Conformational Analysis of *oligo*-1,3-Dioxan-4-yls[‡]

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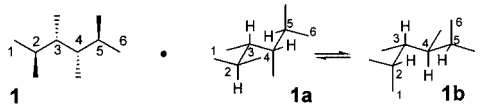
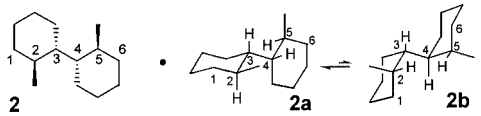
Whereas simple 4,4′-bi(1,3-dioxanyl)s **16** and **19** displayed little conformational preference at the inter-ring bond, their derivatives **4** and **13**, with equatorial methyl groups in the 5- and 5′-positions, each showed a strong conformational preference to populate a conformation with a *gauche* arrangement of the oxygen atoms. These results form the basis of a modular approach to *oligo*-1,3-dioxanyls **5**, **6**, and **29**, in each of which a strong conformational preference prevails at all of the inter-ring bonds.

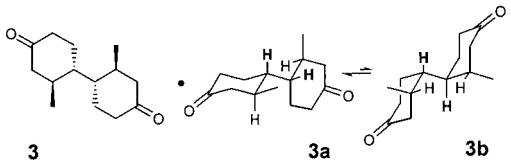
To relate material properties or biological functions of a flexible compound to structure − that is, to constitution − an understanding of the number and nature of low-energy conformations available to such a molecule is essential. In this context, we are interested in learning what modification of flexible alkane chains gives them the property that they populate predominantly one single conformation, or put another way, that they adopt a distinct shape despite maintaining flexibility. The key is to destabilize all the undesired backbone conformations related to the one desired conformation by suitable placement of substituents. A conceivable starting point for such an undertaking is represented by alkane chains bearing a single substituent at each of their secondary carbon atoms, such as 2,3,4,5-tetramethylhexane. We reported recently on the conformational analysis of *meso*-2,3,4,5-tetramethylhexane and of some of its derivatives.[2] The D,L isomer **1** should posess a distinctly different conformational behaviour. We elaborate here on how compounds with strong conformational preferences may be attained by structural modification of D,L-2,3,4,5-tetramethylhexane.





D,L-2,3,4,5-Tetramethylhexane **1** has two low-energy conformations, **1a** and **1b**, which, according to MM3* force-field calculations should be 67 and 27% populated at room temperature. To reach a mono-conformational situation, a structural modification resulting in a selective energetic destabilization of one of these two conformers would be needed. One such modification would be the annelation of two cyclohexane rings, as shown, for instance, in **2**. Conformation **2a** (corresponding to **1a**) would now have all the substituents on both cyclohexane rings equatorial, while in **2b** all the substituents would be in axial positions. Therefore, **2a** would now be expected to be the only conformation of **2** to be significantly populated. This has been supported by force-field calculations, according to which conformer **2a** should be 99% populated. For another system in which an inter-ring bond between two cyclohexane rings has a preferred conformation, see refs.[3,4]

Verification of this prediction would require the determination of ^3J coupling constants across the inter-ring bond. The determination of these $^3J_{H,H}$ coupling constants, however, would be likely to be hampered by severe signal overlap with other proton NMR signals. Nevertheless, we succeeded in the case of compound **3**, a derivative of **2**, in determining the $^3J_{H,H}$ coupling constant between the two protons at the inter-ring bond. The value of 3.0 Hz[5] was exactly what would be expected for conformer **3a**, which would therefore have to be the predominant one.



Rather than concentrating our studies on hydrocarbon compounds, we turned to dioxane derivatives **4** (acetonides

[‡] Flexible Molecules with Defined Shape, XIX. Part XVIII: Ref.[1]

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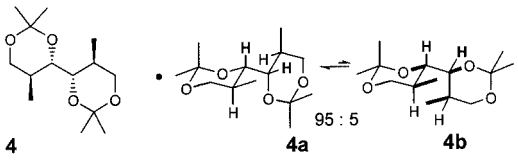
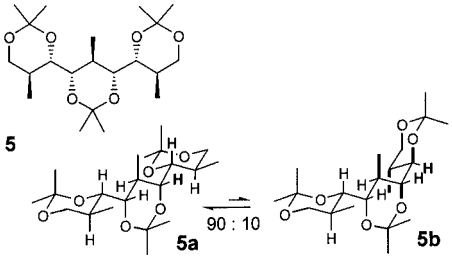
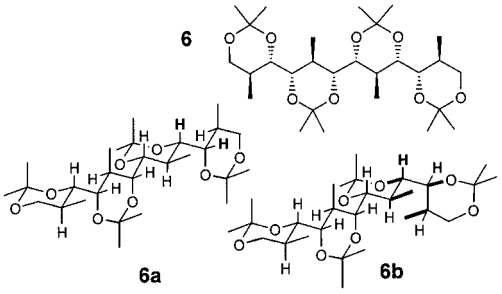
or arylidene acetals) corresponding to **2,** because these systems permit easy synthetic access to larger molecules such as **5** or **6**, containing several of the building blocks **4** connected to one another. The change from a cyclohexane system **2** to a dioxane system **4**, however, does affect the conformational behaviour. While the undesired conformers of **2** at the inter-ring bond are each destabilized by two *syn*-pentane interactions between two CH groups, those of the dioxane **4** involve *syn*-pentane interactions between a CH group and an oxygen atom, which are less destabilizing[6] due to lessened steric interactions. Hence, the calculated conformational preference for **4a** was only 95%, with **4b** amounting to 5%.



For a tris-dioxane **5**, the probability of the occurrence of an undesired conformation at an inter-ring bond should statistically be double that in the case of **4**. In line with this, MM3* calculations predicted a 90:10 conformer equilibrium.



On going to the quater-dioxane **6**, a 90% conformational preference was similarly calculated, representing a 5% probability of the adoption of a conformation with two destabilizing CH/O *syn*-pentane interactions at each of the outer inter-ring bonds. Surprisingly, the calculations predicted no significant population of a conformer with an aberrant conformation at the central inter-ring bond.

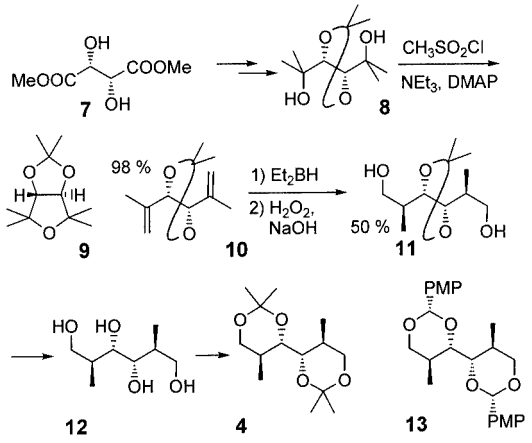


The force-field calculations thus predicted substantial conformational preferences of the order of 90% for these extended molecular backbones, which motivated us to synthesise compounds **4**, **5**, and **6** and to study their conformational behaviour.

Syntheses

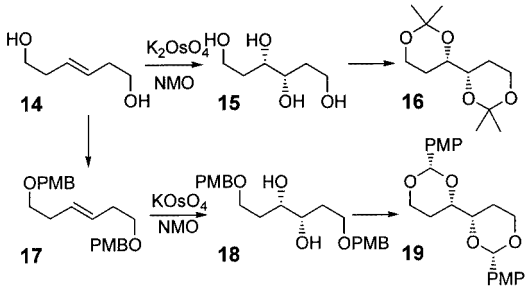
Bi(1,3-dioxan-4-yls)

The synthesis of compound **4** started from dimethyl tartrate **7**, which was converted by known steps[7] to the diol **8**. In order to attain high yields in the dehydration of **8** to the diene **10**, the addition of two equivalents of DMAP was necessary in order to suppress the formation of the tetrahydrofuran **9**.



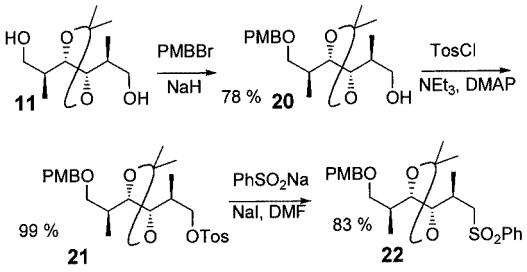
Instead of the previously described hydroboration of **10** by 9BBN (cf. ref.[8,9]), we used diethylborane generated in situ[10] to convert **10** into the diol **11** (50%), which resulted in a diastereoselectivity of 10:1. Cleavage of the acetonide to the tetraol **12** was followed by reacetalisation with 2,2-dimethoxypropane to give the bis-acetonide **4** in 70% yield. Similarly, treatment of the tetraol **12** with *p*-methoxybenzaldehyde diethyl acetal furnished the bis(arylidene) acetal **13** in 60% yield.

Since the methyl groups in **4** and **13** should be the key players in endowing these compounds with high conformational preferences, we were also interested in the corresponding dioxanes **16** and **19**, lacking these methyl groups. Their synthesis started from the diol **14**.[11] Dihydroxylation furnished the tetraol **15** (75%), which was converted into the bis-acetonide **16** with 2,2-dimethoxypropane (80%). The diol **14** was converted into the bis-*p*-methoxybenzyl ether **17** (85%), which after dihydroxylation to **18** (80%) and oxidation with DDQ furnished the bis-acetal **19** in 59% yield.

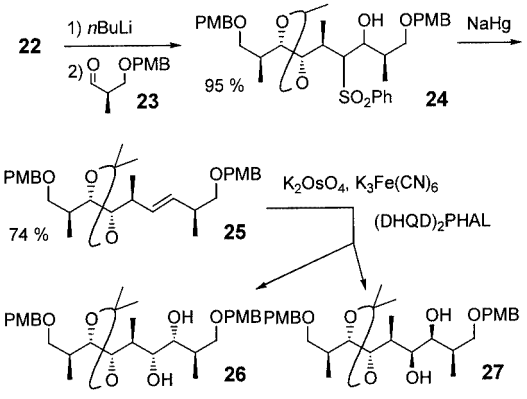


Ter(1,3-dioxan-4-yl)

For the synthesis of the trimer, we planned to combine two chiral building blocks **22** and **23** to give the alkene **25**, it being envisaged that the last two stereogenic centres would be introduced by an asymmetric dihydroxylation reaction. The sequence started with the diol **11**, which was mono-protected as the *p*-methoxybenzyl ether **20** (78%). The hydroxyl function in **20** was converted into the tosylate **21** (99%), followed by substitution with phenylsulfinate to give the sulfone **22** (83%) together with the corresponding phenylsulfinate (12%).

