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Iterative *Syn*-1,3,5-Triol Synthesis Utilizing the Reaction of β-(Trimethylsilyl)alkyl Phenyl Sulphones with Oxiranes#

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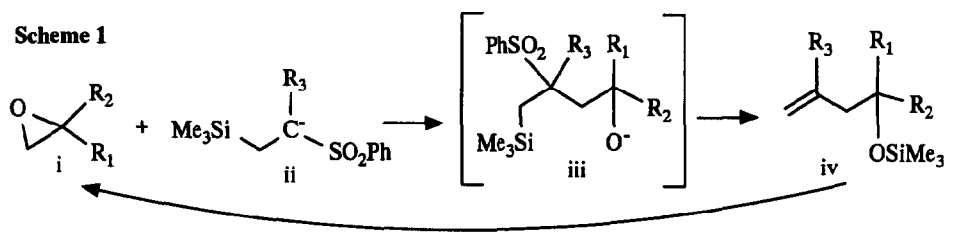
Abstract: Partly protected triols **8a** and **8b** were synthesised from epoxide **1** using β-trimethylsilyl sulphones **2a** and **2a** for the chain elongation and the Cardillo procedure for diastereoselective two-step epoxidation of homoallylic alcohols.

Methodology for stereocontrolled synthesis of acyclic 1,3,5-triols and their congeners with an extended polyol system has recently received a great deal of attention.[1] Although many useful procedures have already been developed, the diversity of the natural products with such a hydroxyl group arrangement and complexity of problems related to their synthesis call for continuous methodological studies.[2] Lipshutz and coworkers[3] have developed succinct iterative[4] synthesis of *syn*-1,3 diols, based upon addition of higher-order vinylic cuprates to optically active epoxides. This method leads to *all-syn* polyols with secondary hydroxyl groups.

Scheme 1



1. protective groups manipulation
2. epoxidation

Our experience with the addition of β-(trimethylsilyl)alkyl phenyl sulphones (which represent a masked vinyl unit) to oxiranes[5] prompted us to examine application of this reaction to stereospecific synthesis of 1,3,5-triols. We expected that the sulphone-based methodology will allow for a convenient approach to *syn* polyols

#This paper is dedicated to the memory of Professor Günther Snatzke.

with differently substituted chains, including those with branched chains and tertiary hydroxyl groups. The planned synthetic approach is presented in Scheme 1. The reaction of sulphonyl anion **ii** with starting chiral epoxide **i** affords protected or free homoallylic alcohol **iv** which is epoxidized with chirality transfer (after appropriate adjustment of the protective groups). The resulting epoxide is subjected to reiterate chain elongation with the use of sulphonyl anion **ii**. The cycle of reactions may be terminated at the stage of homoallylic alcohol (**iv**) or epoxide (**i**), and the products may be further elaborated with the use of terminal functional groups. Additionally, an intermediate with a secondary phenylsulphonyl group (**iii**, R_3=H) may be utilized, if needed, in the reactions of carbon - carbon bond formation. In the study of the reaction sequence presented in Scheme 1 we used four-carbon hydroxy epoxide **1** (Scheme 2, which is available in both enantiomeric forms from L-(-)-malic acid[6,7]) and secondary and primary sulphones, **2a** and **2b**.[8] As the target compounds eight-carbon unsaturated triols **8a** and **8b** were chosen. Now, we present our results.

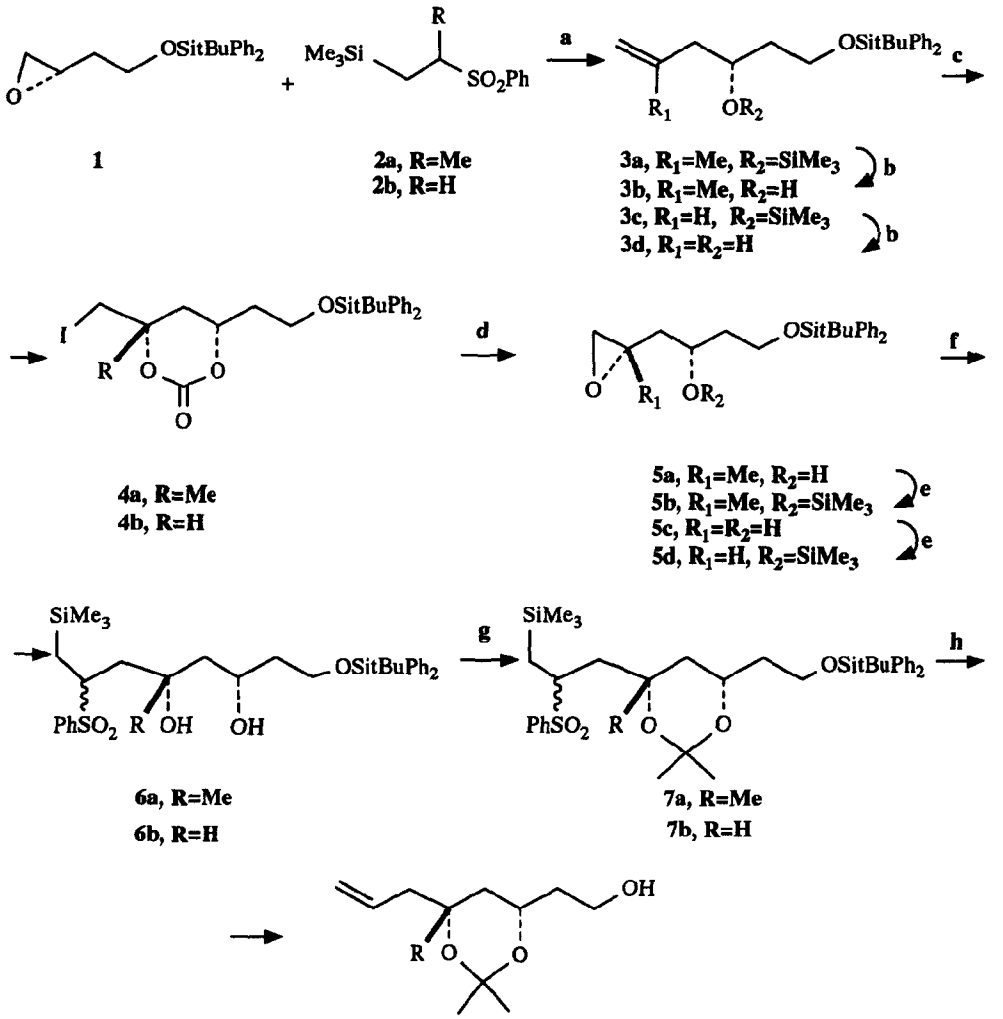
Epoxide **1** in THF solution was allowed to react with the anion generated from sulphone **2a** and butyllithium to afford an adduct which was, without isolation, treated with sodium hydride to effect a shift of the trimethylsilyl group and elimination of the benzenesulphonyl group.[5b] Usual workup of the reaction mixture gave crude trimethylsilyl ether **3a** which partly hydrolysed in the course of chromatography on silica gel to afford **3a** (66% yield) and the corresponding free alcohol **3b** (21% yield). After hydrolysis of the ether fraction, alcohol **3b** was obtained in an over 85% total yield. Likewise, reaction of epoxide **1** with sulphone **2b**, followed by treatment of the immediate adduct with sodium hydride, afforded trimethylsilyl ether **3c** (80% yield after chromatography) which was subsequently hydrolysed to alcohol **3d**.

