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Synthesis of 4-Deoxy-L-(and D-)hexoses from Chiral Noncarbohydrate Building Blocks

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4-Deoxy-L-hexoses were synthesized starting from our previously reported reagent **1** and (*R*)-benzyl glycidyl ether, which led in few steps to a substituted dihydropyran **6**. The stereocontrolled hydroxylation of the latter afforded the corresponding 4-deoxy-L-hexoses **7a**, **9**, and **11**. The same procedure, starting from (*S*)-benzyl glycidyl ether, enabled the preparation of their D-series enantiomers.

Introduction

The rare L-hexoses are key components of numerous biologically potent[1] oligosaccharides, antibiotics,[2] glycopeptides,[3] and terpene glycosides, as well as steroid glycosides and other clinically useful agents such as heparin.[4] They have also demonstrated potential as noncaloric sweeteners[5] and selectively toxic insecticides.[6] Their deoxy derivatives are also valuable tools in the study of biological and biochemical properties of mono-[7] and oligosaccharides,[8] glycoproteins,[9] glycolipids,[10] and antibodies.[11] Deoxy-hexoses most frequently occurring in nature are 2-deoxy-, 6-deoxy-, and 2,6-dideoxy-hexoses, whereas 3-deoxy- and 4-deoxy-hexoses are quite rare compounds. Buchanan and co-workers[12] have recognized methyl 4-deoxy-D-*lyxo*-hexopyranuronate to be the sugar moiety of both neosidomycin and SF-2140, two indole nucleoside antibiotics.[13]

4-Deoxy-L-hexoses, however, are not commercially available compounds. This very fact coupled with practical difficulties in obtaining these rare sugars from natural sources has urged chemists to develop novel, cost-effective, general, simple, and convenient routes for their syntheses.

The most common approach to the preparation of 4-deoxy-hexoses consists of the deoxygenation at C-4 of natural hexoses. The method implies selective protection of the hydroxyl groups at C-1, C-2, C-3, C-5, and C-6 followed by deoxygenation of the sole unprotected hydroxyl group, accomplished according to a rather large variety of protocols.[14] Other approaches involve Kiliani−Fischer homologation of 3-deoxypentoses,[15] hetero-Diels−Alder reactions,[16] and also enzymatic methods.[17]

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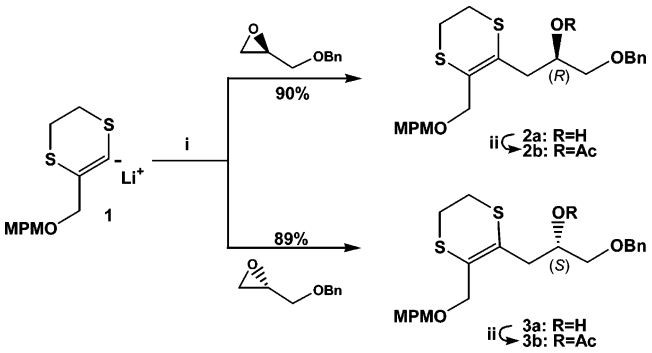
SCHEME 1. Coupling Reactions of 1 with (*R*)- and (*S*)-Benzyl Glycidyl Ether[a]



[a] (i) $Ti(OPr^i)_4$, −78 °C in THF; (ii) Ac_2O in Py.

Furthermore, to the best of our knowledge no general syntheses specifically directed toward the preparation of 4-deoxy-hexoses have been reported as yet. Therefore, in this paper we wish to report a new synthetic route to 4-deoxy-hexoses of both L- and D-series, prepared in good yields from noncarbohydrate starting products.