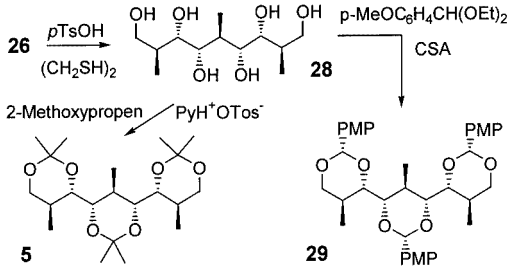


Julia–Lythgoe coupling with the aldehyde **23**[12] furnished the hydroxysulfone **24** (95%). Direct reduction with sodium amalgam afforded the alkene **25** (74%) as a 15:1 *E*/*Z* mixture. In addition, 14% of an alcohol resulting from reduction only of the sulfone moiety was isolated. When the hydroxysulfone **24** was acetylated before treatment with sodium amalgam, the alkene **25** was obtained as a pure *E* isomer, but the overall yield (55%) was inferior to that obtained from the direct reduction of **24**.



Dihydroxylation of **25** could give rise to two diastereomeric diols: **26** and **27**. Simple dihydroxylation with K_2OsO_4 and NMO resulted in a meagre 1.5:1 selectivity in favour of **26**. Fortunately, asymmetric dihydroxylation of **25** with $(DHQD)_2$ PHAL[13] furnished a 74% yield of **26**, with 8% of **27**. The *Z* isomer of **25** did not react under these conditions[14] and could readily be separated at this stage. Structure assignment of **26** (and of **27**) was based on its ultimate conversion into the symmetrical trisacetonide **5.**

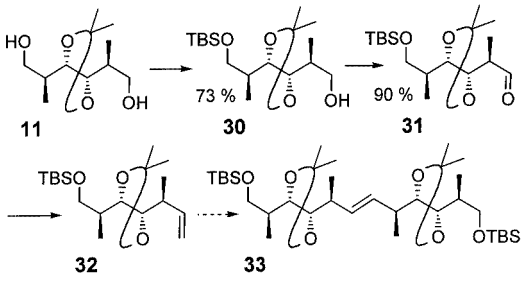
The necessary reaction sequence was initiated by simultaneous deprotection of the acetonide and the *p*-methoxybenzyl ether moieties with ethanedithiol and *p*-toluenesulfonic acid[15] to give the hexaol **28** in 91% yield.



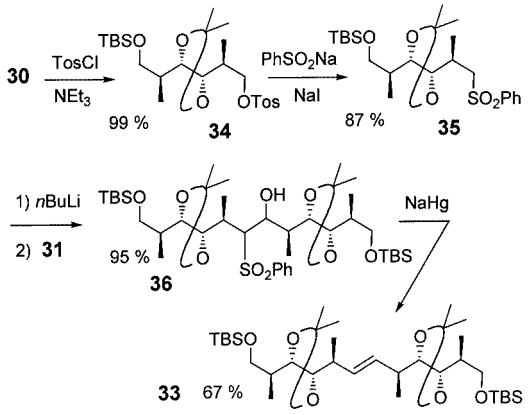
Treatment of this with 2-methoxypropene and pyridinium *p*-toluenesulfonate furnished the desired compound **5** in 70% yield. The symmetrical nature of this compound was evident from the number of signals in the ^{13}C NMR spectrum. Moreover, the positions of the signals at δ = 19.1, 29.7, and 99.2 ppm were characteristic[16,17] of a 4,6-*syn*-disubstituted acetonide. This established the structure of **5** as shown. Finally, treatment of the hexaol **28** with *p*-methoxybenzaldehyde diethylacetal and acid likewise afforded the tris-arylidene acetal **29** in 70% yield.

Quater(1,3-dioxan-4-yl)

The synthesis of the quater-dioxane **6** was based on a TBS protecting group scheme and proceeded through the symmetrical alkene **33** as the key intermediate.

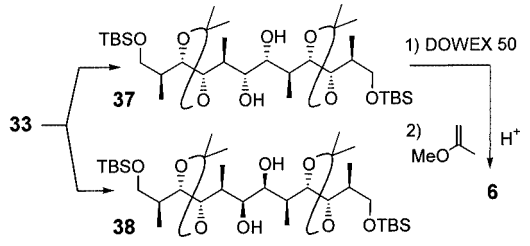


Selective monoprotection of the diol **11**, giving **30**, could be achieved with NaH and TBDMSCl in 73% yield. Oxidation to the aldehyde **31** was accomplished with the Dess–Martin periodinane (90%). Initially, we hoped to obtain the alkene **33** by means of a straightforward alkene cross-metathesis. Hence, the aldehyde **31** was converted into the alkene **32** through a Wittig reaction (65%). Cross-metathesis of **32** did afford the symmetrical alkene **33**, but as an *E*/*Z* mixture. A selective dihydroxylation of the *E* isomer would have been possible (see above), but we pursued another (albeit longer) route to the pure *E* alkene **33**. To this end, the alcohol **30** was tosylated to give **34** (99%) and converted into the phenylsulfone **35** by treatment with sodium phenylsulfinate and sodium iodide in DMF. The sulfone **35** was obtained in 85% yield together with 10% of the corresponding sulfinate, which could be recycled to the alcohol **30**, as discussed in the context of the preparation of the sulfone **22**.



At this point, the stage was set for the Julia−Lythgoe coupling with the aldehyde **31**. The hydroxysulfone **36** could be obtained in 95% yield. Standard conversion into the alkene by acetylation followed by sodium amalgam reduction resulted in low yields (ca. 30%) in our hands. We therefore again resorted to the direct reduction of the hydroxysulfone **36** with NaHg, resulting in a 67% yield of the alkene **33**. Again, an alcohol resulting from reduction of the phenylsulfone moiety alone was formed as a side product (14%). The *E* configuration of the double bond in the alkene **33** was established by a SELINCOR experiment,[18] revealing a 15.9 Hz coupling between the two homotopic olefinic protons.

From the experience gained with **25**, we subjected the alkene **33** to asymmetric dihydroxylation with $(DHQD)_2$ PHAL as chiral promoter. This gave the diols **37** and **38** in 75 and 12% yield, respectively. The structure of the major diastereomer **37** followed from its ultimate conversion into the symmetrical acetonide **6.**

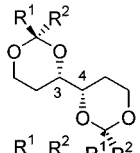
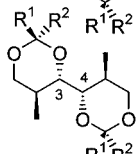
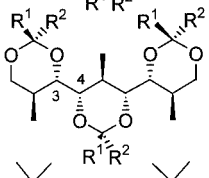
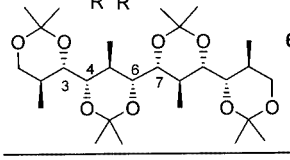


Performance of the dihydroxylation of the alkene **33** with simple K_2OsO_4 and NMO surprisingly resulted in an increase in the selectivity in favour of **37**, giving a 84% yield of **37** and 14% of **38**. The diol **37** was deprotected with DOWEX 50 in methanol, and the resulting octaol was directly treated with 2-methoxypropene and acid to furnish the desired tetrakis-acetonide **6** in 56% yield.

Conformational Analysis

For the systems investigated here, the conformation of only a single type of bond − the inter-ring bond between two 1,3-dioxane rings − had to be considered. Analysis of the characteristic $^3J_{H,H}$ coupling constants[19] was complicated, however, by the C_2 symmetry of the bis-dioxanes **4**, **6**, **13**, **16**, and **19** and the local C_2 symmetry prevailing in compounds **5** and **29**. This rendered the proton signals of interest isochronous, producing higher-order splitting patterns. One way to deal with this is to break the symmetry by recording the ^{13}C-satellite spectra. Therefore, all the $^3J_{H,H}$ coupling constants listed in Table 1 were determined by use of the SELINCOR (selective inverse H,C-correlation by $^1J_{C,H}$) technique.[18]

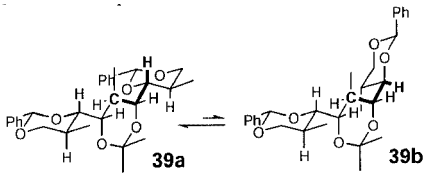
Table 1. $^3J_{H\text{-}3/H\text{-}4}$ coupling constants [±0.2 Hz] at 300 K

			Exptl.	Calcd.*
	**16**	$R^1 = R^2 = CH_3$	5.1	5.2
	19	$R^1 = H$; R^2 = 4-MeOPh	5.4	4.8
	**4**	$R^1 = R^2 = CH_3$	2.6	1.5
	13	$R^1 = H$; R^2 = 4-MeOPh	2.4	1.5
	**5**	$R^1 = R^2 = CH_3$	2.4	2.0
	29	$R^1 = H$; R^2 = 4-MeOPh	2.5	1.8
	**6**	$^3J_{H\text{-}3/H\text{-}4}$:	2.5	2.4
		$^3J_{H\text{-}6/H\text{-}7}$:	2.2	2.3

After Boltzmann averaging over the MM3 energies of the conformers.

The data in the table show that the $^3J_{H,H}$ coupling constants at the inter-ring bond of the oligo-dioxanes with acetonide groups − **4**, **5**, and **6** − as well as those with *p*-methoxybenzylidene acetals − **13** and **29** − were in the 2−3 Hz range. This is in line with predictions made on the basis of the force field calculations. There are, however, two factors that limit the usefulness of conformational analysis based on $^3J_{H,H}$ coupling constants in the case of the compounds studied here. Firstly, the two protons at the inter-ring bond in the major conformer of **4** are in a synclinal arrangement, giving rise to a numerically small (< 3 Hz) coupling constant. Line-broadening and errors associated with the SELINCOR method result in relatively large uncertainties (±0.2 Hz) in the coupling constants obtained. Secondly, the protons at the inter-ring bond are in a synclinal arrangement not only in the major conformer **4a**, but also in the expected minor conformer **4b**. The $^3J_{H,H}$ coupling constants therefore do not reflect the position of the **4a** ⇄ **4b** equilibrium. The only firm conclusion that can be drawn from the coupling constants of 2−3 Hz found for compounds **4**−**6** is that conformers of the type **4a** *and* **4b** were dominant with respect to other conformations regard-

ing the inter-ring bond. Information on the position of the **4a** ⇄ **4b** conformer equilibrium could, however, be obtained from $^3J_{C,H}$ coupling constants. In compound **39** related both to **5** and to **29** we succeeded[20] in measuring the relevant $^3J_{C,H}$ coupling constant as 3.0 Hz. The value expected for **39a** would be 1−3 Hz, that for **39b** between 6 and 8 Hz.[21] Conformer **a** clearly dominated the conformer equilibrium in the case of **39**, and we are confident that this should hold generally for the compounds studied here, because of their similarity to compound **39**.



