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Difunctionalised oxirane systems. Stereodivergent synthesis of 1,4;2,3-dianhydro-5-*O*-benzyl-L-lyxitol and -L-ribitol

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Abstract: A simple, efficient, stereoselective synthesis of the diastereoisomeric cis/trans pair of difunctionalized 1,2-epoxides, 1,4;2,3-dianhydro-5-*O*-benzyl-L-lixitol **1** and 1,4;2,3-dianhydro-5-*O*-benzyl-L-ribitol **2** is described. Starting from D-(+)-xylose, the synthetic approach to **1** and **2** proceeds through the common intermediate, diol **6**, and an appropriate sequence of selective functionalizations. © 1997 Elsevier Science Ltd

The easy accessibility of functionalized and non-functionalized chiral 1,2-epoxides by means of outstandingly effective procedures[1] has extended the use of 1,2-epoxides in organic synthesis, in view of their ability to react with a large variety of nucleophiles.[2] However, for an effective utilization of these versatile synthetic intermediates, the regio- and stereochemical control of the nucleophilic opening of the oxirane ring has to be adequately addressed, thus becoming one of the most qualifying points in the chemistry of 1,2-epoxides.[3] In a program aimed at verifying whether the presence of one or two *O*-heterofunctionalities contemporarily present close to the oxirane ring was able to direct the regioselectivity of the ring opening by means of chelating processes, we needed to obtain the two diastereoisomeric 1,2-epoxides, cis **1** and trans **2**.[4] Epoxides **1** and **2** appeared to be particularly interesting due to the presence of both an endocyclic (tetrahydrofuran oxygen) and an exocyclic (OBn oxygen) *O*-heterofunctionality in an allylic and homoallylic relationship to the oxirane ring, respectively.[5] Previous studies on the synthesis of oxirane systems related to epoxides **1** and **2** were concerned with the preparation of the epoxy alcohols corresponding to L-**1**[6a] and D-**2**[6b] and the corresponding *O*-monomethoxytrityl,[6c] *O*-tosyl and *O*-mesyl derivatives[6a,d] by synthetic procedures different from the one now utilized. Moreover, a simple stereoselective approach to the synthesis of these oxirane systems appeared to be lacking. Here we describe the stereoselective synthesis of enantiomerically pure epoxides L-**1** and L-**2**, starting from commercially available D-(+)-xylose **3**.

The reaction of **3** with isobutylmercaptane afforded the dithioacetal **4**, which, on treatment with TsCl/pyridine, directly afforded the cyclic dithioacetal **6**, reasonably by cyclization in the basic medium of the monotosylate **5**, the primary reaction product (Scheme 1).[7] Diol **6** is the crucial compound in the synthetic pathway to both epoxides **1** and **2**, as it is possible at this point to differentiate the two independent processes (Schemes 2 and 4). On the route to the cis epoxide **1** (Scheme 2), treatment of **6** with *t*-butyldimethylsilyl chloride (TBDMS-Cl, 2 equiv.) in the presence of imidazole afforded the di-*O*-TBDMS protected compound **7**, which was subjected to the known $HgCl_2$/HgO in MeCN protocol[8] in order to obtain the free aldehyde **8**. Subsequent $BH_3 \cdot Me_2S$ reduction of **8** gave the primary alcohol **9**[9] which was transformed into the benzyl ether **10** by means of the BnBr/NaH alkylating mixture. In these conditions, also some amounts (5–10%, ^{1}H NMR) of the regioisomeric ether **11** (Schemes 2 and 3, see below) were formed. Several attempts and reagents were tried in order to deprotect selectively ether **10** to alcohol **12**. The best result was obtained by means of the NBS/DMSO/H_2O protocol at r.t.[10a] which led to an almost 1:1 mixture of alcohol **12** and unreacted starting ether **10** with only a very small amount of a more polar product (diol **16**, TLC).[11] In these conditions, regioisomeric alcohol **13** was not formed or formed at an extent less than 3% (^{1}H NMR). Other deprotection

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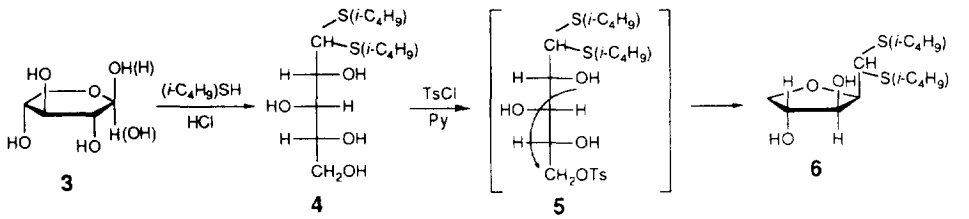
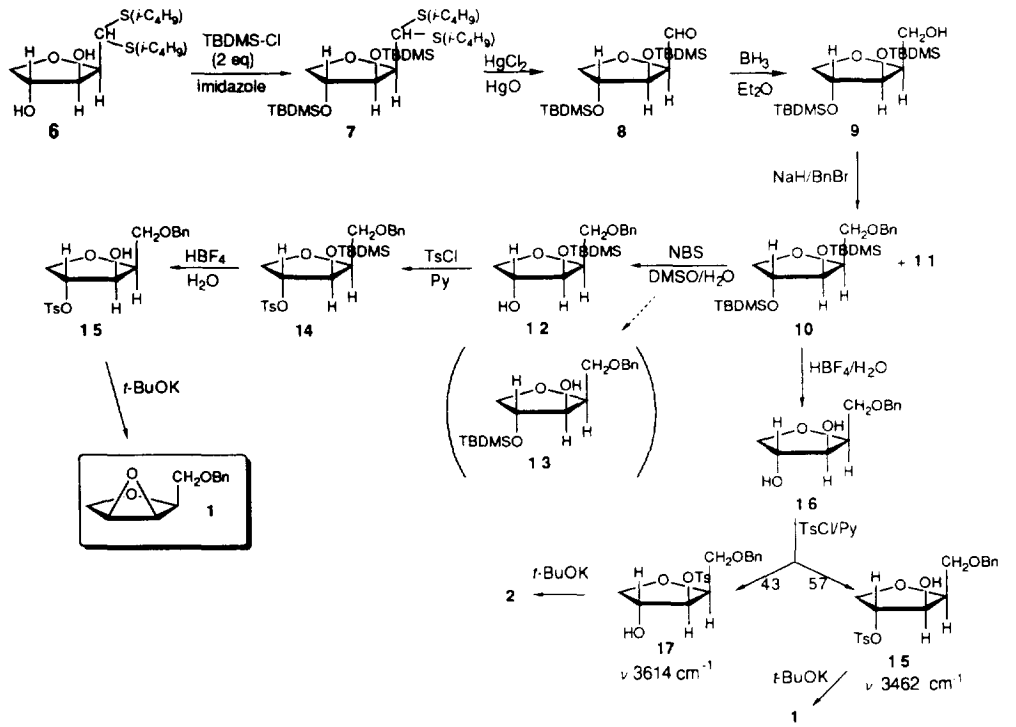
procedures (AcOH–H_2O–THF, HF, HF–Py, TsOH, H_2SiF_6, TBAF/THF)[10b,c] tried on **10** turned out to be unsatisfactory due to a non-selective monodeprotection (formation of a substantial amounts of both **12** and **13**)[12] and/or extensive deprotection (formation of consistent amount of diol **16**). Alcohol **12** and unreacted ether **10** were easily separated by flash chromatography. While ether **10** can be profitably recycled, alcohol **12** was treated with TsCl/pyridine to yield the tosylate **14** which was deprotected by means of 40% aqueous HBF_4 at r.t. in MeCN to give the hydroxy tosylate **15**. Base-catalyzed cyclization of **15** with *t*-BuOK in benzene afforded pure cis epoxide **1**.