Results and Discussion

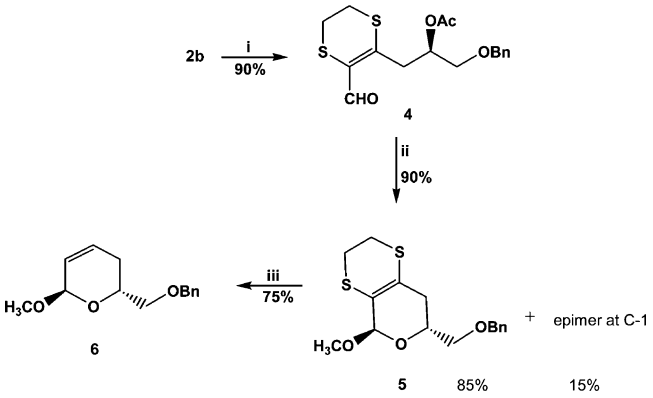
The discovery of 3-*C*-lithiated 5,6-dihydro-1,4-dithiin-2-yl[(4-methoxybenzyl)oxy]methane (**1**), a reagent capable of three-carbon homologation[18] of organic molecules with the introduction of a fully protected allylic alcohol at the new terminus, prompted a new route to 4-deoxy-hexoses.

The synthesis started, in fact, with the coupling of **1** and (*R*)-benzyl glycidyl ether to afford the secondary alcohol **2a** (Scheme 1), which is the precursor of the L-series 4-deoxy-hexoses. In an analogous manner the coupling of **1** with (*S*)-benzyl glycidyl ether led to the enantiomeric alcohol **3a**, precursor of the D-series 4-deoxy-hexoses.

The alcohol **2a** was converted into the corresponding acetate **2b**, and the latter was then treated with DDQ in CH_2Cl_2/H_2O to remove selectively the 4-methoxybenzyl protecting group. As we have previously reported,[18] such removal conditions lead quantitatively to the formation of a formyl function rather than the expected primary alcohol.

The aldehyde **4** thus obtained (Scheme 2) was cyclized in one step, under treatment with TMSOTf and Et_3N in methanol, affording the *O*-methyl acetal **5** in 85% yield beside its C-1 epimer (15% yield). The reagent system $TMSOTf/Et_3N/CH_3OH$ had been chosen with the purpose of converting the formyl group of the aldehyde **4** into its di-*O*-methyl acetal.[19] The latter (which was actually formed and could be isolated) underwent a rapid hydrolysis of the acetoxyl group[20] followed by intramolecular transacetalation[21] affording both **5** and its epimer.

SCHEME 2. Preparation of L-Hexose Precursor[a]



[a] (i) DDQ in CH_2Cl_2/H_2O; (ii) TMSOTf, Et_3N in MeOH; (iii) Raney-Ni in THF.

The subsequent steps of the synthesis were carried out on the more abundant epimer **5**. Actually, it was desulfurized[22] by Raney-Ni in THF, leading to the unsaturated pyranosyl derivative **6**, which can be regarded as the α-anomer of a C-2,C-3,C-4-trideoxy L-sugar *O*-methyl glycoside.

Therefore, the stereocontrolled hydroxylation of the double bond in **6** should afford four different 4-deoxy-L-hexopyranosides, namely, methyl 4-deoxy-α-L-*lyxo*-hexopyranoside, methyl 4-deoxy-α-L-*ara*-hexopyranoside, methyl 4-deoxy-α-L-*xylo*-hexopyranoside, and methyl 4-deoxy-α-L-*ribo*-hexopyranoside.

The first attempt to introduce two hydroxyl groups onto **6** was the osmylation[23] of the double bond by OsO_4/NMO (Scheme 3), which led to a sole *cis*-2,3-dihydroxylated compound whose structure, **7a** (methyl 4-deoxy-α-L-*lyxo*-hexopyranoside), was assigned by ^1H NMR analysis. The compound **7a** and its diacetyl derivative **7b** were already known.[24] Physical and spectroscopic features of our compounds were identical with those reported in the literature.

No traces of the diastereomeric diol (namely, methyl 4-deoxy-α-L-*ribo*-hexopyranoside) coming from the other *syn* hydroxylation of **6** could be detected. On the other hand, such a result was predictable because it is known[25] that the osmylation reaction occurs from the sole face of the double bond that is opposite to the anomeric substituent.