Alcohol **3b** was treated, accordingly to the procedure of Cardillo et al.,[9] consecutively with butyllithium, CO_2 and with I_2 to afford iodocarbonate **4a**. The latter, without purification, was subjected to alkaline hydrolysis and the product was chromatographed on silica gel. Some unreacted alcohol **3b** was recovered and epoxide **5a** was obtained in a 69% over-all yield (60% conversion). The presence of small amounts of *anti* diastereomer in this product was evident by its high-field ^{1}H NMR spectrum; the diastereomer ratio was 20:1. The hydroxyl group in **5a** was protected with the trimethylsilyl group to give ether **5b** (80% yield).

An analogous sequence of reactions starting with homoallylic alcohol **3d** afforded iodolactone **4b** (60% yield, 60% conversion) and then epoxide **5c** (90% yield). In the ^{1}H NMR spectra of compounds **4b** and **5c** no signals of the minor diastereomer could be detected. However, the corresponding trimethylsilyl ether **5d** (obtained from **5c** in 88% yield) showed a 12:1 diastereomer ratio.

Reaction of epoxide **5b** with the anion generated from sulphone **2b** afforded the crude adduct. We did not succeed in inducing carbon-to-oxygen shift of the terminal trimethylsilyl group with elimination of benzenesulphonyl group, by exposing the adduct to an excess of sodium hydride. It is likely that the stability

Scheme 2



Reagents and conditions: a. BuLi/THF-hexane,-78 °C → rt and then NaH, reflux; b. PPTS/MeOH, **3b** 87% from **1** with **2a**, **3d** 74% from **1** with **2b**; c. BuLi / THF-hexane, 0 °C → rt and then CO_2 and I_2; d. K_2CO_3/MeOH, **5a** 69% from **3b** (60% conversion), **5c** 90% from **4b** (60% conversion); e. TMSCl-Py/THF-hexane, **5b** 80%, **5d** 88%; f. **2a**-BuLi/THF-hexane, -78 °C→ rt and then PPTS/MeOH, **6a** 66% from **5b**, **6b** 85% from **5c**; g. 2-methoxypropen - p-TSA/CH_2Cl_2, **7a** 85% from **6a**, **7b** 82% from **6b** ; h. TBAF $3H_2O$/MeCN, reflux, **8a** 94% from **7a**, **8b** 83% from **7b**.

of this adduct, as compared to the adduct obtained in the previous cycle, reflects the interaction of the oxido group with the neighbouring trimethylsilyloxy group. The difficulty in the formation of the double bond at the stage of adduct was easily circumvent. Namely, the crude adduct was treated with pyridinium p-toluenesulphonate (PPTS) in methanol in order to hydrolyse the O-trimethylsilyl group. After chromatography, diol **6a** was obtained in 66% yield. As expected, compound **6a** was formed as a mixture of epimers on the carbon bearing the benzenesulphonyl group. Diol **6a** was further transformed to acetonide **7a** (85% yield) using 2-methoxypropene and p-toluenesulphonic acid (p-TSA) in dichloromethane. Finally, acetonide **7a** was treated with tetrabutylammonium fluoride (TBAF) trihydrate in boiling acetonitrile, which resulted in formation of a double bond and de-protection of the terminal hydroxyl group to give compound **8a** in 94% yield (after chromatography on silica gel). No trace of contamination of compound **8a** with its diastereomer could be detected on examination of its ^{1}H and ^{13}C NMR spectra.

In a similar way, reaction of epoxide **5d** with the anion generated from sulphone **2b**, followed by hydrolysis of the crude adduct, afforded diol **6b** in 85% yield. Diol **6b** was converted to the isopropylidene derivative **7b** (82% yield, after chromatography) and the latter was treated with TBAF·$3H_2O$ in boiling acetonitrile to give the triol derivative **8b** in 83% yield. No traces of diastereomer could be detected by TLC and NMR analysis of compound **8b**.

In conclusion, β-(trimethylsilyl)alkyl phenyl sulphones may be used as a convenient vinyl anion equivalent in iterative synthesis of 1,3-*syn*-diols and related systems. The efficiency of the syntheses involving secondary sulphone **2a** in respect of high yield of homoallylic alcohol formation and high diastereoselectivity of epoxidation, is noteworthy.

