 ml of petroleum ether were added over 10 min at -20°C 1.68 g (10.0 mmol) of 2-propenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.[14] After stirring for 12 h at room temperature 10 ml of water were added, the phases were separated and the aqueous phase was extracted four times with 10 ml each of ether. The combined organic phases were washed with brine and dried with $MgSO_4$. The solvents were removed i.vac. and the residue was purified by flash chromatography over silica gel with petroleum ether/ether = 4:1 to give 1.76 g (70%) of **33a** as a colorless liquid. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.88 (broad s, 1 H), 2.14 - 2.35 (m, 2 H), 2.45 (m, 2 H), 3.89 (m, 1 H), 5.16 (m, 2 H), 5.77 (m, 1 H), 5.86 (dd, *J* = 6.8 and 6.9 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.5, 42.9, 52.0, 68.9, 119.3, 133.3. - $C_6H_{10}Br_2O$ (258.0): calcd. C 27.91, H 3.88; found C 27.89, H 3.81.

2. 1,1-Dibromo-3-trimethylsilyloxy-5-hexene (**34a**): 2.33 ml (15.9 mmol) of trimethylsilyl-imidazole were added dropwise to a solution of 2.73 g (10.6 mmol) of the alcohol **34a** in 20 ml of anhydrous ether. After stirring for 12 h 20 ml of water were added, the phases were separated and the aqueous phase was extracted three times with 10 ml each of petroleum ether. The combined organic phases were washed with brine and dried over Na_2SO_4. The solvent was removed i. vac. and the residue was purified by flash chromatography with petroleum ether / ether = 10 : 1 containing 0.1 % triethylamine to give 3.38 g (97%) of **34a** as a colorless liquid. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.14 (s, 9H), 2.24 (t, *J* = 7.0 Hz, 2 H), 2.47 (m, 2 H), 3.91 (m, 1 H), 5.08 (m, 2 H), 5.65 - 5.79 (m, 2 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 41.8, 43.4, 52.3, 70.4, 118.2, 133.5. - $C_9H_{18}Br_2OSi$ (330.2): calcd. C 32.73, H 5.46; found 32.61, H 5.48.

3. 2-(2,2-Dibromoethyl)-tetrahydropyran (**6**): 12.3 ml (6.15 mmol) of a 0.5 M solution of 9-BBN in THF were added at 0°C to a solution of 1.36 g (4.13 mmol) of the alkene **34a** in 20 ml of THF. After stirring for 12 h the mixture was held under reflux for 1.5 h. After cooling to 0°C 4.13 ml (4.13 mmol) of a 1.0 M solution of potassium triisopropoxyborohydride in THF were added. Dry carbon monoxide was passed through the solution for 20 min at 0°C and for further 30 min at 20°C. The mixture was recooled to 0°C and a nitrogen atmosphere was established. 10 ml of pH-7 buffer and 4 ml of 30% aqueous H_2O_2 were added. The mixture was stirred for 30 min a 0°C and 30 min at 20°C. The mixture was acidified with 4 N hydrochloric acid and stirred for 30 min. After TLC indicated complete oxidation the mixture was neutralised with 2 N postassium hydroxide and the aqueous phase was saturated with potassium carbonate. The phases were separated and the aqueous phase was extracted five times with 10 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether / ether = 5 : 1 furnished 0.92 g (78%) of an anomeric mixture of tetrahydropyranols.

62 µl (0.80 mmol) of trifluoroacetic acid were added at -78°C to a solution of 76.7 mg (0.27 mmol) of these tetrahydropyranols in 5 ml of anhydrous dichloromethane. After stirring for 10 min 130 µl (0.81 mmol) of triethylsilane were added and the mixture was allowed to reach room temperature. After TLC indicated complete reaction the mixture was poured into 10 ml of ice-cold saturated aqueous $NaHCO_3$-solution. The phases were separated and the aqueous phase was extracted four times with 10 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether / ether = 20 : 1 furnished 61 mg (83%) of **6** as a colorless liquid. - ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.31 (m, 1 H), 1.52 (m, 4 H), 1.83 (m, 1 H), 2.40 (ddd, J = 14.7, 10.7, and 2.7 Hz, 1 H), 2.55 (ddd, J = 14.7, 9.7, and 3.2 Hz, 1 H), 3.40 (ddd, J = 11, 11, and 3.5 Hz, 1 H), 3.47 (dddd, J = 10.5, 10.5, 2.3, and 2.3 Hz, 1 H), 3.93 (ddd, J = 11.3, 2.3, and 2.3 Hz, 1 H), 5.84 (dd, J = 10.7 and 3.2 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6, 26.3, 31.6, 43.3, 52.6, 68.8, 76.0. - $C_7H_{12}Br_2O$ (272.1): calcd. C 30.88, H 4.41; found C 31.09, H 4.39.

4. (3R*,4S*)-1,1-Dibromo-3-hydroxy-4-methyl-5-hexene (**33b**): 4.8 ml (3.3 mmol) of a 0.7 M solution of chloro-triphenyloxy-titanium[15] were cooled in the lower chamber of a two chamber reaction vessel[5] to -80°C. To this solution were added 8.8 ml (3.0 mmol) of a 0.34 M solution of crotylmagnesium chloride in THF over 1 h via a syringe pump. The mixture was allowed to reach -30°C over 2 h. It was recooled to -100°C and the upper chamber of the two chamber reaction vessel was charged with a solution of 0.5 g (2.3 mmol) of freshly prepared 3,3-dibromo-propionaldehyde (**32**) in 5 ml of dichloromethane. Once the aldehyde solution was cooled to -100°C it was added dropwise to the solution of the titanate. After stirring for 12 h at -100°C the mixture was allowed to reach room temperature. 20 ml of saturated aqueous potassium fluoride solution were added and the mixture was neutralised to pH = 7. The phases were separated and the aqueous phase was extracted four times with 10 ml each of ether. The combined organic phases were washed with brine. The organic phase was extracted twice with 20 ml of aqueous 2 N NaOH and washed with brine until neutral. The organic phase was dried with Na_2SO_4 and concentrated. Flash chromatography of the residue with petroleum ether / ether gave an 88 : 12 anti/syn mixture of the alcohols **33b**. 1.46 g (64%) of the desired anti-isomer **33b** was obtained by MPLC using petroleum ether / ethyl acetate = 15 : 1. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 (d, J = 6.8 Hz, 3 H), 1.92 (broad s, 1 H), 2.20 (sextett, J = 6.8 Hz, 1 H), 2.47 (m, 2 H), 3.61 (ddd, J = 9.3, 6.2, and 3.1 Hz, 1 H), 5.12 (m, 2 H), 5.69 (ddd, J = 18.8, 10.5, and 8.3 Hz, 1 H), 5.87 (dd, J = 9.9 and 3.8 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.2, 44.0, 44.5, 50.1, 72.8, 117.3, 139.2. - $C_7H_{12}Br_2O$ (272.1): calcd. C 30.88, H 4.41; found C 31.05, H 4.53.