The *anti* hydroxylation of **6** was achieved by epoxidation[26] of the double bond followed by alkaline hydrolysis of the resulting epoxide(s). Under our conditions, **6** was treated with 3-chloro-peroxybenzoic acid (Scheme 3),

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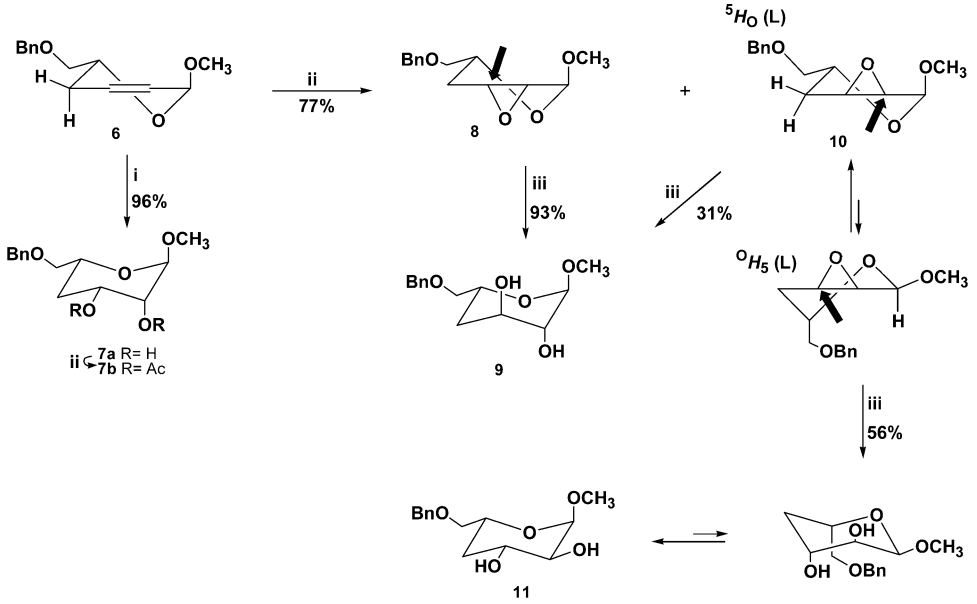
SCHEME 3. Preparation of Methyl 4-Deoxy-L-hexopyranosides[a]



[a] (i) OsO_4/NMO in *tert*-butyl alcohol/acetone; (ii) *m*-CPBA in CH_2Cl_2; (iii) 1 N NaOH.

affording two diastereomeric epoxides **8** and **10** in a 3:2 ratio, as expected[27] in consideration of the steric hindrance of the *pseudo*-axial methoxyl group at one of the sides of the double bond.

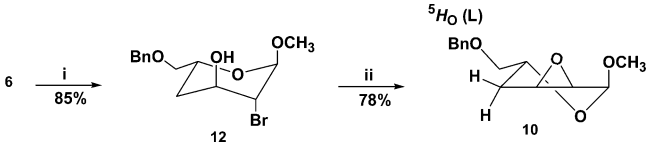
The epoxides were readily separated by chromatography on silica gel, and their structures were assigned by ^{1}H NMR analysis. Evidence could be obtained for both being essentially in ^5H_O (L) conformation with an equatorial benzyloxymethyl group and axial methoxyl group.

The ring opening of the epoxide **8**, carried out by aqueous 1 N NaOH for 2 h at 95 °C, was thoroughly stereospecific, leading to the sole compound **9**. That may be accounted for by the preferred *trans* diaxial opening of the oxirane ring and even the OH^- attack at the relatively unhindered C-3 position of the ^5H_O (L) epoxide **8**. Provided that **9** exists preferably in $^1C_4$ conformation, the rather small $J_{1,2}$ and $J_{2,3}$ ($J_{1,2}$ = 1.1 Hz and $J_{2,3}$ = 3.2 Hz after decoupling) in its ^{1}H NMR spectrum are in good agreement with the assigned structure.

Otherwise, the ring opening of the epoxide **10** was not stereospecific and led to a 76:24 mixture of the diastereomeric 4-deoxy-L-hexopyranosides **9** (identical to that coming from **8**) and **11**. The structure of the latter, which is expected to stay in $^1C_4$ conformation, was assigned by ^{1}H NMR analysis, being significantly supported by the quite large $J_{2,3}$ coupling constant ($J_{2,3}$ = 9.8 Hz).