Experimental Section

Melting points were determined on a hot-stage apparatus and are uncorrected. Spectra were recorded using the following instruments: IR, Beckmann 4240; ^{1}H and ^{13}C NMR, Bruker AM 500 (500 and 125 MHz) or Varian GEM 200 (200 and 50 MHz) (for $CDCl_3$ solutions); mass (MS), AMD 604 - EI mode: 70 eV, 8 kV acc. vol., - LSIMS mode: Cs^+ 10 keV, 8 kV acc. vol., m-nitrobenzyl alcohol matrix. Chemical shifts are reported in δ units, downfield from $(CH_3)_4Si$. All reactions involving organometallic reagents were carried out under argon with stirring. Organic solutions were dried over anhyd. $MgSO_4$ and the solvents were evaporated on a rotary evaporator. Column chromatography was performed on Merck silica gel 60, 230-400 mesh, and TLC - on Merck slica gel G. Optical rotations were measured with a Perkin-Elmer Model 141 polarimeter using a 8 mL capacity cell (10 cm path length) for $CHCl_3$ solutions, unless otherwise stated. Microanalyses were performed at our analytical laboratory.

1-(Trimethylsilyl)-2-(phenylsulphonyl)propane (2a).

To a solution of sulphone **2b** (242 mg, 1 mmol) in THF (2 mL), stirred at -78 °C, BuLi in hexane (1.6 M, 0.75 mL, 1.2 mmol) was added, followed - after 30 min with MeI (0.125 mL, 2 mmol). The mixture was allowed to warm to rt in ca. 1 h whereupon the reaction was quenched with saturated aq. NH_4Cl (1 mL). The product was extracted with toluene (10 mL). The extract was washed consecutively with water and brine, and evaporated. The residue was filtered through SiO_2 (5 g, 1% EtOAc in toluene) to give **2a** (250 mg, 97% yield) as a colourless oil: IR 1300, 1250, 1140, 1080 cm^{-1}; ^1H NMR -0.33 (s, 9, $SiCH_3$), 0.67 (dd, 1, J = 14.2, 12.5 Hz, CHa-Si), 1.22 (dd, 3, J = 6.9, 0.75 Hz, CH_3), 1.31 (dm, 1, J = 14.1 Hz, CHb-Si), 3.07 (m, 1, $CH\text{-}SO_2$), 7.57 and 7.85 (2m, 3 and 2, Ph H); MS EI (m/z) 241 (M^+-CH_3), 214 (M-C_3H_6), 199 (M-CH_3-C_3H_6). Calcd. for $C_{12}H_{20}O_2SSi$ (256.43): C, 56.20; H, 7.86. Found: C, 56.05; H, 8.12.

(3R)-1-O-(t-Butyldiphenylsilyl)-3-O-(trimethylsilyl)-1,3-dihydroxy-5-methylhex-5-ene (3a) and (3R)-1-O-(t-butyldiphenylsilyl)-1,3-dihydroxy-5-methylhex-5-ene (3b).

To a solution of sulphone **2a** (256 mg, 1.0 mmol) in THF (3 mL), stirred at -78 °C, BuLi in hexane (1.6 M, 0.70 mL, 1.1 mmol) was added, followed - after 30 min - by epoxide **1** (326 mg, 1.0 mmol) in THF (1 mL). The solution was allowed to warm to rt within ca. 1.5 h whereupon NaH (washed with hexane, 46 mg, 2 mmol) was added and the mixture was heated under reflux for 30 min. After cooling, the mixture was partitioned between sat. aq. NH_4Cl (1 mL) and hexane (10 mL). The organic layer was washed with water and brine and was evaporated. The residue (404 mg) was chromatographed on SiO_2 (8 g, 1% EtOAc in toluene) to give (in order of elution):

1. **3a** (291, 66%): IR 1650, 1110, 1090 cm^{-1}; ^1H NMR 0.10 (s, 9, $SiCH_3$), 1.06 (s, 9, tBu H), 1.50 - 1.83 (m, 2, C_2 H) overlapping 1.75 (dd, 3, J = 1.3, 0.9 Hz, vinylic CH_3), 2.17 (dm, 2, J = 6.0 Hz, C_4 H), 3.73 (m, 2, C_1 H), 4.09 (m, 1, C_3 H), 4.71 (m, 1, C_6 Ha), 4.78 (m, 1, C_6 Hb), 7.40 and 7.67 (2 m, 6 and 4, arom. H); ^{13}C NMR 0.34 (Si-C), 19.17 (tBu IVry C), 22.97 (vinyl $\underline{C}H_3$), 26.87 (tBu I-ry C), 39.88, 46.47 (C_2, C_4), 60.68 (C_1), 67.74 (C_3), 112.90 (C_6), 127.59, 127.67, 129.53 (arom. C), 133.96 (C_5), 135.57, 142.70 (arom. C); MS EI (m/z) 439 (M^+-H), 385 (M^+-C_4H_7), 383 (M^+-C_4H_9), 355, 293, 271, 251. HRMS. Calcd for $C_{22}H_{33}O_2Si_2$ (M^+-C_4H_7): 385.2019. Found: 385.2015. Calcd for $C_{22}H_{31}O_2Si_2$ (M-C_4H_9): 383.1863; found: 383. 1857.

2. unreacted epoxide **1** (20 mg, 5%)

3. **3b** (85 mg, 21%): $[\alpha]_D^{17}$= +0.4 (c 2.1); IR 3515, 1115, 1080 cm^{-1}; ^1H NMR 1.05 (s, 9, tBu H), 1.70 (m, 2, C_2 H), 1.77 (br s, 3, vinylic CH_3), 2.21 (m, 2, C_4 H), 3.02 (d, 1, J = 2.3 Hz, OH), 3.83 (m, 2, C_1 H), 4.06 (m, 1, C_3H), 4.77 (m, 1, C_6 H_a), 4.84 (m, 1, C_6 H_b), 7.43 and 7.66 (2m, 6 and 4, arom. H); ^{13}C NMR: 19.08 (tBu IVry C), 22.51 (vinyl CH_3), 26.83 (tBu Iry C), 38.36, 46.06 (C_2, C_4), 62.97 (C_1), 68.67 (C_3), 112.98 (C_6), 127.75, 129.77 (arom. C), 133.26 (C_5), 135.56, 142.76 (arom. C); MS LSIMS (m/z) 391 (M^++Na), 369

(M^++1), 351 (M^++1-H_2O), 313 (M^+-C_4H_7), 311 (M^+-C_4H_9), 309 (M^+-H_2O-C_3H_5), 289, 269, 255, 235, 199, 179, 95. HRMS. Calcd for $C_{19}H_{23}O_2Si$ (M^+-C_4H_9): 311.1407. Found: 311.1407.