5. (3R*,4S*)-1,1-Dibromo-3-trimethylsilyloxy-4-methyl-5-hexene (**34b**): 0.81 g (3.0 mmol) of the alcohol **33** were allowed to react with 0.7 ml (4.7 mmol) of trimethylsilyl-imidazole as described under 2. to give a quantitative yield of **34b** as a colorless liquid. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.15 (s, 9 H), 1.01 (d, J = 6.9 Hz, 3 H), 2.24 - 2.52 (m, 3 H), 3.82 (dt, J = 9.5 and 3.4 Hz, 1 H), 5.05 (m, 2 H), 5.64 (dd, J = 10.3 and 3.4 Hz, 1 H), 5.72 (ddd, J = 17.5, 10.6, and 7.3 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 14.4, 43.3, 44.1, 49.1, 74.3, 115.7, 139.4. - $C_{10}H_{20}Br_2OSi$ (344.2): Calcd. C 34.88, H 5.81; found C 35.08, H 5.73.

6. (2S*,3S*)-2-(2,2-Dibromoethyl)-3-methyl-tetrahydropyran (**7**): 401 mg (1.17 mmol) of the alkene **34b** and 3.42 ml (1.76 mmol) of 9-BBN and 1.17 mmol of potassium triisopropoxyborohydride were allowed to react as described under 3. to furnish 206 mg (58%) of the crude tetrahydropyranols as an anomeric mixture. 150 mg of this mixture were reduced as described under 3. with 0.14 ml (1.5 mmol) of trifluoroacetic acid and 0.23 ml (1.5 mmol) of triethylsilane. Flash chromatography with petroleum ether / ether = 20 : 1 furnished 98 mg (70%) of **7** as a colorless liquid. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (d, J = 6.6 Hz, 3 H), 1.14 (m, 1 H), 1.34 (m, 1 H), 1.47 - 1.69 (m, 2 H), 1.76 (m, 1 H), 2.39 (ddd, J = 14.6, 10.2, and 2.6 Hz, 1 H), 2.64 (ddd, J = 14.6, 11.2, and 2.3 Hz, 1 H), 3.06 (td, J = 9.9 and 2.2 Hz, 1 H), 3.31 (td, J = 11.5 and 3.1 Hz, 1 H), 3.90 (m, 1 H), 5.86 (dd, J = 11.3 and 2.5 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.6, 26.4, 32.5, 35.1, 43.8, 49.7, 68.2, 81.4. - $C_8H_{14}Br_2O$ (286.1): calcd. C 33.57, H 4.90; found C 33.80, H 4.95.

7. (3S*,4S*)-1,1-Dibromo-3-hydroxy-4-methyl-5-hexene (**33c**): 5.0 g (19 mmol) of 3,3-dibromo-1-chloro-1-methoxy-propane[10] were stirred for 3 h in 50 ml of water to generate the aldehyde **32**. The phases were separated and the organic

phase was stirred with 10 ml of water for 1 h. The combined aqueous phases were saturated with NaCl and extracted four times with 20 ml each of chloroform. The organic phase was dried with $MgSO_4$ and concentrated. The resulting aldehyde **32** was immediately dissolved in 20 ml of dichloromethane and cooled to -78°C. Then 2.36 ml (18.8 mmol) of BF_3-etherate were added with a syringe. After stirring for 10 min 8.0 g (23 mmol) of crotyl-tributyl-stannane were added with a syringe. The mixture was allowed to reach room temperature over night. 20 ml of aqueous pH-7 buffer were added, the phases were separated and the aqueous phase was extracted four times with 10 ml each of ether. The combined organic phases were washed with 20 ml of brine, dried with Na_2SO_4 and concentrated. Flash chromatography of the residue with petroleum ether / ether = 5 : 1 furnished 1.95 g of a 80 : 20 syn/anti-mixture of the alcohol **33c**. 1.6 g (6.0 mmol) of the desired syn-alcohol **33c** were obtained by MPLC with petroleum ether / ethyl acetate = 15 : 1. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (d, J = 6.9 Hz, 3 H), 2.13 (broad s, 1 H), 2.26 (sextett, J = 6.9 Hz, 1 H), 2.44 (m, 2 H), 3.67 (ddd, J = 8.4, 5.7, and 2.4 Hz, 1 H), 5.07 (m, 1 H), 5.11 (s, 1 H), 5.70 (ddd, J = 18.9, 11.2, and 7.7 Hz, 1 H), 5.84 (dd, J = 10.4 and 3.3 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8, 43.5, 43.7, 49.7, 72.9, 116.5, 139.4. - $C_7H_{12}Br_2O$ (272.1): calcd. C 30.88, H 4.41; found C 31.05, H 4.53.

8. (3S*,4S*)-1,1-Dibromo-3-trimethylsilyloxy-4-methyl-5-hexene (**34c**): 2.0 g (7.7 mmol) of alcohol **33c** were silylated with 1.7 ml (11.5 mmol) trimethylsilyl-imidazole as described under 2. to give a quantitative yield of **34c**. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.15 (s, 9 H), 0.99 (d, J = 7.0 Hz, 3 H), 2.31 (m, 1 H), 2.43 (m, 2 H), 3.76 (ddd, J = 9.3, 6.1, and 5.1 Hz, 1 H), 5.05 (m, 2 H), 5.65 (m, 1 H), 5.81 (ddd, J = 17.4, 10.6, and 6.9 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 15.1, 43.2, 44.2, 49.4, 74.8, 115.6, 139.4. - $C_{10}H_{20}Br_2OSi$ (344.2): calcd. C 34.88, H 5.81; found C 34.72, H 5.82.