Indeed, in the case of compound **6**, the **a**-type conformer was the one present in the solid state, as reflected in the X-ray crystal structure reproduced in Figure 1.

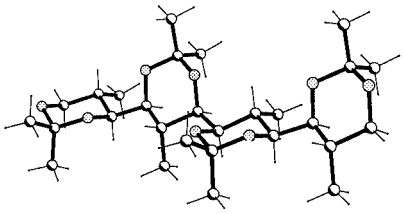
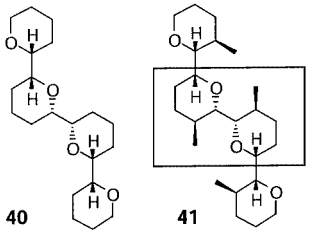


Figure 1. X-ray crystal structure of compound **6**

The point to be demonstrated by this study, however, was to show that the methyl groups on the dioxane rings were essential for establishing strong conformational preferences at the inter-ring bond(s). This becomes evident on comparison of compounds **4** and **13** with the simple bidioxanes **16** and **19**, in which all three diamond lattice type conformers at the inter-ring bond are populated. The powerful effect of these judiciously placed methyl groups on the conformer equilibrium had been postulated before, in seminal studies by W. C. Still.[8,22−28]



Whereas **40** was calculated to be multi-conformational, the corresponding compound **41**, with four methyl groups in the appropriate ring positions, was calculated to be mono-conformational. The central units of compounds **40** and **41** correspond directly to the compounds **4**, **5**, and **6** studied here. The coupling constant for the protons at the inner inter-ring bond of **41** was found to be 2.1 Hz.[22] When the conformation-inducing methyl groups were replaced by "slimmer" benzyloxy groups, the conformational preference was diminished, as evidenced by a larger (2.5 Hz) $^3J_{H,H}$ coupling constant across the inter-ring bond.[29]

Nature amply demonstrates conformation design of flexible molecules, particularly in natural products of polyketide biogenetic origin.[30] Conformation design of flexible backbones should not, however, be restricted only to those flexible structures prevalent in nature. With this study we have identified yet another[2,31−33] structural moiety, **4**, which may be successfully usable in a modular approach[34] towards larger molecular skeletons with a preferred conformation at each freely rotatable bond (cf. **5** and **6**).

Experimental Section

General Remarks: All quoted temperatures are uncorrected. ^{1}H NMR, ^{13}C NMR: Bruker ARX 200, AC 300, WH 400, AM 400, AMX 500. Boiling range of petroleum ether: 40−60 °C. Flash chromatography: SI 60 silica gel, E. Merck KGaA, Darmstadt, 40−63 μm. Buffer (pH 7): $NaH_2PO_4 \cdot 2H_2O$ (56.2 g) and $Na_2HPO_4 \cdot 4H_2O$ (213.6 g) made up to 1 L with water. Conformer populations were estimated by force-field calculations performed with the MM3* force-field implemented in the MACROMODEL program,[35] versions 4.5 and 6.5. Conformers with energies of < 6 kcal·mol^{-1} above the minimum energy conformer were subjected to Boltzmann averaging for 298 K to predict the conformer population.

1. (4*S*,5*S*)-4,5-Diisopropenyl-2,2-dimethyl-1,3-dioxolane (10): Methanesulfonyl chloride (8.90 mL, 114 mmol) was added slowly at 0 °C to a solution of (4*R*,5*R*)-4,5-bis(1-hydroxy-1-methylethyl)-2,2-dimethyl-1,3-dioxolane (**8**,[7] 5.00 g, 22.9 mmol), 4-dimethylaminopyridine (5.60 g, 45.8 mmol), and triethylamine (26.00 mL, 188 mmol) in dichloromethane (130 mL). After the mixture had stirred for 30 h at room temperature, water (80 mL) was added, the phases were separated, and the aqueous phase was extracted with ether (2 × 30 mL). The combined organic phases were washed with brine (50 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/ether, 20:1, furnished the product **10** (4.08 g, 98%) as a colourless liquid. $[\alpha]_D^{20} = -33.6$ ($c = 1.13$, toluene). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.48 (s, 6 H), 1.78 (s, 6 H), 4.19 (s, 2 H), 4.88−4.92 (m, 2 H), 5.04 ppm (s, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.5, 27.0, 83.1, 108.0, 114.4, 141.3 ppm. Cf. the data in ref.[7]

2. (2*S*)-2-{(4*S*,5*S*)-5-[(1*S*)-2-Hydroxy-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}propan-1-ol (11): Borane−dimethyl sulfide (10 M in dimethyl sulfide, 3.6 mL, 36 mmol) was added at 0 °C to a solution of triethylborane (1.0 M in hexane, 72.1 mL, 72.1 mmol). After the mixture had been stirred for 30 min, a solution of the diene **10** (5.25 g, 28.8 mmol) in ether (30 mL) was added and stirring was continued for 12 h. Aqueous NaOH (15%, 30 mL) and aqueous H_2O_2 (30%, 30 mL) were added slowly at 0 °C, and stirring was continued for 4 h at room temperature. Water (50 mL) was added, and the mixture was extracted with ether (5 × 30 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with pentane/ether, 1:1, furnished the diol **11** (3.15 g, 50%). $[\alpha]_D^{20} = -22.9$ ($c = 2.62$, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.92 (d, $J = 7.0$ Hz, 6 H), 1.35 (s, 6 H), 1.79−1.84 (m, 2 H), 2.97 (broad s, 2 H), 3.56−3.63 (m, 4 H), 3.82−3.85 ppm (m, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.4,

27.4, 38.2, 65.4, 83.6, 108.8 ppm. $C_{11}H_{22}O_4$ (218.3): calcd. C 60.52, H 10.16; found C 60.32, H 9.89.

3. (4*S*,5*S*,4′*S*,5′*S*)-2,2,5,2′,2′,5′-Hexamethyl-4,4′-di-1,3-dioxanyl (4): A solution of the diol **11** (151 mg, 0.69 mmol) in aqueous hydrochloric acid (2 M, 1.5 mL) and THF (1.5 mL) was stirred for 1 day. The solvents were removed in vacuo, and the residue was taken up in 2,2-dimethoxypropane (2 mL). Pyridinium *p*-toluenesulfonate (5 mg) was added, and the mixture was stirred for 2.5 h. The solvents were removed in vacuo. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 2:1 to 1:1, furnished the bisacetonide **4** (123 mg, 70%) as a colourless solid of m.p. 122 °C. $[\alpha]_D^{20} = +34.9$ (c = 6.72, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.69 (d, J = 6.7 Hz, 6 H), 1.34 (s, 6 H), 1.36 (s, 6 H), 2.04−2.12 (m, 2 H), 3.47 (t, J = 11.4 Hz, 2 H), 3.50 (d, J = 9.8 Hz, 2 H), 3.66 ppm (dd, J = 11.4, 5.1 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 12.0, 18.5, 28.6, 29.6, 66.2, 73.7, 98.3 ppm. $C_{14}H_{26}O_4$ (258.4): calcd. C 65.09, H 10.14; found C 64.85, H 10.25.

4. (2*S*,4*S*,5*S*)-2-(4-Methoxyphenyl)-4-[(2*S*,4*S*,5*S*)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]-5-methyl-1,3-dioxane (13): A solution of the diol **11** (75 mg, 0.34 mmol) in methanol (2 mL), water (1 mL) and acetic acid (0.5 mL) was heated at 60 °C for 1 day. The solvents were removed in vacuo, and hexane (4 × 20 mL) was distilled from the residue to remove any acetic acid. The residue was taken up in THF (2 mL), and 4-methoxy-benzaldehyde diethylacetal (358 mg, 1.70 mmol) and pyridinium *p*-toluenesulfonate (8 mg, 0.03 mmol) were added. After stirring for 1 day at room temperature the mixture was cooled to 0 °C and petroleum ether (3 mL) was added. The resulting precipitate was filtered and washed with cold petroleum ether (1 mL). The residue was taken up in dichloromethane (0.5 mL). Flash chromatography with pentane/*tert*-butyl methyl ether/triethylamine, 2:1:0.01, furnished the product **13** (83 mg, 60%) as a colourless solid of m.p. 201 °C. $[\alpha]_D^{20} = -33.3$ (c = 1.05, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.88 (d, J = 6.7 Hz, 6 H), 2.44−2.52 (m, 2 H), 3.57 (t, J = 11.3 Hz, 2 H), 3.69 (d, J = 5.3 Hz, 2 H), 3.84 (s, 6 H), 4.17 (dd, J = 11.2, 4.7 Hz, 2 H), 5.47 (s, 2 H), 6.91−6.94 (m, 4 H), 7.46−7.48 ppm (m, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.9, 28.8, 55.3, 73.1, 81.6, 101.5, 113.5, 127.4, 131.2, 159.9 ppm. $C_{24}H_{30}O_6$ (414.5): calcd. C 69.55, H 7.29; found C 69.33, H 7.35.

5. (3*R,4*R**)-Hexane-1,3,4,6-tetraol (15):** Potassium osmate(VI) dihydrate (ca. 10 mg) was added to a suspension of (3*E*)-1,6-dihydroxy-3-hexene (**14**,[11] 177 mg, 1.52 mmol), methanesulfonamide (145 mg, 1.52 mmol), *N*-methylmorpholine *N*-oxide (50% in water, 1.66 g, 4.56 mmol) in acetone (2 mL), *tert*-butyl alcohol (2 mL), and water (4 mL). After the mixture had been stirred for 2 h, the solvents were removed in vacuo and the residue was purified by flash chromatography with ethyl acetate/methanol, 3:1, to give the tetraol **15** (171 mg, 75%) as a colourless oil. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 1.57−1.78 (m, 4 H), 3.62−3.66 (m, 2 H), 3.73 (t, J = 6.2 Hz, 4 H), 3.87 ppm (broad s, 4 H). ^{13}C NMR (75 MHz, [D$_6$]acetone): δ = 36.8, 60.6, 73.3 ppm. $C_6H_{14}O_4$ (HRMS, ESI): calcd. for M + Na^+ 173.0790; found 173.0784.