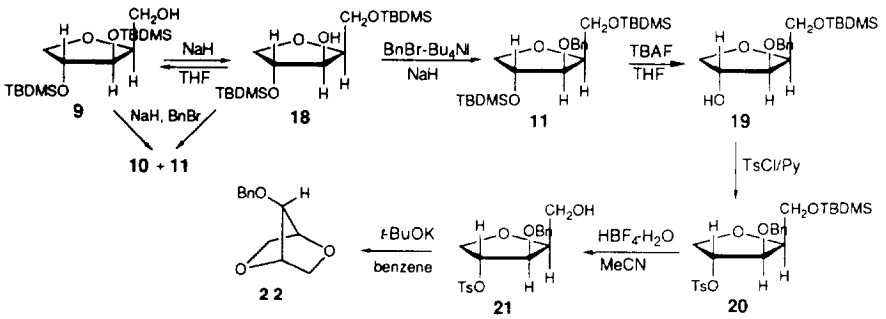


Scheme 1.



Scheme 2.

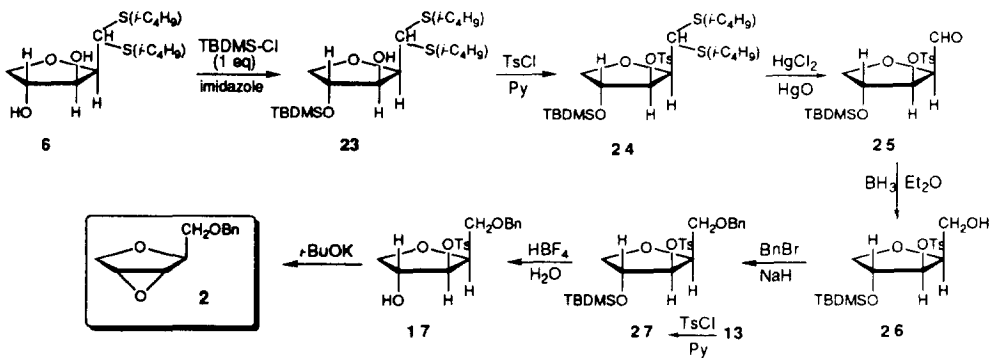
The formation of some amounts of ether **11** in the benzylation reaction of alcohol **9** by the NaH/BnBr protocol (see above) prompted us to examine more closely the process involved in its formation. When alcohol **9** was put in contact with NaH in THF for 18 h at r.t., a 4:6 equilibrating mixture of starting alcohol **9** and regioisomeric alcohol **18** was obtained (Scheme 3), from which pure alcohol **18** was separated by flash chromatography. While the benzylation of **18** by means of the NaH/BnBr protocol afforded an unseparable mixture (75:25) of ethers **10** and **11**, the benzylation of **18** by the Bu_4NI/BnBr/NaH procedure[13] at r.t. afforded only ether **11**. All this reasonably indicated that the formation of ethers **10** and **11** from both alcohols **9** and **18** (Schemes 2 and 3) primarily derives from



Scheme 3

a 1,5-migration of the silyl group between the two cis O-functionalities of the starting alcohols **9** and **18** under the strongly alkaline reaction conditions (NaH/BnBr protocol).[14] Only when, in the case of **18**, less drastic alkylating reaction conditions (Bu_4NI/BnBr/NaH) were used[13] was the migration process prevented. Besides being interesting from a speculative point of view, the obtainment of ether **11** turned out to be also synthetically useful as it provided a simple route to an interesting dioxabicyclo compound. Monodeprotection of ether **11** with TBAF in THF at −10°C afforded alcohol **19** which was transformed into tosylate **20**. Deprotection of **20** with aqueous HBF_4 in MeCN afforded the hydroxy tosylate **21** which was cyclized under basic conditions to the dioxabicyclo compound **22**. Compound **22** is one of the few examples of this class of bicyclo compounds so far described.[15]

The synthesis of the trans epoxide **2** starts from the common intermediate, diol **6** (Scheme 4). Due to the consistently different steric crowding around the two secondary hydroxyl functionalities, treatment of **6** with TBDMS-Cl (1 equiv.) exclusively afforded alcohol **23**, which was transformed into the corresponding tosylate **24**. Deprotection of the carbonyl functionality of **24** with $HgCl_2$/HgO afforded the aldehyde **25** which was reduced to the primary alcohol **26** by $BH_3 \cdot Me_2S$. Benzylation of **26** by the BnBr/NaH alkylating protocol afforded the benzyl ether **27**, which was deprotected to the hydroxy tosylate **17** by treatment with aqueous HBF_4 in MeCN. Base-catalyzed cyclization of **17** with *t*-BuOK yielded the desired trans epoxide **2** (Scheme 4).



Scheme 4

The relative structure and configuration of the two hydroxy tosylates **15** and **17** (Scheme 2) are unequivocally demonstrated on the basis of their method of preparation and confirmed by their ^1H NMR spectra, with appropriate double resonance experiments, and also by examination of their IR spectra in dilute CCl_4 solution (OH stretching band): while hydroxy tosylate **17** showed the presence of only one band at 3614 cm^{-1} attributable to a free OH group, the regioisomer **15** showed only the presence of a characteristic OH···O interaction (3462 cm^{-1}) which is possible only when a

1,3-cis relationship is present in a five-membered substituted ring between the interacting groups,[3a] such as the hydroxyl and benzyloxy groups in **15**, thus confirming the structure given for **15** and **17**. Moreover, hydroxy tosylates **15** and **17** can be obtained as a 57:43 mixture by reaction of the diol **16** with TsCl/pyridine (1 equiv.), thus confirming their regioisomeric structure. The structures of hydroxy tosylates **15** and **17** unequivocally define the structures of the epoxides cis **1** and trans **2**, simply formed by their respective base-catalyzed cyclization.