Partial hydrolysis of 3a.

A solution of ether **3a** (240 mg, 0.54 mmol) in methanol (2.5 mL) containing PPTS (10 mg) was stirred at rt for 15 min and then partitioned between toluene (10 mL) and water (10 mL). Organic layer was washed with water, dried and evaporated. The residue was chromatographed on SiO_2 (5 g, 1% ether in hexane) to give **3b** (198 mg, 99%) identical with the product described above.

(2R,4S)-6-O-(t-Butyldiphenylsilyl)-1,2-epoxy-2-methylhexane-4,6-diol (5a).

To a solution of carbinol **3b** (315 mg, 0.85 mmol) in THF (4 mL), stirred at 0 °C, BuLi in hexane (1.6 M, 0.62 mL, 1 mmol) was added. The mixture was allowed to warm to rt within ca. 30 min, maintained at this temperature for additional 30 min and cooled again to 0 °C. A stream of CO_2 was passed through the mixture for 1 h whereupon I_2 (432 mg, 1.7 mmol) in THF (5 mL) was added dropwise during 15 min and the stirring at 0 °C was continued for 0.5 h. The mixture was diluted with toluene (20 mL) and washed successively with sat. aq. $Na_2S_2O_3$, $NaHCO_3$ and with brine. The solvent was evaporated and the residue (crude iodocarbonate **4a**, 420 mg) was dissolved in methanol (7.5 mL) containing K_2CO_3 (356 mg, 2.6 mmol), and was stirred for 16 h at rt. The solution was diluted with toluene (10 mL), washed with sat. aq. $Na_2S_2O_3$ and then with water and brine. The solvent was evaporated and the residue (311 mg) was chromatographed on SiO_2 (7 g, 1% EtOAc in toluene) to give:

1. unreacted **3b** (130 mg, 41%)

2. **5a** (132 mg, 42%): $[\alpha]_D^{20}$= +7.67 ° (c 1.1); IR 3500, 1110 cm^{-1}; ^1H NMR 1.05 (s, 9, tBu H), 1.39 (s, 3, CH_3), 1.55 - 1.85 (m, 2, C_5 H) overlapping 1.76 (d, 2, J = 6.2 Hz, C_3 H), 2.61 (d, 1, J = 4.7 Hz, C_1 Ha), 2.74 (d, 1, J = 4.7 Hz, C_1 Hb), 3.38 (d, 1, J = 2.2 Hz, OH), 3.85 (m, 2, C_6 H), 4.04 - 4.18 (m, 1, C_4 H); for the minor epimer (2R, 4S) the following signals were recorded: 2.66 (d, J = 4.6 Hz, C_1 H_a), 2.82 (d, J = 4.6 Hz, C_1 Hb), 3.46 (d, J = 2.2 Hz, OH); integration of the C_1 proton signals indicated a 20:1 ratio of the diastereomers; ^{13}C NMR 19.07 (IVry tBu-C), 21.84 (CH_3), 26.83 (Iry tBu-C), 39.11, 43.39 (C_5, C_3), 53.75 (C_1), 55.91 (C_2), 62.89 (C_6), 68.19 (C_4), 127.76, 129.80, 133.08, 133.18, 135.55 (arom C); MS LSIMS (m/z) 407 (M^++Na), 385 (M^++H), 367 (M^+-OH), 327 (M^+-C_4H_9). HRMS. Calcd for $C_{23}H_{32}O_3SiNa$ (M^++Na): 407.2018, found: 407.2020; calcd for $C_{19}H_{23}O_3Si$ (M^+-C_4H_9): 327.1397, found: 327.1397; calcd for $C_{19}H_{21}O_2Si$ (M^+-$C_4H_{11}O$): 309.1296, found: 309.1296.

(2R,4S)-6-O-(t-Butyldiphenylsilyl)-3-O-(trimethylsilyl)-1,2-epoxy-2-methylhexane-4,6-diol (5b).
To a stirred solution of carbinol **5a** (124 mg, 0.3 mmol) in THF (5 mL) Et_3N (0.2 mL, 1.4 mmol) was added, followed by trimethylsilyl chloride (TMSCl, 39 mg, 0.3 mmol). After 16 h the mixture was diluted with hexane (10 mL) and washed successively with sat. aq. $NaHCO_3$, water and brine. The solvent was evaporated. The residue (137 mg) was chromatographed on SiO_2 (3 g, 1% ether in hexane) to give **5b** (118 mg, 80%): IR 1112 and 840 cm^{-1}; ^1H NMR 0.12 (s, 9, $SiCH_3$), 1.06 (s, 9, tBu H), 1.34 (s, 3, CH_3), 1.50 (dd, 1, J = 13.9, 6.8 Hz, C_3 Ha), 1.67 (m, 2, C_5 H), 1.95 (ddd, 1, J = 13.9, 6.2, 1.0 Hz, C_3 Hb), 2.55 (dd, 1, J = 4.9, 1.05 Hz, C_1 Ha), 2.59 (br. d, 1, J = 4.9 Hz, C_1 Hb), 3.72 (m, 2, C_6 H), 4.09 (m, 1, C_4 H), 7.41 and 7.66 (2m, 3 and 2, arom. H); signals for the minor diastereomer could not be detected. ^{13}C NMR: 0.36 (CH_3-Si), 19.13 (tBu IVry C), 21.92 (CH_3), 26.85 (tBu Iry C), 40.22, 44.73 (C_3 and C_5), 53.77, 60.36 (C_1 and C_6), 55.38 (C_2), 67.01 (C_4), 127.62, 129.60, 133.80, 135.54 (arom. C); MS LSIMS (m/z) 479 (M^++Na), 457 (M^++H), 439 (M^+-OH), 424, 399 (M^+-C_4H_9), 309 (M^+-C_4H_9-$OSiMe_3$). HRMS. Calcd for $C_{22}H_{31}O_3Si_2$ (M^+-C_4H_9): 399.1812. Found: 399.1804. Calcd for $C_{19}H_{21}O_2Si$ (M^+-C_4H_9-$OSiMe_3$): 309.1311. Found: 309.1299.