The formation of **11** from the ^5H_O (L) epoxide **10** is likely the consequence of the somewhat difficult oxirane ring opening leading to **9**, where the hydroxide ion must attack the C-2 position of the tetrahydropyran ring from the same side of the ring oxygen atom. Under such circumstances, the attack at C-3 of the less favorable $^OH_5$ (L) conformation of the epoxide **10** may become competitive. The molecular models show that some degree of twisting of the tetrahydropyran ring may reduce significantly the interaction between the nucleophile and the *pseudo*-axial benzyloxymethyl group.

SCHEME 4. Selective Epoxidation of 6 via Bromohydrin 12[a]



[a] (i) NBS in DMSO/H_2O; (ii) NaH in THF.

All that reflects on a wholly more difficult ring opening of the epoxide **10** in comparison with its diastereomer **8**; in fact, under our conditions, the opening rate of the former with sodium hydroxide was nearly 10-fold slower than the rate of the latter.

Following a referee's suggestion, some attempts were made to improve the selectivity of the epoxidation of **6**, which under our conditions led to a 3:2 mixture of the epoxides **8** and **10** (Scheme 3). The dihydropyrane **6** was in fact treated[28] with NBS in DMSO/H_2O and afforded the corresponding bromohydrin **12**. This was then cyclized[29] by NaH in THF, leading as expected to the sole epoxide **10** (Scheme 4) from which both diastereomeric hexopyranosides **9** and **11** are obtained by alkaline hydrolysis (Scheme 3).

Finally, to show the flexibility of our synthetic scheme, the coupling product of **1** with (*S*)-benzyl glycidyl ether, **3a**, was submitted to the same series of reactions described hitherto and gave the enantiomer (D-series analogue) of **6** whose hydroxylation led to the corresponding methyl 4-deoxy-α-D-hexopyranosides.

The synthetic approach described by this paper is quite general and can be conveniently extended to the prepara-

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tion of D and L fully hydroxylated hexoses, by replacing benzyl glycidyl ether with D- and L-glyceraldehyde, respectively. Work is also in progress in our lab to prepare D- and L-iminosugars starting with the coupling of **1** with the enantiomeric Garner aldehydes.

Experimental Section

(2*R*)-1-(Benzyloxy)-3-(3-{[(4-methoxybenzyl)oxy]methyl}-5,6-dihydro-1,4-dithiin-2-yl)propan-2-ol (2a). Typical Coupling Procedure of 1. To a stirred solution of **1** (1.0 g; 3.6 mmol) [prepared in situ according to ref 18] in anhydrous THF (5 mL), at −78 °C and under argon atmosphere, was added dropwise over 10 min a solution of (*R*)-(−)-benzyl glycidyl ether (0.7 mL; 4.4 mmol) and $Ti(OPr^i)_4$ (0.2 mL; 0.9 mmol) in the same solvent (2 mL). The reaction mixture was stirred 1 h at −78 °C and 3 h at −40 °C and then quenched carefully with 10% aqueous NH_4Cl. Usual workup[18] and chromatography on silica gel (hexane/acetone = 8/2) of the crude residue finally afforded pure **2a** (1.4 g; 90%, oily): $[\alpha]^{25}_D$ +8.0 (*c* 2.0, $CHCl_3$); IR (film) 3430 cm^{-1}; ^1H NMR (400 MHz) δ 2.39 (dd, 1H, *J* = 4.5, 15.0 Hz), 2.65 (dd, 1H, *J* = 8.4, 15.0 Hz), 3.12−3.22 (m, 4H), 3.44 (dd, 1H, *J* = 5.8, 10.0 Hz), 3.48 (dd, 1H, *J* = 4.6, 10.0 Hz), 3.78 (s, 3H), 3.90 (d, 1H, *J* = 11.5 Hz), 3.96−4.06 (m, 1H), 4.14 (d, 1H, *J* = 11.5 Hz), 4.46 (s, 2H), 4.57 (s, 2H), 6.83 (d, 2H, *J* = 8.0 Hz), 7.25 (d, 2H, *J* = 8.0 Hz), 7.28−7.38 (m, 5H); ^{13}C NMR (75 MHz) δ 29.6 (2xC), 39.2, 55.2, 69.2, 69.8, 72.0, 73.3, 73.8, 113.7, 122.1, 126.4, 127.6, 128.3, 129.6, 138.1, 159.2. Anal. Calcd for $C_{23}H_{28}O_4S_2$: C, 63.68; H, 6.54. Found: C, 63.75; H, 6.55.