Experimental

Melting points were determined on a Kofler apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were determined with a Bruker AC-200 spectrometer on $CDCl_3$ solutions using tetramethylsilane as the internal standard. Routine IR spectra were taken on paraffin oil mulls while spectra required for the determination of OH stretching bands (compounds **15** and **17**) were taken in dried CCl_4 with a Mattson 3000 FTIR spectrophotometer: the concentration of the solution was 5×10^{-3} M, or lower. Optical rotations were measured with a Perkin–Elmer 241 digital polarimeter with a 1 dm cell. MS spectra of compounds **1** and **2** were recorded on a Hewlett–Packard 5988A spectrometer. All reactions were followed by TLC on Alugram SIL G/UV_{254} silica gel sheets (Macherey–Nagel) with detection by UV or with 0.5% phosphomolybdic acid solution in 95% EtOH. Silica gel 60 (Macherey–Nagel 230–400 mesh) was used for flash chromatography.

Diisobutyl D-*xylose-dithioacetal* ***4***

Following a previously described procedure,[7] isobutyl mercaptane (30 ml, 25.0 g, 0.278 mol) was added dropwise to D-(+)-xylose (**3**) (20.0 g, 0.133 mol) at 0°C under stirring. 36% Aqueous HCl (26.0 ml) was added at the same temperature in one portion, and the resulting rection mixture was vigorously stirred for 30 min at r.t. Dilution with CH_2Cl_2 (200 ml) and evaporation of the washed (saturated aqueous $NaHCO_3$ and water) organic solution afforded a liquid crude reaction product (40.0 g) consisting of practically pure **4** which was utilized in the next step without any further purification. An analytical sample (0.20 g) was filtered by flash chromatography eluting with a 9:0.5:0.5 mixture of AcOEt, hexane, and MeOH to give pure **4** (0.18 g), as a liquid: $[\alpha]_D^{20}$=+71.7 (*c* 1.63, $CHCl_3$) [lit.[16] $[\alpha]_D^{20}$=+14.7 (*c* 3.34, MeOH)]; ^1H NMR δ 4.28–4.44 (m, 1H), 3.76–4.02 (m, 6H), 3.49–3.70 (m, 3H), 2.37–2.62 (m, 4H), 1.68–1.87 (m, 2H), 0.94 (d, 12H, *J*=6.4 Hz). ^{13}C NMR δ 74.36, 74.21, 71.21, 64.68, 56.90, 40.87, 39.27, 29.02, 22.84, 22.72. Anal. Calcd for $C_{13}H_{28}O_4S_2$: C, 49.97; H, 9.03 Found: C, 49.67; H, 8.81.

*Diisobutyl 2,5-anhydro-*D-*xylofuranose dithioacetal* ***6***

A solution of TsCl (27.3 g, 0.144 mol) in anhydrous pyridine (150 ml) was added dropwise at −15°C to a stirred solution of **4** (40.0 g, 0.132 mol) in anhydrous pyridine (200 ml), and the resulting reaction mixture was stirred at the same temperature for 1.5 h, then for two days at r.t. Dilution with $CHCl_3$ and ice-cold water, and evaporation at a temperature not higher than 35°C of the washed (saturated aqueous $NaHCO_3$, and water) organic solvent afforded a crude semisolid residue (38.2 g) which was recrystallized from hexane–$CHCl_3$ to give pure **6** (33.0 g, 85% yield), as a solid, m.p. 93–94°C: $[\alpha]_D^{20}$=+6.22 (*c* 0.74, $CHCl_3$) [lit.[17] m.p. 94°C $[\alpha]_D^{21}$=+11.5 (*c* 0.62, $CHCl_3$)]; ^1H NMR δ 4.09–4.28 (m, 3H), 3.11 (dd, 1H, *J*=9.1 and 3.1 Hz), 3.87–3.92 (m, 1H), 3.65 (dd, 1H, *J*=9.8 and 1.0 Hz), 3.16 (d, 1H, *J*=4.6 Hz), 3.10 (d, 1H, *J*=3.6 Hz), 2.43–2.68 (m, 4H), 1.67–1.84 (m, 2H), 0.93 (d, 12H *J*=6.7 Hz). ^{13}C NMR δ 83.07, 78.42, 77.70, 74.31, 52.11, 39.87, 39.37, 28.98, 28.90, 22.78, 22.64. Anal. Calcd for $C_{13}H_{26}O_3S_2$: C, 53.02; H, 8.90. Found: C, 53.32; H, 8.44.

*Diisobutyl 2,5-anhydro-3,4-di-(*O-t-*butyldimethylsilyl)-*D-*xylofuranose dithioacetal* ***7***

A solution of **6** (6.0 g, 20.4 mmol) in anhydrous DMF (40.0 ml) containing imidazole (6.66 g, 98.0 mmol) was treated at 0°C under stirring with *t*-butyldimethylsilyl chloride (TBDMS-Cl) (7.95 g, 53.0 mmol) and the reaction mixture was stirred for 30 min at the same temperature, and then for 3 days at r.t. Dilution with petroleum ether and evaporation of the washed (saturated aqueous $NaHCO_3$ and

brine) afforded a crude oily product (10.5 g) which was filtered through a short silica gel column. Elution with a 9:1 mixture of hexane and AcOEt afforded pure **7** (10.1 g, 95% yield), as a liquid: $[\alpha]_D^{20}=-32.07$ (*c* 3.48, $CHCl_3$); ^1H NMR δ 4.03–4.14 (m, 3H), 3.98–3.99 (m, 2H), 3.66 (d, 1H, *J*=8.8 Hz), 2.42–2.67 (m, 4H), 1.66–1.93 (m, 2H), 0.98 (d, 6H, *J*=3.8 Hz), 0.95 (d, 6H, *J*=4.0 Hz), 0.85 (s, 9H), 0.84 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H). ^{13}C NMR δ 83.19, 78.60, 78.34, 75.60, 51.89, 40.19, 38.16, 29.73, 26.38, 23.17, 23.09, 22.97, 18.81, 18.64, 18.55, −2.26, −3.45, −4.05. Anal. Calcd for $C_{25}H_{54}O_3S_2Si_2$: C, 57.41; H, 10.41. Found: C, 57.66; H, 10.59.