6. (4*R,4′*R**)-2,2,2′,2′-Tetramethylbi(1,3-dioxan-4-yl) (16):** Pyridinium *p*-toluenesulfonate (ca. 5 mg) was added to a solution of the tetraol **15** (171 mg, 1.14 mmol) in acetone (5 mL) and 2,2-dimethoxypropane (3 mL). After stirring for 12 h, the solution was concentrated and the residue was purified by flash chromatography with pentane/*tert*-butyl methyl ether, 2:1, to give the product **16** (210 mg, 80%) as a colourless solid of m.p. 62 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.34 (s, 6 H), 1.31−1.40 (m, 2 H), 1.42 (s, 6 H), 1.60−1.74 (m, 2 H), 3.82 (ddd, J = 11.7, 8.7, and 2.6 Hz, 2 H), 3.86−4.00 ppm (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2, 25.2, 29.8, 59.7, 70.8, 98.3 ppm. $C_{12}H_{22}O_4$ (258.4): calcd. C 62.58, H 9.63; found C 62.52, H 9.81.

7. (3*E*)-1,6-Bis(4-methoxybenzyloxy)-3-hexene (17): Camphorsulfonic acid (33 mg, 0.20 mmol) was added to a solution of (*E*)-1,6-dihydroxy-3-hexene (232 mg, 2.00 mmol), and 4-methoxybenzyl trichloroacetimidate (1.69 g, 6.31 mmol) in dichloromethane (15 mL). After stirring for 3 days, the solution was washed with saturated aqueous $NaHCO_3$ solution (2 × 10 mL) and brine (2 × 10 mL). The solution was dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 9:1, furnished the product **17** (605 mg, 85%) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27−2.33 (m, 4 H), 3.44 (t, J = 6.9 Hz, 4 H), 3.78 (s, 6 H), 4.43 (s, 4 H), 5.49−5.51 (m, 2 H), 6.84−6.88 (m, 4 H), 7.22−7.27 ppm (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.0, 55.1, 69.6, 72.4, 113.6, 128.4, 129.1, 130.5, 159.0 ppm. $C_{22}H_{28}O_4$ (356.5): calcd. C 74.13, H 7.92; found C 74.34, H 8.04.

8. (3*R,4*R**)-1,6-Bis(4-methoxybenzyloxy)hexane-3,4-diol (18):** Potassium osmate(VI) dihydrate (7.4 mg, 0.02 mmol), potassium hexacyanoferrate(III) (1.98 g, 6.00 mmol), potassium carbonate (830 mg, 6.00 mmol), and methanesulfonamide (190 mg, 2.00 mmol) were dissolved sequentially in a mixture of water (10 mL) and *tert*-butyl alcohol (10 mL). After the mixture had been cooled to 0 °C, (3*E*)-1,6-bis(4-methoxybenzyloxy)-3-hexene (**17**, 713 mg, 2.00 mmol) was added with vigorous stirring. After the mixture had been stirred for 2 days at room temperature, sodium sulfite (3.00 g, 23.8 mmol) was added. After stirring for 1 h, the mixture was extracted with dichloromethane (5 × 10 mL). The combined organic phases were washed with aqueous KOH (0.5 N, 20 mL) and dried (Na_2SO_4). Silica gel (3 g) was added and the solvents were removed. Flash chromatography with petroleum ether/*tert*-butyl methyl ether, 1:1, furnished the diol **18** (614 mg, 80%) as a colourless solid of m.p. 92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.77−1.83 (m, 4 H), 3.17 (broad s, 2 H), 3.61−3.69 (m, 6 H), 3.79 (s, 6 H), 4.44 (s, 4 H), 6.85−6.88 (m, 4 H), 7.22−7.26 ppm (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.0, 55.2, 68.0, 72.9, 73.0, 113.8, 129.4, 130.0, 159.0 ppm. $C_{22}H_{30}O_6$ (390.5): calcd. C 67.67, H 7.74; found C 67.47, H 7.51.

9. (2*R,4*R**)-2-(4-Methoxyphenyl)-4-[(2*R**,4*R**)-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]-1,3-dioxane (19):** A solution of the diol **18** (456 mg, 1.17 mmol) in dichloromethane (20 mL) was stirred with molecular sieves (3A, powdered, 750 mg) for 1 h. Dichlorodicyanoquinone (824 mg, 3.63 mmol) was added at −20 °C and the mixture was allowed to come to room temperature over 4 h. The mixture was filtered and the residue was washed with dichloromethane (5 mL). The combined filtrates were washed with saturated aqueous $NaHCO_3$ solution (20 mL), the aqueous phase was extracted with dichloromethane (5 × 15 mL), and the combined organic phases were washed with brine (20 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 1.5:1 to 1:1, furnished the product **19** (267 mg, 59%) as a colourless solid of m.p. 125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (dd, J = 13.2, 1.3 Hz, 2 H), 1.94−2.06 (m, 2 H), 3.79 (s, 6 H), 3.98 (td, J = 9.3, 2.5 Hz, 2 H), 4.04−4.09 (m, 2 H), 4.30 (ddd, J = 11.4, 5.0, and 1.3 Hz, 2 H), 5.50 (s, 2 H), 6.86−6.90 (m, 4 H), 7.40−7.43 ppm (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.3, 54.8, 66.4, 77.9, 100.8, 113.1, 127.0, 130.7, 159.5 ppm. $C_{22}H_{26}O_6$ (386.4): calcd. C 68.38, H 6.78; found C 68.11, H 6.63.

10. (2*S*)-2-{(4*S*,5*S*)-5-[(1*S*)-2-(4-Methoxybenzyloxy)-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}propan-1-ol (20): Sodium hydride

(60% in white oil, 260 mg, 6.5 mmol) was added to a solution of the diol **11** (1.42 g, 6.5 mmol) in THF (5 mL). After the mixture had stirred for 30 min, 4-methoxybenzyl bromide (1.31 g, 6.5 mmol) was added. Tetrabutylammonium iodide (ca. 5 mg) was added, and the mixture was stirred for 18 h. Water (25 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (5 × 15 mL). The combined organic phases were washed with brine (15 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 3:1, furnished the product **20** (1.72 g, 78%) as a slightly yellowish oil. In addition, the doubly protected diol (197 mg, 7%) and unchanged starting material (142 mg, 10%) were obtained. $[\alpha]_D^{20} = -20.0$ (c = 1.05, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.95 (d, J = 7.0 Hz, 3 H), 1.02 (d, J = 7.0 Hz, 3 H), 1.34 (s, 3 H), 1.40 (s, 3 H), 1.84−1.89 (m, 1 H), 1.97−2.02 (m, 1 H), 2.85 (t, J = 5.4 Hz, 1 H), 3.33 (dd, J = 9.2, 6.1 Hz, 1 H), 3.59−3.73 (m, 3 H), 3.80 (s, 3 H), 3.84 (t, J = 5.4 Hz, 1 H), 3.95 (t, J = 6.8 Hz, 1 H), 4.43 (s, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 7.25 ppm (d, J = 8.6 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0, 15.4, 27.3, 27.5, 36.6, 38.1, 55.2, 66.3, 71.1, 72.8, 81.9, 83.1, 108.4, 113.7, 129.2, 130.3, 159.1 ppm. $C_{19}H_{30}O_5$ (338.4): calcd. C 67.43, H 8.93; found C 67.69, H 8.94.

11. (4*S*,5*S*)-5-[(1*S*)-2-(4-Methoxybenzyloxy)-1-methylethyl]-2,2-dimethyl-4-[(1*S*)-1-methyl-2-(4-methylphenylsulfonyloxy)ethyl]-1,3-dioxolane (21): A solution of the alcohol **20** (1.72 g, 5.1 mmol), triethylamine (1.28 mL, 9.1 mmol), 4-dimethylaminopyridine (310 mg, 2.54 mmol), and *p*-toluenesulfonyl chloride (1.69 g, 8.87 mmol) in dichloromethane (18 mL) was stirred for 12 h. Silica gel (ca. 5 g) was added and the suspension was concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 3.5:1, furnished the tosylate **21** (2.47 g, 99%) as a colourless oil. $[\alpha]_D^{20}$ = −33.1 (c = 1.60, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (d, J = 6.8 Hz, 3 H), 0.96 (d, J = 6.8 Hz, 3 H), 1.24 (s, 3 H), 1.27 (s, 3 H), 1.88−1.99 (m, 2 H), 2.42 (s, 3 H), 3.31 (dd, J = 9.3, 6.6 Hz, 1 H), 3.57 (dd, J = 9.3, 4.9 Hz, 1 H), 3.73−3.76 (m, 2 H), 3.79 (s, 3 H), 3.93 (dd, J = 9.5, 7.1 Hz, 1 H), 4.21 (dd, J = 9.5, 4.1 Hz, 1 H), 4.41 (s, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 7.24 (d, J = 8.6 Hz, 2 H), 7.31 (d, J = 8.2 Hz, 2 H), 7.78 ppm (d, J = 8.2 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 14.9, 27.1, 27.3, 27.4, 36.7, 36.8, 55.1, 71.2, 72.0, 72.6, 80.0, 81.6, 108.5, 113.6, 127.7, 129.0, 129.7, 130.4, 132.4, 144.5, 159.0 ppm. $C_{26}H_{36}O_7S$ (492.6): calcd. C 63.39, H 7.37; found C 63.56, H 7.25.

12. (4*S*,5*S*)-4-[(1*S*)-2-(4-Methoxybenzyloxy)-1-methylethyl]-2,2-dimethyl-5-[(1*R*)-1-methyl-2-phenylsulfonylethyl]-1,3-dioxolane (22): A solution of the tosylate **21** (461 mg, 0.94 mmol), sodium iodide (282 mg, 1.88 mmol) and sodium phenylsulfinate (540 mg, 3.29 mmol) in DMF (7 mL) was heated at 70 °C for 12 h. Water (20 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 10 mL). The combined organic phases were washed with water (10 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 3.5:1, furnished the sulfone **22** (359 mg, 83%). $[\alpha]_D^{20} = -26.8$ (c = 1.90, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, J = 6.8 Hz, 3 H), 1.18 (d, J = 6.6 Hz, 3 H), 1.28 (s, 6 H), 1.83−1.90 (m, 1 H), 2.08−2.19 (m, 1 H), 2.90 (dd, J = 14.6, 9.8 Hz, 1 H), 3.26 (dd, J = 9.3, 6.6 Hz, 1 H), 3.45−3.58 (m, 3 H), 3.74 (t, J = 5.9 Hz, 1 H), 3.81 (s, 3 H), 4.40 (s, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 7.24 (d, J = 8.6 Hz, 2 H), 7.51−7.65 (m, 3 H), 7.90 ppm (d, J = 7.1 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6, 18.0, 27.3, 27.4, 32.1, 37.4, 55.3, 58.0, 71.4, 72.7, 81.2, 82.5, 108.9, 113.7, 127.7, 127.9, 129.1, 129.3, 130.6, 133.6, 159.6 ppm. $C_{25}H_{34}O_6S$ (462.6): calcd. C 64.91, H 7.41; found C 64.91, H 7.26.