9. (2S*,3S*)-2-(2,2-Dibromoethyl)-3-methyl-tetrahydropyran (**8**): 388 mg (1.13 mmol) of alkene **34c**, 3.3 ml of a 0.5 M solution of 9-BBN in THF and 1.13 mmol of potassium triisopropoxyborohydride were allowed to react as described under 3. to furnish 131 mg (39%) of the tetrahydropyranols as an anomeric mixture. 0.50 g (1.7 mmol) of this mixture in 10 ml of dichloromethane were reduced with 0.35 ml (5.1 mmol) of trifluoroacetic acid and 0.81 ml (5.1 mmol) of triethylsilane as described under 3. to give 273 mg (56%) of **8** as a colorless liquid. - ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.96 (d, J = 7.0 Hz, 3 H), 1.29 (m, 1 H), 1.61 (m, 1 H), 1.69 (m, 1 H), 1.74 (m, 2 H), 2.24 (ddd, J = 14.7, 10.7, and 2.5 Hz, 1 H), 2.59 (ddd, J = 14.7, 10.1, and 3.1 Hz, 1 H), 3.41 (m, 1 H), 3.58 (dt, J = 10.1 and 2.5 Hz, 1 H), 3.88 (m, 1 H), 5.78 (dd, J = 10.7 and 3.1 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.2, 22.4, 30.7, 30.9, 43.5, 49.0, 68.3, 76.4. - $C_8H_{14}Br_2O$ (286.1): calcd. C 33.57, H 4.90; found C 33.61, H 4.79.

10. 1,1-Dibromo-4,4-dimethyl-3-trimethylsilyloxy-5-hexene (**34d**): 2.4 g (8.4 mmol) of alcohol **33d**[5] were silylated with 1.85 ml (12.6 mmol) of trimethylsilyl-imidazole as described under 2. to give 2.74 g (99%) of **34d** as a colorless liquid. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.20 (s, 9 H), 1.01 (s, 6 H), 2.47 (m, 2 H), 3.60 (dd, J = 9.2 and 2.8 Hz, 1 H), 5.03 (dd, J = 17.4 and 1.4 Hz, 1 H), 5.07 (dd, J = 10.8 and 1.4 Hz, 1 H), 5.60 (dd, J = 10.4 and 3.6 Hz, 1 H), 5.79 (dd, J = 17.4 and 10.8 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.8, 22.7, 24.0, 41.5, 44.8, 49.0, 78.5, 112.8, 144.8. - $C_{11}H_{22}Br_2OSi$ (358.2): calcd. C 36.86, H 6.14; found C 36.57, H 6.29.

11. 2-(2,2-Dibromoethyl)-3,3-dimethyl-tetrahydropyran (**9**): 1.79 g (5.42 mmol) of alkene **34d**, 8.13 mmol of 9-BBN and 5.42 mmol of potassium triisopropoxyborohydride were allowed to react as described under 3. to give 0.93 g (54%) of the tetrahydropyranols as an anomeric mixture. 866 mg (2.74 mmol) of this mixture were reduced with 0.62 ml (9.0 mmol) of trifluoroacetic acid and 1.4 ml (9 mmol) of triethylsilane as described under 3. to give 0.63 g (81%) of **9** as a colorless liquid. - ^{1}H NMR (500 MHz, toluene-D_8): δ = 0.51 (s, 3 H), 0.63 (s, 3 H), 0.90 (m, 1 H), 0.95 (td, J = 13.3 and 4.3 Hz, 1 H), 1.07 (m, 1 H), 1.46 (m, 1 H), 2.28 (m, 2 H), 2.98 (m, 2 H), 3.66 (m, 1 H), 5.75 (m, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 22.8, 27.2, 32.3, 39.0, 44.6, 46.4, 68.9, 83.3. - $C_9H_{16}Br_2O$ (300.0): calcd. C 36.00, H 5.33; found C 35.91, H 5.15.

12. 4,4-Dibromo-butane-1,2-diol (**37**): 32 mg (0.09 mmol) of potassium osmate dihydrate was added at 0°C under stirring to a solution of 2.24 g (10.5 mmol) of the alkene **36**),[12] 2.98 g (15.3 mmol) of a 60% aqueous solution of N-methyl-morpholine-N-oxide and 0.33 g (1.5 mmol) of 1-benzoyloxy-2-(N,N-diethylamino)-ethane in 5 ml of acetone.

After stirring for 3 d at room temperature 0.5 g of $NaHSO_3$ were added. The mixture was stirred for 1 h and 10 g of Na_2SO_4 and 20 ml of CH_2Cl_2 were added. After stirring for 1 h the mixture was filtered and the residue was washed four times with 15 ml each of CH_2Cl_2. The combined filtrates were concentrated i.vac. and the residue was purified by flash chromatography with t-butyl-methyl-ether/petroleum ether = 1 : 1 to give 2.50 g (96%) of **37** as a colorless oil, which solidified on standing. M.p. 77 - 79°C. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.88 - 1.98 (m, 1 H), 2.38 - 2.44 (m, 1 H), 2.43 (ddd, J = 14.7, 10.0, and 2.9 Hz, 1 H), 2.58 (ddd, J = 14.7, 9.6, and 3.7 Hz, 1 H), 3.51 (ddd, J = 11.2, 6.4, and 5.8 Hz, 1 H), 3.70 (ddd, J = 11.0, 5.3, and 3.3 Hz, 1 H), 3.96 (m, 1 H), 5.88 (dd, J = 10.0 and 3.6 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.1, 48.5, 65.8, 70.5. - $C_4H_8Br_2O_2$ (247.9): calcd. C 19.38, H 3.25; found C 19.50, H 3.24.

13. 4-(2,2-Dibromoethyl-2,2-dimethyl-1,3-dioxolane (**15**): To a solution of 1.27 g (5.1 mmol) of the diol **37** in 10 ml of 2,2-dimethoxypropane were added 6 mg (0.03 mmol) of p-toluene-sulfonic acid monohydrate. After stirring for 2 h at room temperature 5 drops of triethylamine were added and the solvents were removed i. vac. Flash chromatography of the residue with t-butyl-methyl-ether/petroleum ether = 1 : 3 furnished 1.46 g (99%) of **15** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (s, 3 H), 1.40 (s, 3 H), 2.53 (ddd, J = 14.5, 10.0, and 3.6 Hz, 1 H), 2.66 (ddd, J = 14.5, 8.8, and 3.5 Hz, 1 H), 3.62 (dd, J = 8.2 and 5.9 Hz, 1 H), 4.11 (dd, J = 8.3 and 6.2 Hz, 1 H), 4.28 (dddd, J = 8.6, 6.1, 6.1, and 3.6 Hz, 1 H), 5.78 (dd, J = 10.0 and 3.5 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.4, 27.0, 41.5, 49.9, 68.4, 73.8, 109.6. - $C_7H_{12}Br_2O_2$ (288.0): calcd. C 29.19, H 4.20; found C 28.91, H 4.04.