*2,5-Anhydro-3,4-di-(*O-t-*butyldimethylsilyl)-*D-*xylofuranose* ***8***

Following a previously described procedure,[8] a solution of **7** (10.7 g, 20.5 mmol) in MeCN (200 ml) was added dropwise at r.t to a stirred suspension of $HgCl_2$ (12.3 g, 45.3 mmol) and HgO (4.9 g, 22.6 mmol) in a 4:1 MeCN:H_2O mixture (200 ml). The reaction mixture was stirred for 1 h at the same temperature, then filtered on Celite, washing the residue with a 1:1 mixture of hexane and CH_2Cl_2 (300 ml). Evaporation of the washed (5 M aqueous $MeCOONH_4$, saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude reaction product (6.64 g, 90% yield) consisting of aldehyde **8** practically pure which was rapidly utilized in the next step without any further purification. An analytical sample (0.15 g) was purified by flash chromatography: elution with a 8:2:0.5 mixture of hexane, AcOEt and NEt_3 afforded pure **8** (0.110 g), as a liquid: $[\alpha]_D^{20}=+53.03$ (*c* 1.41, $CHCl_3$); ^1H NMR δ 9.62 (d, 1H, *J*=1.6 Hz), 4.28–4.33 (m, 2H), 4.22 (dd, 1H, *J*=8.9 and 2.9 Hz), 4.06 (d, 1H, *J*=3.0 Hz), 3.82 (d, 1H, *J*=8.9 Hz), 0.85 (s, 9H), 0.80 (s, 9H), 0.06 (s, 3H), 0.05 (s, 6H), 0.04 (s, 3H). ^{13}C NMR δ 203.81, 86.31, 81.05, 78.62, 76.18, 26.31, 26.18, 18.48, −4.03, −4.60. Anal. Calcd for $C_{17}H_{36}O_4Si_2$: C, 56.61; H, 10.06. Found: C, 56.26; H, 10.37.

*1,4-Anhydro-2,3-di-(*O-t-*butyldimethylsilyl)-*L-*xylitol* ***9***

10 M $BH_3 \cdot Me_2S$ (5.3 ml) was added dropwise at 0°C to a stirred solution of aldehyde **8** (7.30 g, 20.4 mmol) in anhydrous ether (400 ml) and stirring was prolonged for 2 h at r.t. After cooling to 0°C, MeOH (35 ml) was added and the reaction mixture was stirred at r.t. overnight. Evaporation of the solvent afforded an oily reaction product (6.6 g, 93% yield) consisting of practically pure alcohol **9** which was utilized in the next step without any further purification. An analytical sample (0.10 g) was purified by preparative TLC (an 8:2 mixture of hexane and AcOEt was used as the eluant): extraction of the most intense band afforded pure alcohol **9** (0.075 g), as a liquid: $[\alpha]_D^{20}=-9.8$ (*c* 1.10, $CHCl_3$); ^1H NMR δ 3.95–4.09 (m, 4H), 3.68–3.83 (m, 2H), 3.56–3.63 (m 1H), 0.85 (s, 9H), 0.83 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H). ^{13}C NMR δ 81.10, 79.78, 79.16, 74.16, 62.90, 26.34, 18.53, −3.97, −4.43. Anal. Calcd for $C_{17}H_{38}O_4Si_2$: C, 56.30; H, 10.56. Found: C, 56.65; H, 10.72.

*1,4-Anhydro-2,3-di-(*O-t-*butyldimethylsilyl)-5-*O-*benzyl-*L-*xylitol* ***10***

A solution of alcohol **9** (6.60 g, 18.2 mmol) in anhydrous THF (20 ml) was added to a stirred suspension of NaH (2.18 g of a 60% dispersion in mineral oil, 54.4 mmol) in anhydrous THF (50 ml) containing benzyl bromide (2.15 ml, 18.2 mmol) and the resulting reaction mixture was stirred at 50°C for 18 h. After cooling, ether (120 ml) and water (10 ml) were carefully added in order to destroy the excess of hydride. Evaporation of the washed (brine) organic solution afforded a crude liquid product (7.9 g) mostly consisting of benzyl ether **10** which was filtered through a short silica gel column. Elution with a 9:1 mixture of petroleum ether and ether afforded pure **10** (7.31 g, 89% yield), as a liquid: $[\alpha]_D^{20}=+3.94$ (*c* 1.14, $CHCl_3$); ^1H NMR δ 7.26–7.38 (m, 5H), 4.58 and 4.52 (ABdd, 2H, *J*=10.9 Hz), 4.18–4.23 (m, 1H), 4.04–4.10 (m, 2H), 3.98 (dd, 1H, *J*=3.0 and 1.0 Hz), 3.61–3.68 (m, 3H), 0.88 (s, 18H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H). ^{13}C NMR δ 138.87, 128.97, 128.60, 128.22, 80.30, 78.91, 78.64, 74.67, 74.23, 69.72, 26.64, 26.37, 18.65, 18.56, −3.91, −4.01, −4.46. Anal. Calcd for $C_{24}H_{44}O_4Si_2$: C, 63.66; H, 9.79. Found: C, 63.49; H, 9.64.

In some cases, compound **10** turned out to be inquinated by some amounts of regioisomeric compound **11** (5–10%) (Schemes 2 and 3). **10** and **11** could not be separated due to unsurmontable chromatographic separation problems and their mixture was directly utilized in the next step.

1,4-Anhydro-3-(O-t-butyldimethylsilyl)-5-O-benzyl-L-xylitol ***12***

A solution of ether **10** (0.60 g, 1.33 mmol) in a 95:5 DMSO–H_2O mixture (6 ml) was treated with *N*-bromosuccinimide (NBS) (0.26 g, 1.46 mmol) and the reaction mixture was stirred in the dark for 12 h at r.t. Dilution with ether and evaporation of the washed (10% aqueous $Na_2S_2O_3$ and brine) afforded a crude product (0.385 g) which was subjected to flash chromatography (an 8:2 hexane/AcOEt was used as the eluant) to give starting ether **10** (0.112 g) and alcohol **12** (0.12 g), as a liquid: $[\alpha]_D^{20}$=+12.07 (*c* 0.78, $CHCl_3$); ^{1}H NMR δ 7.25–7.34 (m, 5H), 4.58 and 4.50 (ABdd 2H, *J*=9.5 Hz), 4.21–4.29 (m, 1H), 4.09–4.19 (m, 3H), 3.68–3.72 (m, 1H), 3.59–3.63 (m, 2H), 0.86 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H). ^{13}C NMR δ 138.72, 128.96, 128.53, 128.24, 80.39, 78.59, 78.26, 74.12, 74.00, 69.53, 26.30, 18.61, −4.10, −4.60. Anal. Calcd for $C_{18}H_{30}O_4Si$: C, 63.87; H, 8.93. Found: C, 64.12; H, 8.67.