In addition, a sulfinate corresponding to **20** was obtained as 1:1 diastereomeric mixture (52 mg, 12%).

13. (2*R*,3*RS*,4*RS*,5*R*)-1-(4-Methoxybenzyloxy)-5-{(4*S*,5*S*)-5-[(1*S*)-2-(4-methoxybenzyloxy)-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-2-methyl-4-(phenylsulfonyl)hexan-3-ol (24): *n*-Butyllithium (1.53 M in hexane, 0.51 mL, 0.78 mmol) was added dropwise at −78 °C to a solution of the sulfone **22** (359 mg, 0.78 mmol) in THF (4 mL). After the mixture had been stirred for 15 min, (2*R*)-3-(4-methoxybenzyloxy)-2-methylpropanal (**23**,[12] 162 mg, 0.78 mmol) in THF (1 mL) was added. After the mixture had been stirred for 1 h at −78 °C, water (15 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 10 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 1.5:1 to 1:1, furnished the major diastereomer of the product (342 mg, 65%), together with further diastereomers (154 mg, 30%), as a colourless oil. Major diastereomer: $[\alpha]_D^{20} = -28.4$ (c = 2.50, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.8 Hz, 3 H), 1.07 (s, 3 H), 1.09 (d, J = 6.7 Hz, 3 H), 1.13 (s, 3 H), 1.78−1.88 (m, 1 H), 2.11−2.19 (m, 1 H), 2.56−2.61 (m, 1 H), 3.20 (dd, J = 9.3, 6.1 Hz, 1 H), 3.33−3.39 (m, 2 H), 3.50 (dd, J = 9.3, 4.4 Hz, 1 H), 3.60 (t, J = 4.9 Hz, 1 H), 3.66 (t, J = 4.2 Hz, 1 H), 3.70 (s, 3 H), 3.71 (s, 3 H), 3.79−3.81 (m, 2 H), 4.02 (d, J = 4.9 Hz, 1 H), 4.28−4.37 (m, 4 H), 6.76−6.80 (m, 4 H), 7.13−7.17 (m, 4 H), 7.37−7.52 (m, 3 H), 7.84 ppm (d, J = 7.1 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1, 14.2, 15.7, 27.1, 27.6, 36.8, 37.2, 37.6, 55.1, 65.1, 71.0, 72.7, 72.8, 73.8, 74.5, 80.0, 83.3, 108.9, 113.6, 113.7, 128.7, 128.8, 129.0, 129.2, 129.8, 130.1, 130.5, 140.9, 159.1, 159.2 ppm. $C_{37}H_{50}O_9S$ (670.9): calcd. C 66.24, H 7.51; found C 66.23, H 7.62.

14. (4*S*,5*S*)-4-[(1*S*,2*E*,4*S*)-5-(4-Methoxybenzyloxy)-1,4-dimethyl-2-pentenyl]-5-[(1*S*)-2-(4-methoxybenzyloxy)-1-methylethyl]-2,2-dimethyl-1,3-dioxolane (25): Disodium hydrogen phosphate (383 mg, 2.70 mmol) and sodium amalgam (6%, 2.0 g) were added to a solution of the hydroxysulfone **24** (359 mg, 0.54 mmol) in methanol/ethyl acetate (2:1, 6 mL) at 0 °C. After the mixture had been stirred for 12 h at room temperature, water (10 mL) was added. The aqueous phase was decanted and extracted with *tert*-butyl methyl ether (4 × 5 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 3.5:1, furnished the product (205 mg, 74%) as a 15:1 *E*/*Z* mixture, and in addition the alcohol (4*S*,5*S*)-4-[(1*S*,3*RS*,4*S*)-3-hydroxy-5-(4-methoxybenzyloxy)-1,4-dimethyl-2-pentyl]-5-[(1*S*)-2-(4-methoxybenzyloxy)-1-methylethyl]-2,2-dimethyl-1,3-dioxolane (38 mg, 14%).

Compound 25: $[\alpha]_D^{20} = -22.9$ (c = 1.18, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (d, J = 7.1 Hz, 3 H), 1.00 (d, J = 7.1 Hz, 3 H), 1.09 (d, J = 6.8 Hz, 3 H), 1.32 (s, 3 H), 1.34 (s, 3 H), 1.90−2.00 (m, 1 H), 2.21−2.29 (m, 1 H), 2.41−2.51 (m, 1 H), 3.19−3.26 (m, 2 H), 3.32 (dd, J = 9.0, 6.8 Hz, 1 H), 3.62 (dd, J = 9.0, 4.9 Hz, 1 H), 3.65−3.82 (m, 8 H), 4.37−4.46 (m, 4 H), 5.35 (dd, J = 15.6, 6.8 Hz, 1 H), 5.51 (dd, J = 15.6, 8.1 Hz, 1 H), 6.85−6.88 (m, 4 H), 7.23−7.26 ppm (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6, 17.1, 18.6, 27.2, 27.4, 36.8, 36.9, 39.2, 55.2, 72.0, 72.5, 72.7, 75.2, 80.3, 82.8, 108.0, 113.6, 129.1, 130.4, 130.6, 134.1, 159.1 ppm. $C_{31}H_{44}O_6$ (exact mass, FAB): calcd. 512.3138; found 512.3096.

(4*S*,5*S*)-4-[(1*S*,3*RS*,4*S*)-3-Hydroxy-5-(4-methoxybenzyloxy)-1,4-dimethyl-2-pentyl]-5-[(1*S*)-2-(4-methoxybenzyloxy)-1-methylethyl]-2,2-dimethyl-1,3-dioxolane: $[\alpha]_D^{20} = -21.8$ (c = 1.19, $CHCl_3$). ^{1}H

NMR (300 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.6 Hz, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 1.29−1.37 (m, 2 H), 1.34 (s, 3 H), 1.36 (s, 3 H), 1.76−1.81 (m, 1 H), 1.96−1.98 (m, 2 H), 3.29−3.35 (m, 1 H), 3.43−3.49 (m, 2 H), 3.54−3.67 (m, 2 H), 3.76−3.82 (m, 2 H), 3.79 (s, 6 H), 4.43 (s, 4 H), 6.55−6.88 (m, 4 H), 7.24−7.38 ppm (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 15.1, 17.0, 26.9, 27.6, 32.6, 37.0, 37.4, 39.3, 55.2, 71.8, 72.7, 73.1, 73.3, 74.8, 81.3, 84.2, 108.2, 113.7, 113.8, 129.1, 129.3, 130.8, 130.9, 159.2, 159.3 ppm.

15. (2*R*,3*R*,4*R*,5*S*)-1-(4-Methoxybenzyloxy)-5-{(4*S*,5*S*)-5-[(1*S*)-2-(4-methoxybenzyloxy)-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-2-methylhexane-3,4-diol (26): The alkene **25** (313 mg, 0.61 mmol) was added to a mixture of potassium osmate(VI) dihydrate (11.1 mg, 0.03 mmol), $(DHQD)_2PHAL$ (55 mg, 0.07 mmol), potassium hexacyanoferrate(III) (603 mg, 1.83 mmol), potassium carbonate (253 mg, 1.83 mmol), and methanesulfonamide (58 mg, 0.61 mmol) in water/*tert*-butyl alcohol (1:1, 6 mL). After the mixture had been stirred for 4 h, sodium sulfite (3 g) was added. Stirring was continued for 1 h and water (10 mL) was added. The phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (6 × 5 mL). The combined organic phases were washed with aqueous KOH (0.5 N, 5 mL), dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 3.5:1, furnished the diol **26** (249 mg, 74%) and the diastereomeric diol **27** (30 mg, 8%). The *Z* alkene (19 mg, 7%) corresponding to **25** was recovered.

Compound 26: $[\alpha]_D^{20}$ = −22.8 (*c* = 1.62, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.82 (d, *J* = 6.6 Hz, 3 H), 0.84 (d, *J* = 6.6 Hz, 3 H), 0.97 (d, *J* = 7.1 Hz, 3 H), 1.27 (s, 3 H), 1.32 (s, 3 H), 1.83−1.95 (m, 2 H), 2.01−2.09 (m, 1 H), 3.23 (dd, *J* = 9.0, 6.3 Hz, 1 H), 3.37 (d, *J* = 5.4 Hz, 1 H), 3.41−3.47 (m, 3 H), 3.51−3.60 (m, 2 H), 3.72 (s, 6 H), 3.85 (dd, *J* = 6.6, 4.4 Hz, 1 H), 3.93 (d, *J* = 3.4 Hz, 1 H), 3.96−4.01 (m, 1 H), 4.35−4.38 (m, 4 H), 6.78−6.81 (m, 4 H), 7.16−7.19 ppm (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1, 14.0, 16.0, 27.4, 27.5, 36.1, 36.5, 40.0, 55.2, 71.1, 72.8, 72.9, 74.1, 74.3, 74.5, 82.2, 82.9, 108.5, 113.7, 113.8, 129.2, 129.3, 130.1, 130.5, 159.1, 159.2 ppm. $C_{31}H_{46}O_8$ (546.7): calcd. C 68.11, H 8.48; found C 67.98, H 8.53.

The minor diastereomer **27** had the following data: $[\alpha]_D^{20}$ = −37.4 (*c* = 1.23, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6.6 Hz, 3 H), 0.96 (d, *J* = 7.3 Hz, 3 H), 0.99 (d, *J* = 7.3 Hz, 3 H), 1.35 (s, 3 H), 1.39 (s, 3 H), 1.70−1.76 (m, 1 H), 1.83−1.86 (m, 1 H), 1.94−2.00 (m, 1 H), 2.81 (broad s, 1 H), 3.10 (broad s, 1 H), 3.35 (dd, *J* = 8.6, 6.6 Hz, 1 H), 3.41−3.53 (m, 2 H), 3.62 (dd, *J* = 9.0, 4.9 Hz, 1 H), 3.77−3.81 (m, 8 H), 3.87−3.92 (m, 1 H), 4.00 (t, *J* = 6.1 Hz, 1 H), 4.39−4.45 (m, 4 H), 6.86−6.99 (m, 4 H), 7.14−7.26 ppm (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.5, 11.2, 15.2, 27.4, 27.9, 35.2, 37.0, 37.6, 55.2, 71.3, 71.4, 72.8, 73.0, 73.6, 81.7, 82.5, 108.5, 113.7, 113.8, 127.4, 129.1, 129.2, 130.6, 159.2 ppm.