(2ξ,4S,6S)-8-O-(t-Butyldiphenylsilyl)-4-methyl-2-phenylsulphonyl-1-(trimethylsilyl)octane-4,6,8-triol (6a).
To a solution of sulphone **2b** (605 mg, 2.5 mmol) in dimethoxyethane (DME, 4 mL), stirred at -78 °C, BuLi in hexane (1.6 M, 1.6 mL, 2.5 mmol) was added within 5 min, followed - after 30 min - with epoxide **5b** (216 mg, 0.47 mmol) in DME (3.5 mL). The mixture was allowed to warm to rt within 30 min, stirred for 3 h and then it was partitioned between sat. aq. NH_4Cl (2 mL) and toluene (10 mL). The organic layer was washed with water and brine, dried and evaporated. The residue (adduct, 850 mg) was dissolved in methanol (8.5 mL) containing PPTS (2 mg). After 30 min the solvent was evaporated and the residue (805 mg) was chromatographed on SiO_2 (10 g, toluene, then 10% EtOAc in toluene) to give:

1. unreacted sulphone **2b** (500 mg)
2. unreacted epoxide **5b** (48 mg)
3. **6a** (193 mg, 66% from **5b**): IR 3455, 1112 cm^{-1}; ^1H NMR 0.03 (s, 9, $SiCH_3$), 0.79 (dd, 1, J = 14.5, 10.9 Hz, C_1 Ha), 1.05 (s, 9, tBu H), 1.26 (m, 1, C_5 Ha), 1.35 (s, 3, CH_3) overlapping 1.41 (d, 1, J = 10.7 Hz, C_1 Hb), 1.48 - 1.88 (m, 4, C_3 Ha, C_5 Hb, C_7 Ha, C_7 Hb), 2.19 (dd, 1, J = 15.9, 6.6 Hz, C_3 Hb), 3.40 - 3.58 (m, 1, C_2 H), 3.74 - 3.96 (m, 2, C_8 H), 4.30 (m, 1, C_6 H); ^{13}C NMR: -0.81 ($SiCH_3$), -0.01 (C_1), 19.07 (tBu, IVry C), 19.85 (CH_3), 26.81 (tBu Iry C), 39.41, 43.61, 47.22 (C_3, C_5, C_7), 58.82 (C_2), 62.64 (C_8), 68.43 (C_6), 71.67 (C_4), 127.53, 127.64, 127.76, 129.02, 129.22, 129.48, 129.79, 133.06, 133.19, 133.63, 135.52, 136.65 (arom C); MS LSIMS (m/z) 649 (M^++Na), 627 (M^++H), 591, 569 (M^+-C_4H_9), 551, 535, 531, 513, 507, 473, 449, 412, 409, 393, 389, 313, 297, 287, 269, 255, 239, 235, 215, 199, 193, 179, 157, 135, 125. HRMS. Calcd for $C_{34}H_{51}O_5SSi_2$ (M^++H): 627.2996. Found: 627.2977.

(2ξ,4S,6S)-8-O-(t-Butyldiphenylsilyl)-(4,6-O-isopropylidene)-4-methyl-2-phenylsulphonyl-1-(trimethylsilyl)octane-4,6,8-triol (7a).

To a solution of diol **6a** (295 mg, 0.47 mmol) in CH_2Cl_2 (10 mL), stirred at 0 °C, 2-methoxypropen (105 μL, 1.1 mmol) was added, followed by p-TSA (2 mg). The mixture was set aside at rt for 16 h whereupon powdered $NaHCO_3$ (100 mg) was added. After 20 min the solid material was filtered off and the solvent was evaporated. The residue (315 mg) was chromatographed on SiO_2 (8 g, 1% EtOAc in toluene) to give:

1. **7a** (276 mg, 85%): ^{1}H NMR (δ) 0.12 (s, 9, $SiCH_3$), 1.03 (s, 9, tBu), 1.24 and 1.29 (2s, 3 and 3, acetonide CH_3), 1.40 (s, 3, CH_3) overlapping 0.82 - 1.74 (m, 7, C_1 Ha, C_1 Hb, C_3 Ha, C_5 Ha, C_5 Hb, C_7 Ha, C_7 Hb), 1.95 (dd, 1, J = 15.1, 2.9 Hz, C_3 Hb), 3.43 (m, 1, C_2 H), 3.63 (m, 1, C_8 Ha), 3.78 (m, 1, C_8 Hb), 4.20 (m, 1, C_6 H), 7.15 - 7.90 (m, 15, arom. H); ^{13}C NMR 0.01 ($SiCH_3$), 19.19 (C_1), 19.40 (tBu IVry C), 24.79 (CH_3), 26.80 (tBu Iry C), 28.17 (CH_3), 32.00 (CH_3), 37.73, 39.00, 45.57 (C_7, C_5, C_3), 58.15, 61.85 (C_6 and C_2), 59.43 (C_8), 72.58 (C_4), 98.48 (acetonide, IVry C); MS LSIMS (m/z) 689 (M^++Na), 679, 667, 651, 609 (M^+-C_4H_9). HRMS. Calcd for $C_{37}H_{54}O_5Si_2SNa$ (M^++Na): 689.3127. Found: 689.3128.