14. 1,1-Dibromo-3,4-epoxy-4-methyl-pentane (**17**): Into a solution of 1.16 g (4.8 mmol) of the alkene **38**[2] in 10 ml of CH_2Cl_2 was added at 20°C a solution of 1.30 g (ca. 5.4 mmol) of m-chloroperbenzoic acid in 10 ml of CH_2Cl_2, which had been dried with $MgSO_4$. After stirring for 2 h 20 ml of aqueous $NaHCO_3$-solution was added. The phases were separated and the aqueous phase was extracted three times with 10 ml of dichloromethane. The combined organic phases were washed with 10 ml of brine, dried with Na_2SO_4 and concentrated. Flash chromatography of the residue with t-butyl-methyl-ether / petroleum ether = 1 : 10 furnished 0.97 g (78%) of **17** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (s, 3 H), 1.33 (s, 3 H), 2.59 (ddd, J = 15.0, 6.4, and 4.6 Hz, 1 H), 2.68 (ddd, J = 15.0, 8.0, and 5.0 Hz, 1 H), 2.95 (dd, J = 6.4 and 5.0 Hz, 1 H), 5.78 (dd, J = 8.0 and 4.5 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2, 24.5, 41.0, 44.4, 58.4, 61.6. - $C_6H_{10}Br_2O$ (258.0): calcd. C 27.94, H 3.91; found C 27.84, H 3.96.

15. 4-Benzyloxy-1,1-dibromo-3-trimethylsilyloxy-butane (**19**): 190 mg (0.56 mmol) of 4-benzyloxy-1,1-dibromo-3-hydroxy-butane[6] were silylated with 0.10 ml (0.7 mmol) of trimethylsilyl-imidazole as described under 2. to give a quantitative yield of **19**. - ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.13 (s, 9 H), 2.34 - 2.52 (m, 2 H), 3.18 - 3.32 (m, 2 H), 4.02 (dddd, J = 8.1, 5.2, 5.2, and 5.2 Hz, 1 H), 4.53 (s, 2 H), 5.72 (dd, J = 8.1 and 5.9 Hz, 1 H), 7.24 - 7.40 (m, 5 H). - ^{13}C NMR (50 MHz, $CDCl_3$): δ = 0.3, 43.1, 50.1, 70.0, 73.4, 73.7, 127.7, 127.8, 128.4, 137.8. - $C_{14}H_{22}Br_2O_2Si$ (410.2): calcd. C 40.99, H 5.41; found C 41.10, H 5.45.

16. 1,1-Dibromo-3-t-butyldimethylsilyloxy-4,4,5,5-trimethyl-5-hexene (**23**): 0.80 ml (3.5 mmol) of tert.-butyl-dimethylsilyl triflate were added at 20°C to a solution of 0.85 g of 1,1-dibromo-3-hydroxy-4,4,5-trimethyl-5-hexene[6] and of 0.60 ml (5.2 mmol) of 2,6-lutidine in 3 ml of CH_2Cl_2. After stirring for 2 h 2 ml of ethanol was added, the mixture was stirred for 15 min and the solvents were removed i.vac. The residue was purified by flash chromatography with t-butyl-methyl-ether/petroleum ether = 1:10 to furnish 1.08 g (92%) of **23** as a colorless oil which crystallized in the refrigerator. M.p. 58 - 61 °C. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.10 (s, 3 H), 0.16 (s, 3 H), 0.91 (s, 9 H), 1.02 (s, 3 H), 1.03 (s, 3 H), 1.76 (s, 3 H), 2.38 (ddd, J = 15.0, 8.5, and 3.5 Hz, 1 H), 2.49 (ddd, J = 15.0, 10.7, and 2.0 Hz, 1 H), 3.75 (dd, J = 8.5 and 2.0 Hz, 1 H), 4.81 (s, 2 H), 5.66 (dd, J = 10.7 and 3.4 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -3.8, -3.6, 18.5, 19.9, 20.4, 26.1, 26.2, 44.2, 44.9, 50.3, 75.8, 111.6, 150.3. - $C_{15}H_{30}Br_2OSi$ (414.3): calcd. C 43.49, H 7.30; found C 43.55, H 7.14.

17. 4-Benzyloxy-1,1-dibromo-4-methyl-3-trimethylsilyloxy-pentane (**25**): 0.49 g (1.34 mmol) of 4-benzyloxy-1,1-dibromo-4-methyl-3-pentanol[6] were silylated in 10 ml of petroleum ether with 0.35 ml (2.4 mmol) of N-trimethylsilyl-imidazole as described under 2. Flash chromatography with t-butyl-methyl-ether/petroleum ether = 1:10 furnished 0.55

g (94%) of **25** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.16 (s, 9 H), 1.19 (s, 3 H), 1.25 (s, 3 H), 2.51 (ddd, J = 14.5, 9.2, and 3.7 Hz, 1 H), 2.73 (ddd, J = 14.5, 10.3, and 3.0 Hz, 1 H), 3.81 (dd, J = 9.2 and 2.9 Hz, 1 H), 4.44 (d, J = 11.3 Hz, 1 H), 4.51 (d, J = 11.3 Hz, 1 H), 5.73 (dd, J = 10.3 and 3.7 Hz, 1 H), 7.23 - 7.34 (m, 5 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.7, 20.6, 21.8, 44.7, 48.6, 64.0, 77.4, 77.8, 127.2, 127.3, 128.3, 139.3. - $C_{16}H_{26}Br_2O_2Si$ (438.3): calcd. C 43.85, H 5.98; found C 43.84, H 5.98.

18. 2-(3,3-Dibromo-1-trimethylsilyloxy-propyl)-2-methyl-1,3-dioxolane (**27**): 1.40 g (4.6 mmol) of 2-(3,3-dibromo-1-hydroxy-propyl)-2-methyl-1,3-dioxolane[6] were silylated with 1.20 ml (8.2 mmol) of N-trimethylsilyl-imidazole as described under 2. Flash chromatography with t-butyl-methyl-ether/petroleum ether = 1:1 furnished 1.72 g (99%) of **27** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.15 (s, 9 H), 1.25 (s, 3 H), 2.51 (ddd, J = 14.5, 9.5, and 3.8 Hz, 1 H), 2.61 (ddd, J = 14.5, 10.4, and 3.2 Hz, 1 H), 3.70 (dd, J = 9.5 and 3.1 Hz, 1 H), 3.82 - 3.99 (m, 4 H), 5.67 (dd, J = 10.3 and 3.8 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.3, 19.6, 43.8, 48.5, 64.8, 65.1, 74.5, 109.9. - $C_{10}H_{20}Br_2O_3Si$ (376.2): calcd. C 31.93, H 5.36; found C 31.83, H 5.28.