The *Z* alkene had the following data: $[\alpha]_D^{20}$ = −35.9 (*c* = 1.40, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 6.7 Hz, 3 H), 1.00 (d, *J* = 7.0 Hz, 3 H), 1.05 (d, *J* = 7.0 Hz, 3 H), 1.34 (s, 3 H), 1.35 (s, 3 H), 1.87−2.02 (m, 1 H), 2.57−2.76 (m, 2 H), 3.25 (dd, *J* = 6.8, 1.5 Hz, 1 H), 3.56−3.74 (m, 3 H), 3.75 (s, 6 H), 3.77−3.90 (m, 2 H), 4.43 (s, 4 H), 5.23 (t, *J* = 10.1 Hz, 1 H), 5.44 (t, *J* = 10.1 Hz, 1 H), 6.85−6.90 (m, 4 H), 7.21−7.26 ppm (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0, 17.7, 19.2, 27.2, 27.3, 29.9, 34.5, 37.1, 55.3, 71.9, 72.6, 72.8, 75.0, 81.0, 81.9, 108.1, 113.7, 129.0, 129.1, 130.6, 131.1, 159.0 ppm.

16. (4*R*,5*s*,6*S*)-2,2,5-Trimethyl-4-[(4*R*,5*R*)-2,2,5-trimethyl-1,3-dioxan-4-yl]-6-[(4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxan-4-yl)-1,3-dioxane (5): A solution of the diol **26** (62 mg, 0.11 mmol), ethane-1,2-dithiol (28 μL, 0.33 mmol), and *p*-toluenesulfonic acid (ca 2 mg) in chloroform (0.5 mL) was heated under reflux for 4 h. Pentane (0.5 mL) was added, and the resulting precipitate was filtered and dried. The hexaol **28** was obtained as a colourless solid (26 mg, 91%) and was used as obtained. ^1H NMR (300 MHz, CD_3OD): δ = 0.47 (d, *J* = 6.8 Hz, 9 H), 1.40−1.49 (m, 2 H), 1.53−1.67 (m, 1 H), 3.07−3.34 ppm (m, 8 H). ^{13}C NMR (75 MHz, CD_3OD): δ = 15.1, 15.4, 39.6, 39.8, 67.0, 75.9, 76.9 ppm.

The hexaol **28** (26 mg, 0.10 mmol), 2-methoxypropene (36 mg, 0.50 mmol), and *p*-toluenesulfonic acid (ca. 2 mg) were dissolved in DMF (0.3 mL) at 0 °C and stirred for 4 h. Saturated aqueous $NaHCO_3$ solution (2 mL) was added, the phases were separated, and the aqueous phase was extracted with ether (4 × 2 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 5:1, 1% triethylamine) furnished compound **5** (27 mg, 70%) as a colourless solid of m.p. 168 °C. ^1H NMR (500 MHz, C_6D_6): δ = 0.56 (d, *J* = 6.7 Hz, 6 H), 0.86 (d, *J* = 6.7 Hz, 3 H), 1.21 (s, 3 H), 1.25 (s, 6 H), 1.46 (s, 6 H), 1.48 (s, 3 H), 2.34−2.41 (m, 2 H), 2.64−2.70 (m, 1 H), 3.37 (t, *J* = 11.3 Hz, 2 H), 3.53 (dd, *J* = 10.2, 2.5 Hz, 2 H), 3.58 (dd, *J* = 10.2, 2.5 Hz, 2 H), 3.68 ppm (dd, *J* = 11.3, 5.1 Hz, 2 H). ^{13}C NMR (75 MHz, C_6D_6): δ = 11.3, 12.6, 19.0, 19.1, 29.6, 29.7, 30.4, 30.6, 66.8, 74.5, 76.6, 99.1, 99.2 ppm. $C_{21}H_{38}O_6$ (exact mass, FAB): calcd. 386.2668; found 386.2648.

17. (2*R*,4*R*,5*s*,6*S*)-2-(4-Methoxyphenyl)-4-[(2*R*,4*R*,5*R*)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]-6-[(2*S*,4*S*,5*S*)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]-5-methyl-1,3-dioxane (29): The hexaol **28** obtained under 16. (160 mg, 0.60 mmol), *p*-methoxybenzaldehyde diethylacetal (631 mg, 3.00 mmol), and camphorsulfonic acid (ca. 5 mg) were dissolved in dichloromethane (1.5 mL) and DMF (1.5 mL). After the mixture had been stirred for 8 h, water (5 mL) was added and the phases were separated. The aqueous phase was extracted with ether (6 × 3 mL). The combined organic phases were washed with water (5 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 3:1 to 1:1, 1% triethylamine, furnished the product **29** (261 mg, 70%) as a colourless solid of m.p. 251 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.7 Hz, 6 H), 1.03 (d, *J* = 6.6 Hz, 3 H), 2.47−2.53 (m, 2 H), 2.77−2.82 (m, 1 H), 3.60 (t, *J* = 11.3 Hz, 2 H), 3.75 (dd, *J* = 10.1, 2.4 Hz, 2 H), 3.78 (dd, *J* = 10.1, 2.4 Hz, 2 H), 3.85 (s, 6 H), 3.87 (s, 3 H), 4.20 (dd, *J* = 11.3, 4.7 Hz, 2 H), 5.50 (s, 2 H), 5.54 (s, 1 H), 6.87−6.90 (m, 4 H), 6.93−6.94 (m, 2 H), 7.45−7.47 (m, 4 H), 7.48−7.50 ppm (m, 2 H). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 11.0, 11.7, 28.7, 29.3, 55.5, 55.6, 73.3, 80.7, 81.5, 101.3, 101.4, 113.7, 127.5, 127.6, 131.7, 160.1, 160.2 ppm. $C_{36}H_{44}O_9$ (exact mass, FAB): calcd. 620.2985; found 620.2980.

18. (2*S*)-2-{(4*S*,5*S*)-5-[(1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}propan-1-ol (30): A solution of the diol **11** (2.31 g, 9.30 mmol) in THF (5 mL) was added dropwise at 0 °C to a suspension of sodium hydride (60% in white oil, 223 mg, 9.30 mmol) in THF (30 mL). After the mixture had been stirred for 30 min at 0 °C, *tert*-butylchlorodimethylsilane (50% in toluene, 2.80 g, 9.3 mmol) was added. After the mixture had then been stirred at room temperature for 1 h, water (40 mL) was added and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (4 × 20 mL). The combined organic phases were washed with brine (30 mL), dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 20:1 to 10:1, furnished the product **30** (2.25 g,

73%) as a colourless oil, together with recovered starting material (273 mg, 12%).

Compound 30: $[\alpha]_D^{20} = -18.3$ ($c = 7.43$, $CHCl_3$): ^1H NMR (300 MHz, $CDCl_3$): $\delta = -1.49$ (s, 3 H), 0.01 (s, 3 H), 0.87 (s, 9 H), 0.91 (d, $J = 6.9$ Hz, 3 H), 0.93 (d, $J = 7.0$ Hz, 3 H), 1.35 (s, 3 H), 1.38 (s, 3 H), 1.77−1.88 (m, 2 H), 2.86 (broad s, 1 H), 3.46 (dd, $J = 10.0$, 6.2 Hz, 1 H), 3.61 (dd, $J = 11.2$, 6.4 Hz, 1 H), 3.67−3.82 (m, 3 H), 3.96 ppm (t, $J = 6.7$ Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.4$, 14.5, 14.9, 18.4, 26.1, 27.6, 27.7, 38.4, 39.2, 64.5, 66.4, 82.1, 83.7, 108.7 ppm. $C_{17}H_{36}O_4Si$ (332.2): calcd. C 61.40, H 10.91; found C 61.29, H 11.08.

19. (2*R*)-2-{(4*S*,5*S*)-5-[(1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}propanal (31): Dess−Martin periodinane (527 mg, 1.24 mmol) was added to a solution of the alcohol **30** (336 mg, 1.01 mmol) in dichloromethane (7 mL). After stirring for 4 h, the mixture was poured onto a solution of potassium carbonate (4 g) in saturated aqueous $Na_2S_2O_3$ solution (20 mL). After this mixture had been stirred for 10 min, the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (2 × 10 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ solution (10 mL) and brine (10 mL). The solution was dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 10:1, furnished the aldehyde **31** (319 mg, 96%) as a colourless oil. $[\alpha]_D^{20} = -35.9$ ($c = 9.63$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.03$ (s, 3 H), 0.04 (s, 3 H), 0.88 (s, 9 H), 0.95 (d, $J = 7.0$ Hz, 3 H), 1.18 (d, $J = 7.1$ Hz, 3 H), 1.35 (s, 3 H), 1.37 (s, 3 H), 1.80−1.90 (m, 1 H), 2.50−2.57 (m, 1 H), 3.51 (dd, $J = 10.0$, 5.8 Hz, 1 H), 3.76 (dd, $J = 10.0$, 5.3 Hz, 1 H), 3.86 (t, $J = 6.8$ Hz, 1 H), 4.14 (dd, $J = 7.2$, 5.2 Hz, 1 H), 9.77 ppm (d, $J = 2.6$ Hz, 1 H). ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -5.5$, 11.9, 14.3, 18.2, 25.8, 27.3, 38.9, 48.5, 64.3, 80.1, 81.0, 108.7, 203.7 ppm.

20. (4*S*,5*S*)-4-[(1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-5-[(1*S*)-1-methyl-2-propenyl]-1,3-dioxolane (32): A solution of *n*-butyllithium (1.38 M in hexane, 2.60 mL, 3.6 mmol) was added to a suspension of methyltriphenylphosphonium iodide (1.39 g, 3.90 mmol) in diethyl ether (10 mL). After the mixture had been stirred for 20 min, a solution of the aldehyde **31** (992 mg, 3.00 mmol) in THF (6 mL) was added slowly. After the mixture had been stirred for a further 12 h, water (20 mL) was added and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 10 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 20:1, furnished the product **32** (641 mg, 65%) as a colourless oil. $[\alpha]_D^{20} = -18.1$ ($c = 7.31$, $CHCl_3$): ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.04$ (s, 6 H), 0.89 (s, 9 H), 0.94 (d, $J = 7.0$ Hz, 3 H), 1.11 (d, $J = 7.0$ Hz, 3 H), 1.34 (s, 3 H), 1.36 (s, 3 H), 1.74−1.87 (m, 1 H), 2.24−2.41 (m, 1 H), 3.48 (dd, $J = 9.7$, 6.5 Hz, 1 H), 3.68 (t, $J = 7.2$ Hz, 1 H), 3.77 (dd, $J = 9.7$, 4.6 Hz, 1 H), 3.85 (dd, $J = 7.4$, 4.0 Hz, 1 H), 4.96−5.10 (m, 2 H), 5.86 ppm (ddd, $J = 17.3$, 10.5, and 8.5 Hz, 1 H). ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -5.4$, 14.1, 18.3, 18.4, 25.9, 27.5, 28.3, 39.4, 40.9, 64.8, 80.3, 82.7, 107.9, 115.6, 139.6 ppm. $C_{18}H_{36}O_3Si$ (328.6): (exact mass, ESI, M + Na^+): calcd. 351.2331; found 351.2318.