Reaction of ether ***10*** *with TBAF/THF*

A solution of ether **10** (2.0 g, 4.42 mmol) in anhydrous THF (140 ml) was treated at −35°C under nitrogen with a 1 M TBAF solution in THF (4.4 ml), added over 40 min, and the resulting reaction mixture was stirred for 1 h at the same temperature, then left to warm to −10°C (1 h) and stirred for an additional hour at this temperature. The reaction was quenched at −10°C with water (50 ml) and ether (50 ml). Evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude reaction product (1.40 g) consisting of a 75:25 mixture of ethers **12** and **13** which was subjected to flash chromatography. Elution with a 7:3 mixture of hexane and AcOEt afforded pure **12** (0.96 g, 62% yield) and 1,4-anhydro-2-(*O-t*-butyldimethylsilyl)-5-*O*-benzyl-L-xylitol **13** (0.30 g, 20% yield), as a liquid: $[\alpha]_D^{20}$=−13.62 (*c* 0.71, $CHCl_3$); ^{1}H NMR δ 7.30–7.35 (m, 5H), 4.64 and 4.55 (ABdd, 2H, *J*=12.0 Hz), 4.15–4.24 (m, 2H), 4.05–4.14 (m, 2H), 3.85–3.94 (m, 2H), 3.59–3.69 (m, 1H), 3.50–3.56 (m, 1H), 0.87 (s, 9H), 0.07 (s, 6H). ^{13}C NMR δ 137.97, 129.22, 128.66, 128.54, 79.95, 79.00, 78.92, 75.11, 74.78, 69.81, 26.40, 18.64, −4.10, −4.20. Anal. Calcd for $C_{18}H_{30}O_4Si$: C, 63.87; H, 8.93. Found: C, 63.61; H, 9.19. Compound **13** can be utilized in the synthesis of the trans epoxide **2** (see below and Scheme 4).

Following standard described procedures,[10b,c] other deprotection procedures (AcOH–H_2O–THF, HF, HF–Py, TsOH, H_2SiF_6, TBAF/THF) were tried on ether **10**, affording unsatisfactory results.

1,4-Anhydro-2-O-tosyl-3-(O-t-butyldimethylsilyl)-5-O-benzyl-L-xylitol ***14***

A solution of alcohol **12** (1.60 g, 4.80 mmol) in anhydrous pyridine (15 ml) was treated at 0°C with TsCl (1.82 g, 9.60 mmol) and the reaction mixture was stirred for 3 days at r.t. The usual work-up afforded a crude oily residue (2.30 g) mostly consisting of tosylate **14** which was filtered through a short silica gel column. Elution with an 8:2 mixture of hexane and AcOEt afforded pure **14** (2.12 g, 90% yield) as a solid m.p. 63–64°C: $[\alpha]_D^{20}$=+10.65 (*c* 0.77, $CHCl_3$); ^{1}H NMR δ 7.75–7.81 (m, 2H), 7.26–7.36 (m, 7H), 4.63–4.72 (m, 1H), 4.52 and 4.50 (ABdd, 2H, *J*=12.2 Hz), 4.29 (m, 1H), 4.04–4.19 (m, 2H), 3.78 (d, 1H, *J*=10.7 Hz), 3.56–3.59 (m, 2H), 2.44 (s, 3H), 0.82 (s, 9H), 0.02 (s, 6H). ^{13}C NMR δ 145.88, 138.64, 134.13, 130.67, 129.01, 128.48, 128.30, 85.6, 80.42, 76.08, 74.14, 71.29, 68.81, 26.23, 22.32, 18.54, −4.32, −4.77. Anal. Calcd for $C_{25}H_{36}O_6SSi$: C, 60.94; H, 7.36. Found: C, 60.76; H, 7.70.

1,4-Anhydro-2-O-tosyl-5-O-benzyl-L-xylitol ***15***

A solution of the tosylate **14** (2.0 g, 4.06 mmol) in MeCN (16 ml) was treated with a 48% aqueous HBF_4 solution (1.0 ml) and the reaction mixture was stirred for 2 h at r.t. Dilution with ether and evaporation of the washed (saturated aqueous $NaHCO_3$ and water) ether solution afforded a crude reaction product (1.52 g) consisting of **15** practically pure which was filtered through a short silica gel column. Elution with a 1:1 mixture of hexane:AcOEt afforded pure hydroxy tosylate **15** (1.30 g, 85% yield), as a liquid: $[\alpha]_D^{20}$=−17.52 (*c* 1.01, $CHCl_3$); IR (CCl_4) 3462 cm^{-1} (1,3 OH···O); ^{1}H NMR δ 7.78 (d, 2H, *J*=8.3 Hz), 7.25–7.36 (m, 7H), 4.79–4.82 (m, 1H), 4.58 and 4.52 (ABdd, 2H, *J*=11.7 Hz), 4.34 (m, 1H), 4.20 (dd, 1H, *J*=10.8 and 4.6 Hz), 4.08 (q, 1H, *J*=3.8 Hz), 3.77–3.84 (m, 4H), 2.44

(s, 3H); ^{13}C NMR δ 145.91, 137.72, 133.88, 130.70, 129.22, 128.72, 128.49, 85.94, 79.11, 77.12, 74.70, 71.52, 69.27, 22.33. Anal. Calcd for $C_{19}H_{22}O_6S$: C, 60.30; H, 5.86. Found: C, 60.11; H, 5.48.

*1,4;2,3-Dianhydro-5-*O*-benzyl-*L*-lyxitol* ***1***

Hydroxy tosylate **15** (0.535 g, 1.41 mmol) was dissolved in anhydrous benzene (40 ml) and treated under stirring with two portions (0.213 g × 2) of *t*-BuOK over 2 h. Evaporation of the filtered organic solvent afforded a crude product (0.293 g) consisting of epoxide **1** which was purified by flash chromatography. Elution with a 7:3 mixture of hexane and AcOEt and few drops of NEt_3 afforded pure **1** (0.28 g, 96% yield), as a liquid: $[\alpha]_D^{20}$=+66.09 (*c* 1.28, $CHCl_3$); ^{1}H NMR δ 7.24–7.35 (m, 5H), 4.59 and 4.56 (ABdd, 2H, *J*=11.9 Hz) 4.04 (d, 1H, *J*=10.6 Hz), 4.00 (t, 1H, *J*=6.2 Hz), 3.76 (dd, 2H, *J*=5.4 and 3.3 Hz), 3.69 (d, 1H, *J*=10.2 Hz), 3.65 (d, 2H, *J*=6.2 Hz). ^{13}C NMR δ 138.51, 130.43, 129.02, 128.38, 128.39, 76.91, 74.23, 70.81, 69.22, 68.34, 57.22, 56.64. MS (*m/e*) 206 (M^+), 158, 145, 117, 91, 85, 69, 65. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 70.10; H, 6.52.