19. 4,4-Dibromo-2-hydroxybutyl 2,2-dimethylpropanoate (**39**): Into a solution of 1.31 g (5.3 mmol) of the diol **37** in 5 ml of pyridine were added 0.72 g (6.0 mmol) of pivaloyl chloride. After stirring for 2 h 10 ml of water were added. The phases were separated and the aqueous phase was extracted three times with 10 ml each of t-butyl-methyl-ether. The combined organic phases were washed three times with 10 ml each of 2 N hydrochloric acid and once with 10 ml of brine. After removal of the solvent the residue was purified by flash chromatography with t-butyl-methyl-ether/petroleum ether = 1 : 3 to give 1.59 g (90%) of **39** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (s, 9 H), 2.46 (broad s, 1 H), 2.48 (ddd, J = 14.6, 9.9, and 3.0 Hz, 1 H), 2.57 (ddd, J = 14.6, 9.1, and 3.8 Hz, 1 H), 4.01 - 4.18 (m, 3 H), 5.87 (dd, J = 9.9 and 3.8 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.2, 38.9, 41.8, 48.9, 67.5, 68.6, 178.8. - $C_9H_{16}Br_2O_3$ (332.1): calcd. C 32.56, H 4.86; found C 32.40, H 4.88.

20. 4,4-Dibromo-2-(t-butyldimethylsilyloxy)-butyl-2,2-dimethylpropanoate (**40**): 0.94 g (2.8 mmol) of the alcohol **39**, 0.65 ml (5.6 mmol) of 2,6-lutidine and 0.85 ml (3.7 mmol) tert.-butyl-dimethylsilyl triflate were allowed to react as described under 16. Flash chromatography with t-butyl-methyl-ether/petroleum ether = 1 : 30 furnished 1.25 g (99%) of **40** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 3 H), 0.13 (s, 3 H), 0.88 (s, 9 H), 1.21 (s, 9 H), 2.53 (ddd, J = 14.5, 9.7, and 3.1 Hz, 1 H), 2.61 (ddd, J = 14.5, 8.4, and 4.0 Hz, 1 H), 3.93 (dd, J = 10.3 and 5.4 Hz, 1 H), 3.97 - 4.06 (m, 1 H), 4.07 (dd, J = 10.4 and 3.3 Hz, 1 H), 5.70 (dd, J = 9.9 and 4.0 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -4.7, -4.4, 17.9, 25.7, 27.2, 38.8, 42.1, 50.8, 66.8, 68.9, 178.1. - $C_{15}H_{30}Br_2O_3Si$ (446.3): calcd. C 40.37, H 6.78; found C 40.62, H 6.70.

21. 4,4-Dibromo-2-(t-butyldimethylsilyloxy)-1-butanol (**41**): Into a solution of 1.25 g (2.8 mmol) of the pivalate **40** in 20 ml of CH_2Cl_2 was added at -78°C 2.5 ml (3.5 mmol) of a 1.4 M solution of diisobutylaluminium hydride in toluene. After the temperature reached -30°C over 2 h, 20 ml of saturated aqueous NH_4Cl-solution were added. The phases were separated and the aqueous phase was extracted three times with 20 ml each of t-butyl-methyl-ether. The combined organic phases were washed with 20 ml of brine and concentrated. Flash chromatography of the residue with t-butyl-methyl-ether/petroleum ether = 1:7 to 1:3 furnished 0.79 g (78%) of **41** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 3 H), 0.14 (s, 3 H), 0.89 (s, 9 H), 2.01 (broad s, 1 H), 2.53 (ddd, J = 14.6, 9.6, and 3.7 Hz, 1 H), 2.72 (ddd, J = 14.6, 8.7, and 4.4 Hz, 1 H), 3.50 (dd, J = 11.4 and 3.5 Hz, 1 H), 3.62 (dd, J = 11.4 and 4.1 Hz, 1 H), 3.94 (dddd, J = 8.6, 3.8, 3.8, and 3.8 Hz, 1 H), 5.67 (dd, J = 9.5 and 4.4 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -4.6, -4.4, 18.0, 25.8, 42.5, 49.8, 65.8, 71.3. - $C_{10}H_{22}Br_2O_2Si$ (362.2): calcd. C 33.16, H 6.12; found C 33.25, H 6.10.

22. 4,4-Dibromo-2-(t-butyldimethylsilyloxy)-butyric acid (**42**): Into a solution of 0.77 g (2.1 mmol) of the alcohol **41** in 5 ml of CCl_4, 5 ml of acetonitrile and 5 ml of water were added 2.20 g (10.3 mmol) of sodium meta-periodate and 17 mg of ruthenium dioxide. After stirring for 16 h 5 ml of water were added. The phases were separated and the aqueous phase was extracted five times with 10 ml each of ether. The combined organic phases were filtered over a small pad of silica gel, dried with Na_2SO_4 and concentrated at 20°C/0.2 Torr to give 0.62 g (79%) of the acid **42** as a colorless oil. -

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.14 (s, 3 H), 0.14 (s, 3 H), 0.92 (s, 9 H), 2.77 (ddd, J = 14.5, 8.2, and 5.1 Hz, 1 H), 2.84 (ddd, J = 14.5, 8.6, and 4.5 Hz, 1 H), 4.40 (dd, J = 8.3 and 4.5 Hz, 1 H), 5.74 (dd, J = 8.7 and 5.2 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.1, -4.9, 18.2, 25.6, 40.5, 50.1, 70.5, 176.2. - $C_{10}H_{20}Br_2O_3Si$ (376.2): calcd. C 31.93, H 5.36; found C 31.74, H 5.26.