2. unreacted diol **6a** (29 mg).

(3S,5R)-(3,5-O-Isopropylidene)-5-methyl-1,3,5-trihydroxyoct-7-ene (8a).

A solution of sulphone **7a** (200 mg, 0.31 mmol) and TBAF·3H_2O (260 mg, 0.83 mmol) in acetonitrile (10 mL) was heated under refluxed for 3 h. After cooling, toluene (10 mL) was added and the bulk of solvent was evaporated. The residue was chromatographed on SiO_2 (4 g, 10% EtOAc in toluene) to give **8a** (60 mg, 94% yield): $[\alpha]_D^{23}$= -46.9 (c 2.3); ^{1}H NMR 1.30 (dd, 1, J = 12.8, 2.4 Hz, C_4 Ha), 1.32 (s, 3, CH_3), 1.37 (d, 3, J = 0.6 Hz, acetonide CH_3a), 1.49 (d, 3, J = 0.6 Hz, acetonide CH_3b), 1.59 (d, 1, J = 12.8 Hz, C_4 Hb), 1.67 (m, 2, C_2 H), 2.22 (m, 2, C_6 H), 2.56 (t, 1, J = 5.5 Hz, OH), 3.81 (q, 2, J = 5.5 Hz, C_1 H) 4.21 (m, 1, C_3 H), 5.04 (dm, 1, J = 10.6 Hz, C_8 Ha), 5.11 (m, 1, C_8 Hb), 5.95 - 5.73 (m, 1, C_7 H); ^{13}C NMR 25.01 (CH_3), 26.26 (CH_3), 31.76 (CH_3), 38.10, 38.95, 49.86 (C_2, C_4 and C_6), 61.02 (C_1), 65.81 (C_3), 72.56 (acetonide IVry C), 98.45 (C_5), 117.83 (C_8), 133.96 (C_7); MS EI (m/z) 199 (M^+-CH_3), 173 (M^+-C_3H_5), 139, 121. HRMS. Calcd for $C_{11}H_{19}O_3$ (M^+-CH_3): 199.1334. Found: 199.1334.

(3R)-1-O-(t-Butyldiphenylsilyl)-3-O-(trimethylsilyl)-1,3-dihydroxyhex-5-ene (3c).

To a solution of sulphone **2b** (484 mg, 2 mmol) in DME (3 mL), stirred at -78 °C, BuLi in hexane (1.6 M, 1.4 mL, 2.2 mmol) was added, followed - after 30 min - by epoxide **1** (652 mg, 2 mmol) in DME (2 mL). The mixture was allowed to warm to rt within ca. 2 h whereupon NaH (washed in hexane, 48 mg, 2 mmol) was added. The mixture was heated under reflux for 30 min, cooled and partitioned between aq. sat. NH_4Cl (1 mL) and hexane (20 mL). The organic layer was washed with water and brine, dried and evaporated. The

residue (855 mg) was filtered through SiO_2 (10 g) in hexane to give **3c** (510 mg, 80%): $[\alpha]_D^{23}$= -13.7 (c 1.9); IR 1640, 1105 cm^{-1}; ^1H NMR 0.05 (s, 9, $SiCH_3$), 1.02 (s, 9, tBu H), 1.65 (m, 2, C_2 H), 2.19 (m, 2, C_4 H), 3.69 (m, 2, C_1 H), 3.93 (m, 1, C_3 H), 4.97 (m, 1, C_6 Ha), 5.04 (m, 1, C_6 Hb), 5.65 - 5.88 (m, 1, C_5 H), 7.37 and 7.64 (2m, 6 and 4, arom. H); MS EI (m/z) 385 (M^+-C_3H_5) , 369 (M^+-C_4H_9), 341, 271, 211, 199, 193, 133, 91, 81, 57. HRMS. Calcd for $C_{22}H_{33}O_2Si_2$ (M^+-C_3H_5): 385.2019. Found: 385.2015. Calcd for $C_{21}H_{29}O_2Si_2$ (M^+-C_4H_9): 369.1706. Found: 369.1706.

(3R)-1-O-(t-Butyldiphenylsilyl)-1,3-dihydroxyhex-5-ene (3d).

A solution of **3c** (483 mg, 1.1 mmol) in methanol (5 mL) containing PPTS (2 mg) was stirred at rt for 15 min and then diluted with toluene (25 mL) and concentrated *in vacuo*. The remainder (ca. 20 mL) was washed with water and brine. The solvent was evaporated and the residue (402 mg) was chromatographed on SiO_2 (8 g, 2% ether in hexane) to give **3d** (373 mg, 93%): $[\alpha]_D^{20}$= +2.3 (c 1.4); IR 3660, 3500, 1640, 1110 cm^{-1}; ^1H NMR 1.05 (s, 9, tBu H), 1.71 (m, 2, C_2 H), 2.27 (br. t, 2, J = 7 Hz, C_4 H), 3.26 (br. d, 1, J = 2.4 Hz, OH), 3.86 (m, 2, C_1 H), 3.96 (m, 1, C_3 H), 5.07 (m, 1, C_6 Ha), 5.14 (dm, 1, J = 5 Hz, C_6 Hb), 5.84 (m, 1, C_5 H), 7.42 and 7.69 (2m, 6 and 4, arom. H); ^{13}C NMR 19.09 (tBu IVry C), 26.61 (tBu Iry C), 37.91, 42.01 (C_2 and C_4), 63.33 (C_1), 70.93 (C_3), 117.47 (C_6), 127.77 (C_5), 127.82, 129.70, 129.87, 134.85, 135.00, 135.23, 135.61 (arom. C); MS EI (m/z) 297 (M^+-C_4H_9), 281, 256, 241, 227, 214, 199, 181, 166, 151, 135, 121, 73. HRMS. Calcd for $C_{18}H_{21}O_2Si$ (M^+-C_4H_9): 297.1311. Found: 297.1311.