21. (4*S*,5*S*)-5-[(1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-4-[(1*S*)-1-methyl-2-(4-methylphenylsulfonyloxy)ethyl]-1,3-dioxolane (34): A solution of the alcohol **30** (4.89 g, 14.7 mmol), triethylamine (3.70 mL, 26.5 mmol), 4-dimethylaminopyridine (899 mg, 7.36 mmol), and *p*-toluenesulfonyl chloride (4.91 g, 25.8 mmol) in dichloromethane (100 mL) was stirred for 12 h. Water (40 mL) was added, the phases were separated, and the aqueous phase was extracted with dichloromethane (3 × 20 mL). The combined organic phases were washed with water (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 20:1 to 10:1, furnished the tosylate **34** (7.08 g, 99%) as a colourless oil. $[\alpha]_D^{20} = -30.8$ ($c = 7.51$, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.03$ (s, 6 H), 0.88 (s, 9 H), 0.90 (d, $J = 7.0$ Hz, 3 H), 0.97 (d, $J = 7.0$ Hz, 3 H), 1.24 (s, 3 H), 1.30 (s, 3 H), 1.71−1.80 (m, 1 H), 1.92−1.99 (m, 1 H), 2.44 (s, 3 H), 3.44 (dd, $J = 10.0$, 6.4 Hz, 1 H), 3.69−3.79 (m, 3 H), 3.92 (dd, $J = 9.6$, 7.3 Hz, 1 H), 4.20 (dd, $J = 9.6$, 5.5 Hz, 1 H), 7.76−7.81 (m, 2 H), 7.31−7.35 ppm (m, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -5.4$, 14.5, 14.7, 18.3, 21.6, 25.9, 27.6, 36.8, 39.3, 64.3, 72.1, 80.3, 81.6, 108.6, 128.0, 129.8, 133.0, 144.6 ppm. $C_{24}H_{42}O_6SSi$ (486.7): calcd. C 59.22, H 8.70; found C 59.37, H 8.66.

22. (4*S*,5*S*)-4-[(1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-5-[(1*R*)-1-methyl-2-phenylsulfonylethyl]-1,3-dioxolane (35): A solution of the tosylate **34** (150 mg, 0.31 mmol), sodium iodide (93 mg, 0.62 mmol), and sodium phenylsulfinate (179 mg, 1.09 mmol) in DMF (2 mL) was heated for 12 h at 70 °C. Water (10 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 5 mL). The combined organic phases were washed with water (5 mL) and brine (5 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 20:1 to 10:1, furnished the sulfone **35** (125 mg, 87%), and the corresponding sulfinate (15 mg, 10%).

Sulfone 35: $[\alpha]_D^{20} = -27.2$ ($c = 7.95$, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): $\delta = -1.30$ (s, 3 H), 0.00 (s, 3 H), 0.77 (d, $J = 6.9$ Hz, 3 H), 0.85 (s, 9 H), 1.16 (s, 3 H), 1.17 (d, $J = 7.3$ Hz, 3 H), 1.27 (s, 3 H), 1.63−1.79 (m, 1 H), 2.06−2.21 (m, 1 H), 2.88 (dd, $J = 14.6$, 9.6 Hz, 1 H), 3.34−3.48 (m, 3 H), 3.65−3.80 (m, 2 H), 7.49−7.62 (m, 3 H), 7.86−7.91 ppm (m, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -5.5$, 14.0, 18.1, 18.2, 25.9, 27.3, 27.4, 32.0, 39.7, 57.9, 64.4, 81.1, 82.5, 108.7, 127.9, 129.2, 133.5, 139.6 ppm. $C_{23}H_{40}O_5SSi$ (456.2): calcd. C 60.49, H 8.83; found C 60.44, H 8.87.

23. (2*R*,3*RS*,4*RS*,5*R*)-2,5-Bis{(4*S*,5*S*)-5-[(1*S*)-2-*tert*-butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-1,3-dioxolane-4-yl}-4-phenylsulfonylhexan-3-ol (36): *n*-Butyllithium (1.37 M in hexane, 1.60 mL, 2.2 mmol) was added at −78 °C to a solution of the sulfone **35** (1.048 g, 2.29 mmol) in THF (17 mL). After the resulting yellow solution had been stirred for 15 min, a solution of the aldehyde **31** (656 mg, 1.98 mmol) in THF (5 mL) was added slowly. After the mixture had been stirred for 2 h at −78 °C, water (25 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 10 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 10:1 to 5:1, furnished the hydroxysulfone **36** (654 mg, 42%) as a single diastereomer, together with a diastereomer mixture of hydroxysulfones (955 mg, 53%). In addition, starting sulfone **35** (119 mg, 11%) could be reisolated.

Hydroxysulfone 36: $[\alpha]_D^{20} = -25.7$ ($c = 1.32$, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): $\delta = -0.02$ (s, 3 H), −0.01 (s, 3 H), 0.02 (s, 3 H), 0.03 (s, 3 H), 0.86 (s, 9 H), 0.87 (d, $J = 7.4$ Hz, 3 H), 0.89 (s, 9 H), 0.97 (s, 3 H), 0.98 (d, $J = 6.9$ Hz, 3 H), 1.01 (d, $J = 7.1$ Hz, 3 H), 1.19 (d, $J = 7.0$ Hz, 3 H), 1.28 (s, 3 H), 1.35 (s, 3 H), 1.43 (s, 3 H), 1.67−1.72 (m, 1 H), 1.79−1.84 (m, 1 H), 2.17−2.23 (m, 1 H), 2.49−2.53 (m, 1 H), 3.39 (dd, $J = 10.0$, 7.2 Hz, 1 H), 3.47 (dd, $J = 10.0$, 7.1 Hz, 1 H), 3.51 (dd, $J = 6.8$, 6.2 Hz, 1 H), 3.72

(dd, J = 10.0, 4.5 Hz, 1 H), 3.81−3.84 (m, 2 H), 3.90 (t, J = 7.1 Hz, 1 H), 4.01 (dd, J = 7.4, 3.8 Hz, 1 H), 4.24 (dd, J = 8.9, 5.0 Hz, 1 H), 4.72 (dd, J = 10.0, 1.5 Hz, 1 H), 7.50−7.55 (m, 2 H), 7.57−7.61 (m, 1 H), 7.83−7.85 ppm (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4, 11.3, 11.5, 14.3, 14.9, 18.3. 26.0, 27.2, 27.6, 27.8, 28.1, 37.9, 38.2, 39.5, 39.9, 64.1, 64.3, 64.8, 67.5, 80.7, 81.8, 83.3, 83.8, 108.5, 108.9, 128.4, 129.1, 133.5, 139.0 ppm. $C_{40}H_{74}O_9SSi_2$ (787.3): calcd. C 61.03, H 9.47; found C 60.86, H 9.32.

24. (4*S*,5*S*)-4-[(1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl]-5-[(1*S*,2*E*,4*S*)-4-{(4*S*,5*S*)-5-[(1*S*)-2-*tert*-butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-1-methyl-2-pentenyl]-2,2-dimethyl-1,3-dioxolane (33): Disodium hydrogen phosphate (818 mg, 5.65 mmol) and sodium amalgam (6%, 3.8 g) were added at −20 °C to a solution of the hydroxysulfone **36** (759 mg, 0.96 mmol) in a mixture of methanol and ethyl acetate (2:1, 15 mL). The mixture was allowed to come to room temperature whilst stirring. After 12 h, water (20 mL) was added, the mixture was decanted, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 15 mL). The combined organic phases were washed with brine (15 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 9:1, furnished the alkene **33** (403 mg, 67%) and the alcohol (4*S*,5*S*)-4-[(1*S*)-2-*tert*-butyldimethylsilyloxy-1-methylethyl]-5-(1*S*,3*RS*,4*S*)-4-{(4*S*,5*S*)-5-[(1*S*)-2-*tert*-butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-3-hydroxy-1-methyl-2-pentyl]-2,2-dimethyl-1,3-dioxolane (87 mg, 14%).

Alkene 33: $[\alpha]_D^{20}$ = −19.8 (c = 5.09, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 (s, 12 H), 0.89 (s, 18 H), 0.95 (d, J = 6.6 Hz, 6 H), 1.10 (d, J = 6.8 Hz, 6 H), 1.34 (s, 6 H), 1.36 (s, 6 H), 1.71−1.86 (m, 2 H), 2.24−2.33 (m, 2 H), 3.35 (dd, J = 9.9, 7.0 Hz, 2 H), 3.58 (t, J = 7.0 Hz, 2 H), 3.75−3.83 (m, 4 H), 5.36−5.53 ppm (m, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.5, −5.4, 14.2, 18.2, 18.6, 25.9, 27.4, 39.4, 39.5, 64.8, 80.5, 82.9, 107.8, 132.1 ppm. $C_{34}H_{68}O_6Si_2$ (629.1): calcd. C 64.92, H 10.90; found C 64.87, H 11.02.

(4*S*,5*S*)-4-[(1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl]-5-[(1*S*,3*RS*,4*S*)-4-{(4*S*,5*S*)-5-[(1*S*)-2-*tert*-butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-3-hydroxy-1-methyl-2-pentyl]-2,2-dimethyl-1,3-dioxolane: $[\alpha]_D^{20}$ = −35.3 (c = 6.44, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.00 (s, 12 H), 0.83−0.84 (m, 21 H), 0.89 (d, J = 7.2 Hz, 3 H), 0.90 (d, J = 7.0 Hz, 3 H), 0.96 (d, J = 6.8 Hz, 3 H), 1.32 (s, 9 H), 1.36 (s, 3 H), 1.61−1.85 (m, 6 H), 2.99 (d, J = 2.7 Hz, 1 H), 3.44 (dd, J = 9.8, 6.7 Hz, 1 H), 3.48 (dd, J = 9.8, 6.1 Hz, 1 H), 3.63−3.81 (m, 5 H), 3.96 (dd, J = 7.0, 4.5 Hz, 1 H), 4.07 ppm (t, J = 6.0 Hz, 1 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.1, 11.5, 14.7, 15.0, 18.1, 18.6, 26.3, 27.6, 28.0, 28.1, 34.3, 36.4, 38.8, 39.9, 40.0, 64.8, 69.5, 81.2, 81.6, 83.9, 84.3, 108.6, 108.7 ppm. $C_{34}H_{70}O_7Si_2$ (647.1): calcd. C 63.11, H 10.90; found C 62.99, H 10.89.