23. 3-[4,4-Dibromo-2-(t-butyldimethylsilyloxy)-butanoyloxymethyl]-3-methyl-oxetane (**43**): Into a solution of 324 mg (0.86 mmol) of the acid **43** and of 0.30 ml (3.7 mmol) of pyridine in 5 ml of CH_2Cl_2 was added dropwise at 20°C 0.10 ml (1.1 mmol) $POCl_3$. After stirring for 15 min and cooling to 0°C 0.16 ml (1.6 mmol) of 3-hydroxymethyl-3-methyl-oxetane were added and the mixture was allowed to reach 20°C over 12 h. 10 ml of saturated aqueous NH_4Cl-solution were added, the phases were separated and the aqueous phase was extracted three times with 10 ml each of t-butyl-methyl-ether. The combined organic phases were washed with 10 ml of brine and concentrated. Flash chromatography of the residue with t-butyl-methyl-ether/petroleum ether = 1:3 furnished 193 mg (49%) of the ester **43** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.10 (s, 6 H), 0.91 (s, 9 H), 1.34 (s, 3 H), 2.77 (dd, J = 6.9 and 6.3 Hz, 2 H), 4.23 (d, J = 11.1 Hz, 1 H), 4.27 (d, J = 11.1 Hz, 1 H), 4.38 (dd, J = 6.8 and 5.9 Hz, 1 H), 4.40 (d, J = 6.0 Hz, 2 H), 4.49 (d, J = 6.0 Hz, 2 H), 5.74 (dd, J = 7.3 and 6.5 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.2, -4.8, 18.2, 21.1, 25.7, 39.2, 40.9, 50.3, 69.6, 70.7, 79.4, 79.5, 172.1. - $C_{15}H_{28}Br_2O_4Si$ (460.3): calcd. C 39.14, H 6.13; found C 39.44, H 6.26.

24. 1-[3,3-Dibromo-1-(t-butyldimethylsilyloxy)-propyl]-4-methyl-2,6,7-trioxa[2.2.2]bicyclooctane (**29**): To a solution of 117 mg (0.25 mmol) of the ester **43** in 5 ml of CH_2Cl_2 were added at -50°C 70 μl (0.06 mmol) of a 10 % solution of BF_3-etherate in CH_2Cl_2. The mixture was allowed to reach 20°C over 4 h. When TLC indicated complete reaction, 5 drops of triethylamine were added and the solvent was removed i.vac. Flash chromatography of the residue with CH_2Cl_2/petroleum ether = 1:2 furnished 43 mg (37%) of the orthoester **29** as a colorless solid, m.p. 69 -70 °C. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 3 H), 0.11 (s, 3 H), 0.80 (s, 3 H), 0.88 (s, 9 H), 2.61 (ddd, J = 14.7, 10.2, and 3.5 Hz, 1 H), 2.71 (ddd, J = 14.7, 9.2, and 4.0 Hz, 1 H), 3.81 (dd, J = 9.2 and 3.4 Hz, 1 H), 3.87 (s, 6 H), 5.72 (dd, J = 10.1 and 4.0 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.2, -4.3, 14.3, 18.5, 26.2, 30.6, 43.7, 50.3, 72.5, 72.8, 107.7. - $C_{15}H_{28}Br_2O_4Si$ (460.3): calcd. C 39.14, H 6.13; found C 39.18, H 6.32.

25. Bromine/Lithium Exchange on the Dibromo Compounds and Formation of the Epoxides: The procedure used was described in detail in ref.[5].

26. 2-(2,3-Epoxy-3-methylbutyl)-tetrahydropyran (**10**): From 0.386 g (1.42 mmol) of **6**; flash chromatography with ether/petroleum ether = 6:1 gave 0.274 g (88%) of **10** as a colorless liquid. The diastereomer ratio was found to be 76:24 from the ^{1}H- and ^{13}C-NMR-spectra. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 3 H), 1.26 (s, 3 H), 1.29 - 1.81 (m, 8 H), 2.81 (t, J = 6.4 Hz, 0.77 H), 2.88 (dd, J = 4.0 and 7.8 Hz, 0.23 H), 3.40 (m, 2 H), 3.94 (m, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer: δ = 18.8, 23.5, 24.7, 25.9, 31.5, 35.7, 57.6, 61.1, 68.7, 75.8; minor diastereomer: δ = 19.0, 23.4, 24.7, 26.0, 32.2, 36.0, 58.1, 61.4, 68.7, 75.6. - $C_{10}H_{18}O_2$ (170.0): calcd. C 70.59, H 10.59; found C 70.46, H 10.62.

27. 2-(2-Hydroxy-3-methyl-3-butenyl)-tetrahydropyran (**11**): To a solution of 2.0 mmol of lithium diisopropylamide in 20 ml of ether were added at 0°C 224 mg (1.32 mmol) of a 81:19 mixture of the epoxides **10** in 5 ml of ether. After allowing to reach room temperature over 3 h the mixture was held under reflux for 8 h. 20 ml of 2 N hydrochloric acid were added and the mixture was stirred for 30 min before it was neutralised with 1 N NaOH. The phases were separated and the aqueous phase was extracted four times with 20 ml of ether. The combined organic phases were washed with 10 ml of brine, dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ether = 4:1 furnished 128 mg (57%) of **11** as a colorless liquid. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 - 1.79 (m, 12 H), 3.44 (td, J = 11.3 and 3.0 Hz, 1 H), 3.56 (m, 1 H), 3.97 (m, 1 H), 4.25 (dd, J = 9.5 and 2.8 Hz, 1 H), 4.77 (m, 1 H), 4.97 (m, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.9, 23.2, 25.8, 32.3, 41.9, 68.3, 75.8, 79.1, 110.4, 147.2. - $C_{10}H_{18}O_2$ (170.0): calcd. C 70.59, H 10.59; found C 70.34, H 10.58.

28. (2R*,3S*)-2-(2',3'-Epoxy-3'-methylbutyl)-3-methyl-tetrahydropyran (**12**): From 95 mg (0.33 mmol) of the dibromo compound **7**. Flash chromatography with petroleum ether /ether = 6:1; 37.0 mg (61%) of **12** as a colorless liquid. Gas chromatography indicated an 81:9 mixture of diastereomers. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (d, J = 6.6 Hz, 0.6 H), 0.83 (d, J = 6.6 Hz, 2.4 H), 1.23 (s, 0.6 H), 1.25 (s, 2.4 H), 1.30 (s, 3 H), 1.52 - 1.90 (m, 7 H), 2.97 (dd, J = 6.7 and 4.8 Hz, 0.8 H), 3.04 (m, 1.2 H), 3.37 (m, 1 H), 3.98 (m, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer: δ = 17.8, 18.7, 24.6, 26.4, 32.5, 32.7, 34.8, 56.9, 61.2, 68.3, 82.1.