(3S,5S)-5-(Iodomethyl)-3-[2-(t-butyldiphenylsilyloxy)ethyl]-2,6-dioxacyclohexanone (4b).

To a solution of olefin **3d** (278 mg, 0.78 mmol) in THF (5 mL), BuLi in hexane (1.6 M, 0.6 mL, 0.9 mmol) was added at 0 °C. The mixture was stirred at rt for 0.5 h and then was cooled again to 0 °C and saturated with CO_2. After 1 h I_2 (406 mg, 1.6 mmol) in THF (1 mL) was added, the mixture was set aside at rt for 18 h whereupon it was diluted with toluene (30 mL) and was washed successively with sat. aq. $Na_2S_2O_3$, water and brine. The solvent was evaporated and the residue (334 mg) was chromatographed on SiO_2 (8 g, 0.5% EtOAc in toluene) to give:

1. unreacted **3d** (110 mg, 40%)

2. **4b** (247 mg, 60%): IR 1770, 1100 cm^{-1}; ^1H NMR 1.06 (s, 9, tBu H), 1.72 (m, 1, C_4 Ha), 1.85 (m, 2, C_2 H), 2.38 (dm, 1, J = 13.9 Hz, C_4 Ha), 3.26 (dd, 1, J = 10.5, 7.3 Hz, CHa-I), 3.38 (dd, 1, J = 10.5, 4.4 Hz, CHb-I), 3.84 (m, 2, C_1 H), 4.40 (m, 1, C_5 H), 4.67 (m, 1, C_3 H), 7.43 and 7.62 (2m, 6 and 4, arom. H), ^{13}C NMR 5.16 (C_6), 19.20 (tBu IVry C), 26.92 (tBu Iry C), 33.55 (C_2), 37.83 (C_4), 58.96 (C_1), 75.83, 77.28 (C_5 and C_3), 127.69, 127.82, 129.88, 135.50 (arom. C), 192.77 (C=O).

(2R,4S)-(6-O-tButyldiphenylsilyl)-1,2-epoxyhexa-4,6-diol (5c).

A solution of iodocarbonate **4b** (214 mg, 0.41 mmol) in methanol (3.6 mL) containing powdered anhyd. Na_2CO_3 (173 mg, 1.25 mmol) was stirred at rt for 6.5 h whereupon it was diluted with ether (20 mL) and washed successively with sat. aq. $Na_2S_2O_3$, water and brine. The solvent was evaporated and the residue (152 mg) was chromatographed on SiO_2 (4 g, 1% EtOAc in toluene) to give **5c** (136 mg, 90%): IR 3520, 1120, 1085 cm^{-1}; ^1H NMR 1.06 (s, 9, tBu H), 1. 76 (m, 4, C_3 H, C_5 H), 2.52 (dd, 1, J = 5.0, 2.7 Hz, C_1 Ha), 2.80 (dd, 1, J= 4.9, 4.0 Hz, C_1 Hb), 3.12 (m, 1, C_2 H), 3.50 (br. d, 1, J = 2.2 Hz, OH), 3.88 (m, 2, C_6 H), 4.14 (m, 1, C_4 H), 7.41 and 7.68 (2m, 6 and 4, arom. H); ^{13}C NMR: 19.05 (tBu IVry C), 26.84 (tBu Iry C), 38.40, 39.93 (C_3 and C_5), 46.60 (C_6). 49.87 (C_2), 63.20 (C_1), 69.75 (C_4), 127,69, 127.80, 129.85, 135.55 (arom. C); MS LSIMS (m/z) 393 (M^++Na), 371 (M^++H), 313 (M^+-C_4H_9), 255, 235, 215, 199, 179, 167, 117. HRMS. Calcd for $C_{18}H_{21}O_3Si$ (M^+-C_4H_9): 313.1260. Found: 313.1264.

(2R,4S)-(6-O-tButyldiphenylsilyl)-(4-O-trimethylsilyl)-1,2-epoxyhexa-4,6-diol (5d).

To a solution of epoxide **5c** (124 mg, 0.33 mmol) in THF (5 mL), containing Et_3N (250 μL, 2.5 mmol), TMSCl (100 μL, 0.66 mM) was added. The mixture was stirred for 48 h whereupon it was diluted with hexane and washed with sat. aq. $NaHCO_3$. The solvent was evaporated and the residue (135 mg) was quickly filtered through SiO_2 (1 g, 1% EtOAc in hexane containing 0.5% Et_3N) to give **5d** (130 mg, 88%): IR 1250, 1100, 830 cm-1; ^1H NMR 0.11 (s, 9, $SiCH_3$), 1.05 (s, 9, tBu H), 1.70 (m, 4, C_3H and C_5H), 2.42 (dd, 1, J = 5.0, 2.7 Hz, C_1 Ha), 2.74 (dd, 1, J = 5.0, 4.0 Hz, C_1 Hb), 2.99 (m, 1, C_2 H), 3.73 (m, 2, C_6 H), 4.13 (q, 1, J = 6.0 Hz, C_4 H), 7.41 and 7.64 (2m, 6 and 4, arom. H); for the minor epimer (2R, 4S) the following signals were recorded: 0.11 (s, Si-CH_3), 1.07 (s, tBu H), 2.47 (dd, J = 5.2, 2.8 Hz, C_1 Ha), 2.78 (dd, J = 5.0, 4.0 Hz, C_1 Hb); integration of the C_1 proton signals indicated a 12:1 ratio of the diastereomers; MS LSIMS (m/z) 465 (M^+ + Na), 443 (M^+ + H), 385 (M^+ - C_4H_9), 365, 271, 251, 239, 227, 209, 197, 183, 165, 135, 129, 117, 91.

(2ξ,4S,6S)-8-O-(tButyldiphenylsilyl)-2-phenylsulphonyl-1-(trimethylsilyl)hexane-4,6,8-triol (6b).