Under the same conditions, the enantiomer **3a** was obtained from the coupling of **1** with (*S*)-(+)-benzyl glycidyl ether (89% yield): $[\alpha]^{25}_D$ −8.0 (*c* 2.0, $CHCl_3$). Anal. Calcd for $C_{23}H_{28}O_4S_2$: C, 63.86; H, 6.52. Found: C, 63.75; H, 6.55. ^1H NMR and ^{13}C NMR spectra superimposable on those of **2a**.

Data for Compound 2b: oily, $[\alpha]^{25}_D$ +9.0 (*c* 2.5, $CHCl_3$); IR (KBr) 1740 cm^{-1}; ^1H NMR (400 MHz) δ 2.05 (s, 3H), 2.48 (dd, 1H, *J* = 5.8, 14.8 Hz), 2.75 (dd, 1H, *J* = 7.8, 14.8 Hz), 3.07−3.19 (m, 4H), 3.50−3.62 (m, 2H), 3.82 (s, 3H), 4.05 (d, 1H, *J* = 11.9 Hz), 4.21 (d, 1H, *J* = 11.9 Hz), 4.44 (s, 2H), 4.48 (d, 1H, *J* = 12.0 Hz), 4.52 (d, 1H, *J* = 12.0 Hz), 5.21−5.30 (m, 1H), 6.80 (d, 2H, *J* = 8.0 Hz), 7.25−7.40 (m, 7H); ^{13}C NMR (75 MHz) δ 21.1, 28.5, 29.2, 36.3, 55.2, 69.7, 70.4, 71.7, 71.9, 73.1, 73.3, 113.8, 123.8, 124.6, 127.6, 128.4, 129.5, 130.1, 138.1, 159.3, 170.3. Anal. Calcd for $C_{25}H_{30}O_5S_2$: C, 63.26; H, 6.37. Found: C, 63.18; H, 6.39.

Carbaldehyde 4. Oxidative Cleavage of the MPM Protecting Group. To a stirred CH_2Cl_2/H_2O (9:1) emulsion (50 mL) containing the MPM ether **2b** (0.5 g; 1.0 mmol) was added DDQ (0.3 g; 1.3 mmol) in one portion at room temperature. After 1 h, the suspension was filtered, and the solid was washed with CH_2Cl_2. The organic layer was separated and dried (Na_2SO_4), and the solvents were evaporated under reduced pressure. Chromatography of the crude product on silica gel (hexane/acetone = 8/2) gave the pure carbaldehyde **4** (0.32 g; 90%, oily): $[\alpha]^{25}_D$ −22.1 (*c* 3.0, $CHCl_3$); IR (film) 2880, 1705, 1738, 1235 cm^{-1}; ^1H NMR (300 MHz) δ 2.06 (s, 3H), 2.86 (dd, 1H, *J* = 4.4, 14.8 Hz), 3.08−3.18 (m, 2H), 3.26−3.34 (m, 2H), 3.40 (dd, 1H, *J* = 8.8, 14.8 Hz), 3.62 (d, 2H, *J* = 4.6 Hz), 4.58 (s, 2H), 5.24−5.35 (m, 1H), 7.24−7.50 (m, 5H), 9.82 (s, 1H); ^{13}C NMR (75 MHz) δ 20.9, 30.3, 30.8, 35.8, 69.8, 71.5, 73.2, 122.0, 124.2, 127.6, 128.3, 128.7, 137.3, 170.1, 183.2. Anal. Calcd for $C_{17}H_{20}O_4S_2$: C, 57.93; H, 5.72. Found: C, 58.05; H 5.74.