25. (2*S*,3*R*,4*R*,5*S*)-2,5-Bis{(4*S*,5*S*)-5-[(1*S*)-2-*tert*-butyldimethylsilyloxy-1-methylethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}hexane-3,4-diol (37): Potassium osmate(VI) dihydrate (ca. 5 mg) was added to a solution of the alkene **33** (35 mg, 0.06 mmol) and *N*-methylmorpholine *N*-oxide (50%) in water (49 mg, 0.21 mmol) in a mixture of acetone (0.1 mL), *tert*-butyl alcohol (0.1 mL) and water (0.2 mL). After the mixture had been stirred for 3 days, sodium sulfite (300 mg) was added and stirring was continued for 2 h. Water (5 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 3 mL). The combined organic phases were washed with brine (3 mL), dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with pentane/*tert*. butyl methyl ether, 10:1 to 5:1, furnished the diol **37** (31 mg, 84%) and the diastereomeric diol **38** (5 mg, 14%).

Diol 37: $[\alpha]_D^{20}$ = −45.7 (c = 1.37, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 (s, 6 H), 0.02 (s, 6 H), 0.89 (s, 18 H), 0.93 (d, J = 6.9 Hz, 6 H), 1.00 (d, J = 6.8 Hz, 6 H), 1.39 (s, 6 H), 1.41 (s, 6 H), 1.86−1.90 (m, 2 H), 1.99−2.02 (m, 2 H), 3.41 (dd, J = 10.0, 6.4 Hz, 2 H), 3.61 (dd, J = 7.1, 3.7 Hz, 2 H), 3.76 (dd, J = 10.0, 5.4 Hz, 2 H), 3.86−3.92 (m, 4 H), 4.05 ppm (dd, J = 8.1, 6.6 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4, 13.4, 15.4, 18.3, 27.0, 27.5, 27.6, 39.1, 40.3, 64.2, 74.1, 82.6, 82.9, 108.6 ppm. $C_{34}H_{70}O_8Si_2$ (663.1): calcd. C 61.59, H 10.64; found C 61.33, H 10.72.

Diol 38: $[\alpha]_D^{20}$ = −33.3 (c = 0.33, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.04 (s, 12 H), 0.89 (s, 18 H), 0.95 (d, J = 7.0 Hz, 6 H), 0.96 (d, J = 7.0 Hz, 6 H), 1.38 (s, 6 H), 1.40 (s, 6 H), 1.59−1.71 (m, 2 H), 1.76−1.89 (m, 2 H), 3.01 (broad s, 2 H), 3.54 (dd, J = 9.8, 6.2 Hz, 2 H), 3.73−3.83 (m, 4 H), 3.98−4.05 ppm (m, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.4, 10.8, 14.6, 18.3, 25.9, 27.5, 28.1, 37.1, 39.6, 64.4, 71.3, 81.5, 82.6, 108.6 ppm. $C_{34}H_{70}O_8Si_2$ (663.1): calcd. C 61.59, H 10.64; found C 61.67, H 10.53.

26. (4*S*,5*R*,6*R*)-2,2,5-Trimethyl-4-[(4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxan-4-yl]-6-{(4*R*,5*R*,6*S*)-2,2,5-trimethyl-6-[(4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxan-4-yl]-1,3-dioxan-4-yl}-1,3-dioxane (6): DOWEX 50 (ca. 10 mg) was added to a solution of the diol **37** (210 mg, 0.32 mmol) in methanol (2.5 mL). After stirring for 12 h, the mixture was filtered, the residue was washed with methanol (2 mL), and the combined filtrates were concentrated. The crude product was taken up in DMF (3 mL). 2-Methoxypropene (230 mg, 3.20 mmol) and *p*-toluenesulfonic acid (ca 5 mg) were added at 0 °C. After the mixture had been stirred for 1 h, saturated aqueous $NaHCO_3$ solution (5 mL) was added, the phases were separated, and the aqueous phase was extracted with ether (3 × 3 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether, 4:1, containing 1% triethylamine, furnished the product **6** (82 mg, 52%) as a colourless solid of m.p. 225 °C. $[\alpha]_D^{20}$ = +8.5 (c = 1.99, $CHCl_3$). ^{1}H NMR (500 MHz, C_6D_6): δ = 0.68 (d, J = 6.7 Hz, 6 H), 1.01 (d, J = 6.7 Hz, 6 H), 1.33 (s, 6 H), 1.36 (s, 6 H), 1.54 (s, 6 H), 1.55 (s, 6 H), 2.41−2.47 (m, 2 H), 2.76−2.82 (m, 2 H), 3.47 (t, J = 11.3 Hz, 2 H), 3.68 (dd, J = 10.0, 2.5 Hz, 2 H), 3.70 (dd, J = 10.0, 2.5 Hz, 2 H), 3.76 (dd, J = 11.3, 4.8 Hz, 2 H), 3.75−3.77 ppm (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.0, 12.2, 18.5, 18.6, 29.2, 29.5, 30.0, 30.2, 66.4, 74.0, 74.3, 74.5, 98.6, 98.9 ppm. $C_{28}H_{50}O_8$ (exact mass, ESI, M + Na^+): calcd. 537.3403; found 537.3370.

CCDC-177255 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44−1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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[1] R. W. Hoffmann, K. Menzel, K. Harms, *Eur. J. Org. Chem.* **2002**, 2603−2612, preceding paper.
[2] R. W. Hoffmann, K. Menzel, *Eur. J. Org. Chem.* **2001**, 2749−2755.
[3] I. Columbus, S. Cohen, S. E. Biali, *J. Am. Chem. Soc.* **1994**, *116*, 10306−10307.
[4] I. Columbus, R. E. Hoffman, S. E. Biali, *J. Am. Chem. Soc.* **1996**, *118*, 6890−6896.
[5] R. W. Hoffmann, T. Brandl, P. Kirsch, K. Harms, *Synlett* **2001**, 960−963.
[6] E. Kleinpeter, R. Meusinger, C. Duschek, R. Borsdorf, *Magn. Reson. Chem.* **1987**, *25*, 990−995.
[7] D. S. Matteson, E. C. Beedle, A. A. Kandil, *J. Org. Chem.* **1987**, *52*, 5034−5036.
[8] X. Wang, S. D. Erickson, T. Iimori, W. C. Still, *J. Am. Chem. Soc.* **1992**, *114*, 4128−4137.
[9] W. C. Still, J. C. Barrish, *J. Am. Chem. Soc.* **1983**, *105*, 2487−2489.
[10] F. Langer, A. Devasagayaraj, P.-Y. Chavant, P. Knochel, *Synlett* **1994**, 410−412.
[11] B. K. Eya, T. Otsuka, I. Kubo, T. L. Wood, *Tetrahedron* **1990**, *46*, 2695−2706.
[12] K. C. Nicolaou, A. P. Patron, K. Ajito, P. K. Richter, H. Khatuya, P. Bertinato, R. A. Miller, M. J. Tomaszewski, *Chem. Eur. J.* **1996**, *2*, 847−868.
[13] H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483−2547.
[14] D. Xu, G. A. Crispino, K. B. Sharpless, *J. Am. Chem. Soc.* **1992**, *114*, 7570−7572.
[15] D. Redoulès, J. Perié, *Tetrahedron Lett.* **1999**, *40*, 4811−4814.
[16] S. D. Rychnovsky, D. J. Skalitzky, *Tetrahedron Lett.* **1990**, *31*, 945−948.
[17] D. A. Evans, D. L. Rieger, J. R. Gage, *Tetrahedron Lett.* **1990**, *31*, 7099−7100.
[18] T. Fäcke, S. Berger, *Magn. Reson. Chem.* **1995**, *33*, 144−148.
[19] R. Göttlich, B. C. Kahrs, J. Krüger, R. W. Hoffmann, *Chem. Commun.* **1997**, 247−251.
[20] T: Brandl, Dissertation Universität Marburg **2001**; R. W. Hoffmann, G. Mas, T. Brandl, *Eur. J. Org. Chem.*, submitted.
[21] P. E. Hansen, *Progr. NMR Spectroscop.* **1981**, *14*, 175−296.
[22] T. Iimori, S. D. Erickson, A. L. Rheingold, W. C. Still, *Tetrahedron Lett.* **1989**, *30*, 6947−6950.
[23] G. Li, W. C. Still, *Tetrahedron Lett.* **1993**, *34*, 919−922.
[24] G. Li, W. C. Still, *J. Org. Chem.* **1991**, *56*, 6964−6966.
[25] S. D. Erickson, M. H. J. Ohlmeyer, W. C. Still, *Tetrahedron Lett.* **1992**, *33*, 5925−5928.
[26] G. Li, W. C. Still, *Tetrahedron Lett.* **1992**, *33*, 5929−5932.
[27] G. Li, W. C. Still, *J. Am. Chem. Soc.* **1993**, *115*, 3804−3805.
[28] M. T. Burger, A. Armstrong, F. Guarnieri, D. Q. McDonald, W. C. Still, *J. Am. Chem. Soc.* **1994**, *116*, 3593−3594.
[29] S. Tang, W. C. Still, *Tetrahedron Lett.* **1993**, *34*, 6701−6704.
[30] R. W. Hoffmann, *Angew. Chem.* **1992**, *104*, 1147−1157; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1124−1134.
[31] R. W. Hoffmann, *Angew. Chem.* **2000**, *112*, 2134−2150; *Angew. Chem. Int. Ed.* **2000**, *39*, 2054−2070.
[32] D. Stenkamp, R. W. Hoffmann, R. Göttlich, *Eur. J. Org. Chem.* **1999**, 2929−2936.
[33] T. Trieselmann, R. W. Hoffmann, *Org. Lett.* **2000**, *2*, 1209−1212; T. Trieselmann, R. W. Hoffmann, K. Menzel, *Eur. J. Org. Chem.* **2002**, 1292−1304.
[34] R. W. Hoffmann, M. Stahl, U. Schopfer, G. Frenking, *Chem. Eur. J.* **1998**, *4*, 559−566.
[35] F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson, W. C. Still, *J. Comput. Chem.* **1990**, *11*, 440−467.

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