Equilibrating mixture of alcohols ***9*** *and* ***18***

A solution of alcohol **9** (0.90 g, 2.48 mmol) in anhydrous THF (20 ml) was treated under stirring at 0°C with NaH (0.40 g of a 60% dispersion in mineral oil, 10.0 mmol) and the reaction mixture was stirred for 90 min at r.t. Ether and water were carefully added in order to destroy the excess of hydride. Evaporation of the washed (brine) organic solution afforded a crude liquid product (1.0 g) consisting of a 40:60 mixture (^{1}H NMR) of alcohols **9** and **18** which was subjected to flash chromatography: elution with an 8:2 mixture of hexane and AcOEt afforded alcohol **9** (0.25 g, 28% yield) and 1,4-anhydro-2,5-di-(*O-t*-butyldimethylsilyl)-L-xylitol **18** (0.432 g, 48% yield), as a solid m.p. 35–37°C: ^{1}H NMR δ 4.30 (d, 1H, *J*=3.6 Hz), 4.06–4.17 (m, 5H), 4.00 (t, 1H, *J*=3.2 Hz), 3.65 (d, 1H, *J*=8.0 Hz), 0.90 (s, 9H), 0.88 (s, 9H), 0.11 (s, 6H), 0.09 (s, 3H), 0.08 (s, 3H). ^{13}C NMR δ 80.45, 79.21, 79.02, 75.01, 63.73, 26.40, 18.77, 18.68, −4.10, −4.22, −4.83, −4.98. Anal. Calcd for $C_{17}H_{38}O_4Si_2$: C, 56.30; H, 10.56. Found: C, 56.18; H, 10.71.

Prolonged reaction times (two days) led to a complex reaction mixture (extensive decomposition).

*1,4-Anhydro-3-*O*-benzyl-2,5-di-(*O*-t-butyldimethylsilyl)-*L*-xylitol* ***11***

Following a previously described procedure,[13] a solution of alcohol **18** (0.30 g, 0.83 mmol) in anhydrous THF (7 ml) was treated under nitrogen in succession with NaH (0.040 g of a 60% dispersion in mineral oil, 1.0 mmol), tetrabutylammonium iodide (0.036 g, 0.10 mmol) and benzyl bromide (0.12 ml, 1.0 mmol) and the reaction mixture was stirred 16 h at r.t. Dilution with ether, and extraction of the washed (brine) organic solution afforded a crude product (0.565 g) which was filtered through a short silica gel column. Elution with a 95:5 mixture of petroleum ether and ether afforded pure **11** (0.24 g), as a liquid: ^{1}H NMR δ 7.37–7.42 (m, 5H), 4.68 (s, 2H), 4.32–4.35 (m, 1H), 4.11–4.18 (m, 2H), 3.85–3.93 (m, 3H), 3.68 (dd, 1H, *J*=9.1 and 1.7 Hz), 0.97 (s, 9H), 0.92 (s, 9H), 0.13 (s, 6H), 0.08 (s, 3H), 0.06 (s, 3H). ^{13}C NMR δ 138.97, 129.07, 128.38, 128.23, 84.79, 81.48, 76.40, 74.97, 73.05, 61.75, 26.68, 26.42, 19.42, 19.05, 18.67, −4.11, −4.60. Anal. Calcd for $C_{24}H_{44}O_4Si_2$: C, 63.66; H, 9.79. Found: C, 63.54; H, 10.05.

*1,4-Anhydro-3-*O*-benzyl-5-(*O*-t-butyldimethylsilyl)-*L*-xylitol* ***19***

A solution of ether **11** (0.24 g, 0.53 mmol) in anhydrous THF (21 ml) was treated at −40°C under stirring with a 1 M TBAF solution in THF (0.53 ml). The reaction mixture was slowly warmed to −10°C and stirred at this temperature for 3 h. Dilution with ether and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude product (0.15 g) which was subjected to preparative TLC (an 8:2 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the most intense band afforded pure **19** (0.13 g), as a liquid: ^{1}H NMR δ 7.32–7.36 (m, 5H), 4.63–4.65 (m, 2H), 4.34–4.38 (m, 1H), 4.09–4.17 (m, 2H), 3.73–3.93 (m, 5H), 0.92 (s, 9H), 0.09 (s, 6H). ^{13}C NMR 139.01, 129.08, 128.41, 128.20, 84.56, 81.67, 75.90, 74.26, 73.10, 61.73, 26.61, 25.52, 18.98, 18.64, −4.71. Anal. Calcd for $C_{18}H_{30}O_4Si$: C, 63.87; H, 8.93. Found: C, 64.02; H, 8.81.

1,4-Anhydro-2-O-tosyl-3-O-benzyl-5-(O-t-butyldimethylsilyl)-L-xylitol **20**

Following standard procedures, the treatment of a solution of alcohol **19** (0.13 g, 0.39 mmol) in anhydrous pyridine (1.5 ml) with TsCl (0.148 g, 0.78 mmol) for two days at r.t. afforded a crude product (0.173 g) which was subjected to preparative TLC (a 7:3 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the most intense band afforded pure tosylate **20** (0.12 g), as a liquid: ^{1}H NMR δ 7.73 (d, 2H, *J*=8.0 Hz), 7.20–7.36 (m, 7H), 4.93–4.95 (m, 1H), 4.53 and 4.47 (ABdd, 2H, *J*=11.9 Hz), 3.93–4.13 (m, 3H), 3.81–3.69 (m, 3H), 2.42 (s, 3H), 0.84 (s, 9H), 0.00 (s, 6H). ^{13}C NMR δ 145.85, 138.11, 134.16, 130.67, 129.07, 128.47, 128.23, 83.56, 82.03, 81.51, 72.99, 71.58, 61.44, 26.54, 22.34, 18.90, −4.74. Anal. Calcd for $C_{25}H_{36}O_6SSi$: C, 60.94; H, 7.36. Found: C, 60.66; H, 7.24.

1,4-Anhydro-2-O-tosyl-3-O-benzyl-L-xylitol **21**

A stirred solution of ether **20** (0.12 g, 0.28 mmol) in MeCN (3 ml) was treated with 48% aqueous HBF_4 (0.18 ml) for 2 h at r.t. Usual workup afforded a crude product (0.10 g) which was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the most intense band afforded pure hydroxy tosylate **21**, as a solid m.p. 77–78°C; $[\alpha]_D^{20}$=+47.88 (*c* 0.93, $CHCl_3$); ^{1}H NMR δ 7.79 (d, 2H, *J*=8.2 Hz), 7.21–7.39 (m, 7H), 4.94–5.01 (m, 1H), 4.60 and 4.44 (ABdd, 2H, *J*=12.1 Hz), 4.02–4.27 (m, 4H), 3.69–3.82 (m, 3H), 2.46 (s, 3H). ^{13}C NMR δ 146.11, 137.44, 134.01, 130.78, 129.35, 128.97, 128.50, 83.38, 83.42, 80.65, 72.98, 71.37, 61.88, 22.38. Anal. Calcd for $C_{19}H_{22}O_6S$: C, 60.30; H, 5.86 Found: C, 60.46; H, 6.11.