29. (2S*,3S*)-2-(2',3'-Epoxy-3'-methylbutyl)-3-methyl-tetrahydropyran (**13**): From 105 mg (0.37 mmol) of the dibromo compound **8**. Flash chromatography with petroleum ether/ether = 5 : 1; 53 mg (81%) of **13** as a colorless liquid. Gas chromatography revealed the presence of two diastereomers in a 77:23 ratio. - ^{1}H NMR (300 MHz, $CDCl_3$): major diastereomer: δ = 0.95 (d, J = 6.9 Hz, 3 H), 1.25 (s, 3 H), 1.29 (s, 3 H), 1.52 - 1.84 (m, 7 H), 2.80 (dd, J = 6.6 and 5.7 Hz, 1 H), 3.38 (m, 1 H), 3.54 (ddd, J = 8.2, 5.7, and 2.3 Hz, 1 H), 3.93 (m, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer: δ = 12.0, 18.7, 21.0, 24.6, 30.3, 31.0, 31.9, 57.7, 61.7, 68.4, 78.2.

30. 2-(2,3-Epoxy-3-methylbutyl)-3,3-dimethyl-tetrahydropyran (**14**): From 176 mg (0.59 mmol) of the dibromo compound **9**. Flash chromatography with petroleum ether / ether = 5:1. 102 mg (86%) of **14** as a colorless oil. Gas chromatography revealed the presence of two diastereomers in a 90:10 ratio. - ^{1}H NMR (300 MHz, $CDCl_3$): major diastereomer: δ = 0.81 (s, 3 H), 0.92 (s, 3 H), 1.25 (s, 3 H), 1.31 (s, 3 H), 1.30 - 1.81 (m, 6 H), 2.91 (dd, J = 6.9 and 5.4 Hz, 1 H), 3.04 (dd, J = 10.1 and 2.4 Hz, 1 H), 3.35 (m, 1 H), 4.00 (m, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer: δ = 18.8, 19.1, 23.0, 24.9, 27.7, 29.8, 32.8, 39.0, 57.5, 62.8, 68.8, 84.4. - $C_{12}H_{22}O_2$ (198.1): calcd. C 72.73, H 11.11; found C 72.46, H 11.19.

31. 4-(2,3-Epoxy-3-methylbutyl)-2,2-dimethyl-1,3-dioxolane (**16**): From 299 mg (1.04) of the dibromo compound **5**; flash chromatography with t-butyl methyl ether / petroleum ether = 1:4 furnished 151 mg (78%) of **16** as a colorless oil. Gas chromatography showed the presence of two diastereomers in a 62:38 ratio. - *Syn*-**16**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (s, 3H), 1.29 (s, 3 H), 1.33 (s, 3 H), 1.40 (s, 3 H), 1.81 (dd, J = 6.0 and 6.0 Hz, 2 H), 2.81 (dd, J = 6.1 and 6.1 Hz, 1 H), 3.65 (dd, J = 7.7 and 7.5 Hz, 1 H), 4.06 (dd, J = 8.0 and 6.0 Hz, 1 H), 4.23 (dddd, J = 7.3, 5.9, 5.9, and 5.9 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8, 24.7, 25.6, 26.8, 32.5, 57.8, 60.4, 68.7, 73.7, 108.9. - *Anti*-**16**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (s, 3 H), 1.29 (s, 3 H), 1.33 (s, 3 H), 1.38 (s, 3 H), 1.58 (ddd, J = 14.1, 8.0, and 5.5 Hz, 1 H), 1.91 (ddd, J = 14.1, 7.5, and 4.3 Hz, 1 H), 2.90 (dd, J = 7.9 and 4.3 Hz, 1 H), 3.54 (dd, J = 8.1 and 7.2 Hz, 1 H), 4.08 (dd, J = 8.1 and 5.9 Hz, 1 H), 4.19 - 4.29 (m, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.9, 24.7, 25.6, 26.9, 33.4, 58.3, 61.1, 69.4, 73.9, 108.8. - $C_{10}H_{18}O_3$ (186.3): calcd. C 64.49, H 9.74; found C 64.36, H 9.70.

32. 2,3,5,6-Di-epoxy-2,6-dimethyl-heptane (**18**): From 368 mg (1.43 mmol) of the dibromo compound **17**. The resulting 400 mg of product was contaminated by 1-bromo-3,4-epoxy-4-methyl-pentane and solvent. Separation of the epoxide **18** was attained by flash chromatography (t-butyl methyl ether / petroleum ether = 1:20) followed by microdistillation. Gas chromatography revealed a *syn*/*anti*-ratio of 60:40. *Syn*-**18**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (s, 6 H), 1.33 (s, 6 H), 1.73 (dt, J = 14.6 and 6.1 Hz, 1 H), 1.84 (dt, J = 14.6 and 6.6 Hz, 1 H), 2.86 (dd, J = 6.4 and 6.4 Hz, 2 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8, 24.7, 28.5, 57.9, 61.2. *Anti*-**18**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (s, 6 H), 1.33 (s, 6 H), 1.75 (t, J = 6.3 Hz, 2 H), 2.90 (t, J = 6.2 Hz, 2 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.9, 24.7, 29.2, 58.3, 61.5.

33. 6-Benzyloxy-2,3-epoxy-2-methyl-5-trimethylsilyloxy-hexane (**20**): From 200 mg (0.49 mmol) of the dibromo compound **19**. Flash chromatography with t-butyl methyl ether / petroleum ether = 1:3 to 1:1 furnished 99 mg (65%) of **20** as a colorless oil. The diastereomer ratio was found to be 85:15 from the ^{1}H-NMR and ^{13}C-NMR spectra. *Syn*-**20**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.12 (s, 9 H), 1.25 (s, 3 H), 1.29 (s, 3 H), 1.69 - 1.84 (m, 2 H), 2.85 (dd, J = 6.2 and 6.2 Hz, 1 H), 3.43 (dd, J = 9.6 and 5.3 Hz, 1 H), 3.48 (dd, J = 9.6 and 5.6 Hz, 1 H), 4.00 (dddd, J = 5.7, 5.7, 5.7, and 5.7 Hz, 1 H), 4.54 (s, 2 H), 7.23 - 7.35 (m, 5 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.2, 18.8, 24.8, 34.0, 57.6, 61.1, 69.7, 73.3, 74.2, 127.5, 127.6, 128.2, 138.3. The following signals of anti-**20** could be recorded: ^{1}H NMR (300

MHz, $CDCl_3$): δ = 0.13 (s, 9 H), 1.31 (s, 3 H), 2.84 (dd, J = 5.9 and 5.9 Hz, 1 H), 3.38 - 3.47 (m, 2 H), 4.53 (s, 2 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.2, 19.0, 58.4, 61.6, 69.4, 74.7. - $C_{17}H_{28}O_3Si$ (308.5): calcd. C 66.19, H 9.15; found C 65.92, H 9.15.