To a solution of sulphone **2b** (411 mg, 1.7 mmol) in DME (3 mL), stirred at - 78 °C, BuLi in hexane (1.6 M, 1.1 mL, 1.7 mmol) was added, followed - after 30 min - by epoxide **5d** (76 mg, 0.17 mmol) in DME (2 mL). The mixture was allowed to warm to -20 °C within 1.5 h, stirring at -20 °C was continued for 2 h whereupon NaH (washed with hexane, 39 mg, 1.7 mmol) was added. The mixture was heated under reflux for 1.5 h and then was cooled and partitioned between sat. aq. NH_4Cl (2 mL) and toluene (20 mL). The organic layer was washed with water and brine. The solvent was evaporated and the residue (427 mg) was chromatographed on SiO_2 (10 g, 5% EtOAc in hexane) to give:

1. a mixture of epimers **6b** (23 mg)

2. pure more polar epimer **6b** (66 mg): IR 3500, 1100 cm^1; ^1H NMR 0.04 (s, 9, $SiCH_3$), 1.04 (s, 9, tBu H), 0.72 - 2.08 (m, 8, C_7, C_5, C_3, C_1 H), 3.36 (m, 1, C_2 H), 3.86 (t, 2, J = 4.8 Hz, C_8 H), 4.10 (m, 2, C_4 H, C_6 H), 7.40 ,7.60 and 7.90 (3m, 6, 7 and 2, arom. H); for the minor epimer (2R, 4S) the following signals were recorded: 0.03 (s, $SiCH_3$), 1.04 (s, tBu H); ^{13}C NMR: -0.89 (CH_3Si), 16.27 (C_8), 19.01 (tBu IVry C), 26.80 (tBu Iry C) 38.69, 38.69 and 43.62 (C_2, C_4, C_6), 59.45 (C_7), 63. 22 (C_1), 68.99, 72.58 (C_3 and C_5), 127.69, 127.85, 129.05, 129.20, 129.94, 132.86, 132.75, 133.54, 135.53, 137.25 (arom C); MS LSIMS (m/z) 635 (M^++Na), 613 (M^++H), 577 (M^+-35), 555 (M^+-C_4H_9). HRMS. Calcd for $C_{33}H_{48}O_5SSi_2Na$ (M^++Na): 635.2659. Found: 635.2651.

(2ξ,4S,6S)-8-O-(tButyldiphenylsilyl)-4,6-O-isopropylidene-2-(phenylsulphonyl)-1-(trimethylsilyl)hexane-4,6,8-triol (7b).

A solution of diol **6b** (40 mg, 0.06 mmol) in acetone (1 mL) containing p-TSA (2 mg) and anhyd. $CuSO_4$ (10 mg) was stirred at rt for 2.5 h and then was diluted with hexane (5 ml) and concentrated *in vacuo*. The remainder was chromatographed on SiO_2 (1 g, 2% EtOAc in hexane) to give **7b** (35 mg, 82%). IR: 1300, 1240, 1140, 840 cm^{-1}; ^1H NMR 0.80 - 1.93 (m, 8, C_1, C_3, C_5, C_7 H), 1.03 (s, 9, tBu H), 1.25 and 1.37 (2s, 6, acetonide CH_3), 3.23 (m, 1, C_2 H), 3.49 - 3.84 (m, 2, C_4, C_6 H), 4.20 (m, 2, C_8 H), 7.39, 7.61 and 7.86(3m, 6, 7 and 2 arom. H); ^{13}C NMR: 0.66 ($SiCH_3$), 15.41 (C_1), 19.24 (tBu IVry C), 19.92 (acetonide $\underline{C}H_3$), 26.90 (tBu Iry C), 30.16 (acetonide $\underline{C}H_3$), 37.16, 37.46, 39.28 (C_3, C_5 and C_7), 58.51 (C_2), 59.67 (C_8), 65.53, 65.81 (C_4, C_6), 98.54 (acetonide IVry C), 127.62, 127.73, 129.01, 129.08, 129.59, 133.41, 133.97, 135.57, 137.80 (arom. C); MS LSIMS (m/z) 675 (M^++Na), 653 (M^++H), 637 (M^+-CH_3), 595 (M^+-C_4H_9). HRMS calcd for $C_{36}H_{52}O_5SSi_2Na$ (M^++Na): 675.2972. Found: 675.2970.

(3S,5R)-3,5-O-Isopropylidene-1,3,5-trihydroxyoct-7-ene (8b).

A solution of sulphone **7b** (40 mg, 0.06 mmol) in acetonitrile (4 mL) containing TBAF·$3H_2O$ (50 mg, 0.16 mnmol) was heated under reflux for 4 h whereupon the solvent was evaporated *in vacuo*. The residue was chromatographed on SiO_2 (2 g, 10% EtOAc in benzene) to give **8b** (10 mg, 83%): $[\alpha]_D^{16}$= -2.2 (c 0.7); ^1H NMR 1.40 and 1.47 (2s, 6, acetonide CH_3), overlapping 1.18 - 1.51 (m, 2, C_2 H), 1.61 - 1.80 (m, 2, C_4 H), 2.24 (m, 2, C_6 H), 2.58 (m, 1, OH), 3.77 (m, 2, C_1 H), 3.91 (ddt, 1, J = 11.3, 6.4, 2.7 Hz, C_3 H), 4.10 (m, 1, C_5 H), 5.04 (m, 1, C_8 Ha), 5.11 (dm, 1, J = 9 Hz, C_8 Hb), 5.69 - 5.91 (m, 1, C_7 H); ^{13}C NMR: 19.82 and 30.20 (acetonide CH_3), 36.18, 38.11 and 40.73 (C_2, C_4 and C_6), 60.91 (C_1), 68.56 and 69.35 (C_3 and C_5), 98.67 (acetonide IVry C), 117.18 (C_8), 134.02 (C_7); MS EI (m/z) 185 (M^+-CH_3), 159 (M^+-C_3H_5). HRMS. Calcd for $C_{10}H_{17}O_3$ (M^+-CH_3): 185.1178. Found: 185.1177.

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