(1S,4S)-7-Benzyloxy-2,5-dioxabicyclo[2.2.1]heptane **22**

Treatment of a benzene solution (3.0 ml) of hydroxy tosylate **21** (0.122 g, 0.32 mmol) with *t*-BuOK (0.036 g × 2) as usual, afforded a reaction product (0.065 g, 92% yield) consisting of practically pure **22** which was subjected to semipreparative TLC (an 8:2 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the most intense band afforded pure **22** (0.050 g), as a solid, m.p. 53–54°C: $[\alpha]_D^{20}$=−48.14 (*c* 1.43, $CHCl_3$): ^{1}H NMR δ 7.22–7.28 (m, 5H), 4.59 and 4.50 (ABdd, 2H, *J*=11.8 Hz), 4.20 (s, 1H), 3.97–4.12 (m, 3H), 3.90 (d, 1H, *J*=8.4 Hz), 3.83 (s, 1H). ^{13}C NMR δ 138.12, 129.17, 128.68, 128.50, 80.35, 76.55, 76.49, 74.47, 73.51, 72.85. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.65; H, 7.14.

Diisobutyl-2,5-anhydro-4-(O-t-butyldimethylsilyl)-D-xylofuranose dithioacetal **23**

A solution of **6** (6.0 g, 20.4 mmol) in anhydrous DMF (40 ml) containing imidazole (3.33 g, 48.9 mmol) was treated at 0°C with TBDMS-Cl (3.21 g, 21.4 mmol) and the reaction mixture was stirred for 30 min at the same temperature, and then for 3 days at r.t. The usual work-up afforded a crude product (7.7 g) which was filtered through a short silica gel column. Elution with an 8:2 mixture of petroleum ether and AcOEt afforded pure **23** (6.88 g, 82% yield), as a liquid: $[\alpha]_D^{20}$=−6.16 (*c* 1.25, $CHCl_3$); ^{1}H NMR δ 4.05–4.25 (m, 4H), 3.96 (d, 1H, *J*=8.8 Hz), 3.67 (d, 1H, *J*=8.9 Hz), 2.59–2.72 (m, 4H), 1.79–1.89 (m, 2H), 1.03 (s, 6H), 0.99 (s, 6H), 0.88 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H). ^{13}C NMR δ 83.30, 79.24, 78.42, 75.31, 52.46, 40.17, 39.47, 29.22, 29.10, 26.39, 22.91, 22.80, 18.64, −4.15. Anal. Calcd for $C_{19}H_{40}O_3S_2Si$: C, 55.83; H, 9.86. Found: C, 56.13; H, 9.61.

Diisobutyl-2,5-anhydro-3-O-tosyl-4-(O-t-butyldimethylsilyl)-D-xylofuranose dithioacetal **24**

Proceeding as previously described for **14**, a solution of **23** (4.8 g, 11.76 mmol) in anhydrous pyridine (15 ml) was treated with TsCl (4.02 g, 21.17 mmol) to give a crude reaction product (6.3 g) which was subjected to flash chromatography. Elution with a 9:1 mixture of hexane and AcOEt afforded pure **24** (5.3 g, 80% yield), as a liquid: $[\alpha]_D^{20}$=−17.4 (*c* 1.1, $CHCl_3$); ^{1}H NMR δ 7.80 (d, 2H, *J*=8.3 Hz), 7.33 (d, 2H, *J*=8.0 Hz), 4.76 (t, 1H, *J*=0.9 Hz), 4.54 (d, 1H, *J*=4.0 Hz), 4.19 (dd, 1H, *J*=9.6 and 4.1 Hz), 4.08 (dd, 1H, *J*=10.5 and 2.6 Hz), 3.74 (t, 2H, *J*=10.7 Hz), 2.52 (dd, 2H, *J*=6.8 and 4.7 Hz), 2.43 (s, 3H), 2.39 (dd, 2H, *J*=6.8 and 3.0 Hz), 1.52–1.90 (m, 2H), 0.96 (d, 6H, *J*=6.5 Hz), 0.88 (d, 6H, *J*=6.7 Hz), 0.86 (s, 9H), 0.11 (s, 3H), 0.07 (s, 3H). ^{13}C NMR δ 145.71, 134.08,

130.42, 128.67, 85.43, 81.87, 75.71, 75.62, 50.85, 40.43, 38.40, 29.44, 29.01, 26.22, 22.92, 22.84, 22.69, 22.34, 18.37. Anal. Calcd for $C_{26}H_{46}O_5S_3Si$: C, 55.47; H, 8.24. Found: C, 55.29; H, 7.93.

*2,5-Anhydro-3-*O*-tosyl-4-(*O*-t-butyldimethylsilyl)-*D*-xylofuranose* **25**

Following the procedure previously described for the synthesis of **8**, the treatment of **24** (6.0 g, 10.7 mmol) in MeCN (100 ml) with $HgCl_2$ (6.4 g, 23.5 mmol) and HgO (2.5 g, 11.5 mmol) in a 4:1 mixture of MeCN and water (160 ml) afforded a crude liquid product (3.64 g, 85% yield) consisting of practically pure aldehyde **25** which was directly utilized in the next step without any further purification: ^{1}H NMR δ 9.45 (d, 1H, *J*=1.2 Hz), 7.62–7.71 (m, 2H), 7.26–7.34 (m, 2H), 4.76 (dd, 1H, *J*=1.1 and 3.7 Hz), 4.48–4.51 (m, 1H), 4.37 (dd, 1H, *J*=1.3 and 3.7 Hz), 4.22 (dd, 1H, *J*=9.6 and 3.4 Hz), 3.81 (d, 1H, *J*=9.5 Hz), 2.39 (s, 3H), 0.79 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H). ^{13}C NMR δ 199.80, 146.41, 132.90, 130.74, 128.70, 85.49, 83.99, 76.46, 76.17, 26.26, 22.40, 18.51, −4.14, −4.41.

*2,5-Anhydro-3-*O*-tosyl-2-(*O*-t-butyldimethylsilyl)-*L*-xylitol* **26**

Proceeding as previously described for the preparation of **9**, the treatment of aldehyde **25** (3.64 g, 9.1 mmol) in anhydrous ether (160 ml) with 10 M $BH_3 \cdot Me_2S$ (2.3 ml) afforded a crude liquid product (3.5 g, 95% yield) consisting of practically pure alcohol **26** which was directly utilized in the next step without any further purification. An analytical sample (0.10 g) of crude **26** was purified by flash chromatography: elution with a 6:4 mixture of hexane and AcOEt afforded pure **26**, as a liquid: $[\alpha]_D^{20}$=−4.12 (*c* 1.48, $CHCl_3$); ^{1}H NMR δ 7.80 (d, 2H, *J*=8.2 Hz), 7.37 (d, 2H, *J*=8.1 Hz), 4.65 (d, 1H, *J*=2.8 Hz), 4.28–4.30 (m, 1H), 4.18 (ddd, 1H, *J*=8.4, 6.2 and 3.2 Hz), 4.07 (dd, 1H, *J*=9.2 and 3.9 Hz), 3.62–3.73 (m, 3H), 2.46 (s, 3H), 0.82 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H). ^{13}C NMR δ 146.22, 133.48, 130.79, 128.64, 85.23, 80.01, 76.73, 74.76, 60.91, 26.23, 22.41, 18.48, 4.00. Anal. Calcd for $C_{18}H_{30}O_6SSi$: C, 53.70; H, 7.51. Found: C, 53.91; H, 7.22.