34. 5-(t-Butyldimethylsilyloxy)-2,3-epoxy-2,6,6,7-tetramethyl-7-octene (**24**): From 326 mg (0.79 mmol) of the dibromo compound **23**: Flash chromatography with t-butyl methyl ether / petroleum ether = 1:30 furnished 194 mg (78%) of **24** as a colorless liquid alongside with 52 mg (16%) of recovered **23**. The diastereomer ratio of **24** followed from the ^1H-NMR and ^{13}C-NMR-spectra to 91:9. - *Syn*-**24**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.07 (s, 3 H), 0.07 (s, 3 H), 0.90 (s, 9 H), 1.04 (s, 6 H), 1.21 (s, 3 H), 1.28 (s, 3 H), 1.65 (dd, J = 5.7 and 5.7 Hz, 2 H), 1.73 (s, 3 H), 2.85 (dd, J = 6.0 and 6.0 Hz, 1 H), 3.76 (dd, J = 5.4 and 5.4 Hz, 1 H), 4.78 (s, 2 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -4.0, -3.9, 18.3, 18.7, 20.3, 20.9, 24.9, 25.8, 26.1, 33.5, 44.5, 58.6, 62.5, 75.6, 111.4, 150.8. The following signals of *anti*-**24** could be recorded: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 3 H), 0.09 (s, 3 H), 0.91 (s, 9 H), 1.01 (s, 3 H), 1.02 (s, 3 H), 1.19 (s, 3 H), 1.27 (s, 3 H), 1.71 (s, 3 H), 2.84 - 2.90 (m, 1 H), 3.84 (dd, J = 7.9 and 3.0 Hz, 1 H), 4.71 - 4.76 (m, 2 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -3.8, 18.4, 19.0, 20.0, 20.7, 25.7, 26.2, 32.6, 59.0, 62.1, 75.1, 110.7, 151.3. - $C_{18}H_{36}O_2Si$ (312.6): calcd. C 69.17, H 11.61; found C 68.93, H 11.54.

35. 6-Benzyloxy-2,3-epoxy-2,6-dimethyl-5-trimethylsilyloxy-heptane (**26**): From 239 mg (0.55 mmol) of the dibromo compound **25**. Flash chromatography with t-butyl methyl ether / petroleum ether 1:20 to 1:10 furnished 142 mg (77%) of **26** as a colorless oil. The diastereomer ratio followed from the ^1H- and ^{13}C-NMR-spectra to 90:10. - *Syn*-**26**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.12 (s, 9 H), 1.18 (s, 3 H), 1.25 (s, 6 H), 1.27 (s, 3 H), 1.78 (ddd, J = 14.3, 8.3, and 5.7 Hz, 1 H), 1.85 (ddd, J = 14.3, 6.8, and 3.9 Hz, 1 H), 2.90 (dd, J = 6.6 and 5.9 Hz, 1 H), 3.71 (dd, J = 8.2 and 3.9 Hz, 1 H), 4.44 (d, J = 11.4 Hz, 1 H), 4.50 (d, J = 11.4 Hz, 1 H), 7.20 - 7.31 (m, 5 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.6, 18,7, 19.8, 22.4, 24.9, 32.4, 57.9, 62.8, 63.9, 77.4, 78.1, 127.0, 127.2, 128.1, 139.7. - The following signals of *anti*-**26** could be recorded: ^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (dd, J = 9.2 and 3.3 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.7, 19.1, 20.6, 22.3, 24.9, 31.4, 58.8, 62.3, 77.9, 127.2, 128.0. - $C_{19}H_{32}O_3Si$ (336.6): calcd. C 67.81, H 9.58; found C 67.85, H 9.44.

36. 2-(3,4-Epoxy-4-methyl-1-trimethylsilyloxy-pentyl)-2-methyl-1,3-dioxolane (**28**): From 212 mg (0.56 mmol) of the dibromo compound **27**. Flash chromatography with t-butyl methyl ether / petroleum ether = 1 : 5 furnished 120 mg (78 %) of epoxides **28** as a colorless oil. The diastereomer ratio followed from the ^1H- and ^{13}C-NMR-spectra to be 89:11. - *Syn*-**28**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.12 (s, 9 H), 1.26 (s, 3 H), 1.27 (s, 3 H), 1.30 (s, 3 H), 1.71 (ddd, J = 14.3, 6.9, and 3.9 Hz, 1 H), 1.81 (ddd, J = 14.3, 8.5, and 5.7 Hz, 1 H), 2.88 (dd, J = 6.5 and 5.8 Hz, 1 H), 3.65 (dd, J = 8.5 and 3.9 Hz, 1 H), 3.87 - 4.00 (m, 4 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.3, 18.7, 19.5, 24.8, 32.7, 57.7, 62.2, 64.8, 65.2, 74.4, 110.5. The following signals of *anti*-**28** could be recorded: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.13 (s, 9 H), 3.72 (dd, J = 9.7 and 3.1 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.4, 19.0, 24.9, 31.9, 58.6, 62.0, 73.8. - $C_{13}H_{26}O_4Si$ (274.4): calcd. C 56.90, H 9.55; found C 56.87, H 9.56.

37. 1-(1-t-Butyldimethylsilyloxy-3,4-epoxy-4-methyl-pentyl)-4-methyl-2,6,7-trioxa[2.2.2]bicyclooctane (**30**): From 50 mg (0.11 mmol) of the dibromo compound **29**. Flash chromatography with ethyl acetate / petroleum ether = 1 : 10 furnished 29 mg (74 %) of the epoxides **30** as a colorless oil. The diastereomer ratio followed from the ^1H- and ^{13}C-NMR-spectra to be *syn*/*anti* = 88 : 12. *Syn*-**30**: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.07 (s, 3 H), 0.08 (s, 3 H), 0.78 (s, 3 H), 0.87 (s, 9 H), 1.24 (s, 3 H), 1.27 (s, 3 H), 1.78 (ddd, J = 14.4, 7.7, and 4.9 Hz, 1 H), 1.91 (ddd, J = 14.4, 7.8, and 4.9 Hz, 1 H), 2.92 (dd, J = 7.7 and 4.9 Hz, 1 H), 3.73 (dd, J = 7.8 and 5.0 Hz, 1 H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.1, -4.3, 14.4, 18.5, 18.7, 24.9, 26.0, 30.6, 32.2, 58.1, 62.1, 72.5, 72.5, 108.2. - The following signals of *anti*-**30** could be recorded: ^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.0, 19.1, 25.0, 26.1, 29.7, 31.2, 58.8, 61.7, 72.1. - $C_{18}H_{34}O_5Si$ (358.6): calcd. C 60.30, H 9.56; found C 60.37, H 9.53.

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