*1,4-Anhydro-3-*O*-tosyl-2-(*O*-t-butyldimethylsilyl)-5-*O*-benzyl-*L*-xylitol* **27**

a) Proceeding as previously described for the synthesis of **10**, the treatment of a suspension of NaH (1.4 g of a 60% dispersion in mineral oil, 35.0 mmol) in anhydrous THF (90 ml) containing benzyl bromide (1.45 ml, 12.19 mmol) with a solution of alcohol **26** (4.90 g, 12.2 mmol) in anhydrous THF (22 ml) afforded a crude liquid product (5.7 g) which was subjected to flash chromatography. Elution with a 9:1 mixture of hexane and AcOEt afforded pure **27** (5.1 g, 85% yield), as a liquid: $[\alpha]_D^{20}$=+8.15 (*c* 1.08, $CHCl_3$); ^{1}H NMR δ 7.76 (d, 2H, *J*=8.4 Hz), 7.28–7.35 (m, 7H), 4.63 (dd, 1H, *J*=3.1 and 1.1 Hz), 4.45 and 4.41 (ABdd, 2H, *J*=11.9 Hz), 4.40 (dd, 1H, *J*=9.7 and 6.9 Hz), 4.27 (ddd, 1H, *J*=8.6, 6.5 and 3.2 Hz), 4.12 (dd, 1H, *J*=9.4 and 4.1 Hz), 3.66 (dd, 1H, *J*=9.5 and 1.2 Hz), 3.42–3.62 (m, 2H), 2.41 (s, 3H), 0.84 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H). ^{13}C NMR δ 145.82, 138.53, 133.87, 130.58, 129.04, 128.52, 128.42, 128.33, 85.61, 78.68, 76.51, 75.00, 74.20, 68.62, 26.31, 22.33, 18.51, −4.22, −4.41. Anal. Calcd for $C_{25}H_{36}O_6SSi$: C, 60.94; H, 7.36. Found: C, 60.84; H, 7.51.

b) Proceeding as previously described for the preparation of **14**, the treatment of alcohol **13** (0.225 g, 0.67 mmol) in anhydrous pyridine (1.0 ml) with TsCl (0.25 g, 1.33 mmol) afforded crude tosylate **27** (0.32 g) which was purified by flash chromatography as in a) to give pure tosylate **27** (0.25 g).

*1,4-Anhydro-3-*O*-tosyl-5-*O*-benzyl-*L*-xylitol* **17**

Proceeding as previously described for the preparation of **15**, a solution of **27** (1.6 g, 3.25 mmol) in MeCN (16 ml) was treated with 48% aqueous HBF_4 (0.95 ml) to give a crude solid product (1.15 g, 94% yield) consisting of practically pure hydroxy tosylate **17**, as a solid, m.p. 70–71°C (from hexane): $[\alpha]_D^{20}$=+38.98 (*c* 1.18, $CHCl_3$); IR (CCl_4) 3614 cm^{-1} (free OH); ^{1}H NMR δ 7.77 (d, 2H, *J*=8.3 Hz), 7.23–7.38 (m, 7H), 4.77 (dd, 1H, *J*=4.0 and 1.4 Hz), 4.50–4.52 (m, 1H), 4.40 and 4.49 (ABdd, 2H, *J*=12.0 Hz), 4.15–4.28 (m, 2H), 3.66 (dd, 1H, *J*=9.9 and 3.0 Hz), 3.40–3.57 (m, 2H), 2.40 (s, 3H). ^{13}C NMR δ 146.01, 138.40, 133.48, 130.62, 129.03, 128.51, 128.32, 85.88, 78.74, 76.53, 74.12, 73.68, 68.31, 22.34. Anal. Calcd for $C_{19}H_{22}O_6S$: C, 60.30 H, 5.86. Found: C, 60.52; H, 5.55.

*1,4;2,3-Dianhydro-5-O-benzyl-*L*-ribitol* **2**

The treatment of a solution of **17** (1.32 g, 3.49 mmol) in anhydrous benzene (35 ml) with *t*-BuOK (0.39 g × 2) afforded a liquid product consisting of pure epoxide (0.675 g, 94% yield), as a liquid: $[\alpha]_D^{20}$=+16.73 (*c* 1.3, $CHCl_3$); ^{1}H NMR δ 7.25–7.36 (m, 5H), 4.54 (s, 2H), 4.21 (t, 1H, *J*=4.4 Hz), 3.92 (dd, 2H, *J*=10.2 Hz), 3.78 (dd, 2H, *J*=10.8 and 3.4 Hz), 3.52–3.61 (m, 2H). ^{13}C NMR δ 138.48, 129.02, 128.42, 128.14, 77.33, 74.10, 70.92, 68.41, 58.53, 57.02. MS (*m/e*) 206 (M^+), 181, 145, 117, 91, 85, 69, 65. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.66; H, 6.50.

*1,4-Anhydro-5-O-benzyl-*L*-xylitol* ***16***

A solution of ether **10** (0.88 g, 1.90 mmol) in MeCN (8.0 ml) was treated with 48% aqueous HBF_4 (0.8 ml) and the reaction mixture was stirred for 2 h at r.t. Solid $NaHCO_3$ and ether were added: evaporation of the washed (saturated aqueous $NaHCO_3$) organic solution afforded a crude solid product (0.36 g) consisting of diol **16**, which was recrystallized from hexane to give pure (0.27 g), as a solid, m.p. 72–74.5°C: $[\alpha]_D^{20}$=−3.63 (*c* 1.10, $CHCl_3$); ^{1}H NMR δ 7.24–7.35 (m, 5H), 4.54 and 4.58 (ABdd, 2H, *J*=12.4 Hz), 4.14–4.19 (m, 4H), 3.63–3.88 (m, 3H). ^{13}C NMR δ 137.94, 129.21, 128.67, 128.55, 79.15, 78.34, 74.59, 74.02, 69.59. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 63.96; H, 7.39.

Monotosylation reaction of diol ***16***

A solution of diol **16** (0.84 g, 3.75 mmol) in anhydrous pyridine (11 ml) was treated at 0°C with TsCl (0.75 g, 3.95 mmol) and the reaction mixture was stirred at r.t for 48 h. Dilution with ether and evaporation of the washed (10% aqueous HCl, saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude oily product (1.25 g) consisting of a 57:43 mixture (^{1}H NMR) of the monotosylates **15** and **17** which was subjected to flash chromatography. Elution with a 1:1 mixture of hexane and AcOEt gave pure **15** (0.46 g) and **17** (0.42 g).

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