(5*R*,7*R*)-7-[(Benzyloxy)methyl]-5-methoxy-2,3,7,8-tetrahydro-5*H*-[1,4]dithiino[2,3-*c*]pyran (5). To a stirred solution of carbaldehyde **4** (1.0 g; 2.8 mmol) in methanol (5 mL) at room temperature were added TEA (1.95 mL; 14.0 mmol) and then TMSOTf (2.2 mL; 14.0 mmol) portionwise over 1 h. After 2 h, most of the solvent was evaporated under reduced pressure and replaced by EtOAc. The organic phase was washed with brine until neutral and then dried (Na_2SO_4), and the solvents were evaporated under reduced pressure. Chromatography of the crude residue on silica gel (hexane/EtOAc = 8/2) afforded the pure dihydropyran **5**, beside a small amount of its epimer at C-1 (0.83 g, 90% overall yield; diastereomeric ratio 85:15).

Data for dihydropyran 5: lower R_f compound, 0.71 g, oily; $[\alpha]^{25}_D$ +39.0 (*c* 1.4, $CHCl_3$); ^1H NMR (400 MHz) δ 1.95 (dd, 1H, *J* = 3.4, 16.5 Hz), 2.41 (dd, 1H, *J* = 11.6, 16.5 Hz), 3.08−3.18 (m, 2H), 3.21−3.31 (m, 2H), 3.43 (s, 3H), 3.55 (dd, 2H, *J* = 4.6), 4.28−4.34 (m, 1H), 4.57 (d, 1H, *J* = 12.1 Hz), 4.61 (d, 1H, *J* = 12.1 Hz), 4.76 (s, 1H), 7.25−7.38 (m, 5H); ^{13}C NMR (50 MHz) δ 27.3, 28.5, 32.8, 55.2, 66.3, 71.6, 73.1, 98.2, 118.3, 123.5, 127.3, 128.1, 137.8. Anal. Calcd for $C_{16}H_{20}O_3S_2$: C, 59.23; H, 6.21. Found: C, 59.39; H 6.23.

Data for the C-1 epimer of 5: higher R_f compound, 0.12 g, oily; $[\alpha]^{25}_D$ +18.2 (*c* 0.9, $CHCl_3$); ^1H NMR (200 MHz) δ 1.95 (dd, 1H, *J* = 3.3, 16.6 Hz), 2.40 (dd, 1H, *J* = 11.4, 16.6 Hz), 3.00−3.30 (m, 4H), 3.54 (dd, 1H, *J* = 4.5, 10.4 Hz), 3.57 (dd, 1H, *J* = 5.3, 10.3 Hz), 3.83 (s, 3H), 4.30−4.37 (m, 1H), 4.57 (d, 1H, *J* = 12.1 Hz), 4.61 (d, 1H, *J* = 12.1 Hz), 4.85 (s, 1H), 7.20−7.40 (m, 5H); ^{13}C NMR (75 MHz) δ 27.6, 29.7, 33.1, 63.7, 66.6, 71.9, 73.4, 97.4, 118.8, 124.0, 127.6, 128.1, 128.4, 138.1. Anal. Calcd for $C_{16}H_{20}O_3S_2$: C, 59.23; H, 6.21. Found: C, 59.32; H, 6.19.

(2*R*,6*R*)-2-[(Benzyloxy)methyl]-6-methoxy 3,6-dihydro-2*H*-pyran (6). A solution of dihydropyran **5** (0.6 g; 1.85 mmol) in THF (10 mL) was added in one portion to a stirred suspension of Raney-Ni (W2) (5.5 g, wet) in the same solvent (5 mL) at room temperature and under an argon stream. The suspension was stirred for 5 min (TLC monitoring), and then the solid was filtered off and washed with THF. The filtrate was evaporated under reduced pressure to afford a crude residue whose chromatography on silica gel (hexane/acetone = 8/2) gave pure **6** (0.32 g, 75% yield): $[\alpha]^{25}_D$ +23.7 (*c* 1.5, $CHCl_3$); ^1H NMR (500 MHz) δ 1.94 (dddd, 1H, *J* = 1.5, 3.4, 5.6, 17.6 Hz), 2.17 (dddd, 1H, *J* = 2.0, 4.4, 11.3, 17.6 Hz), 3.44 (s, 3H), 3.58 (d, 2H, *J* = 4.88 Hz), 4.08−4.16 (m, 1H), 4.58 (d, 1H, *J* = 12.2 Hz), 4.63 (d, 1H, *J* = 12.2 Hz), 4.91 (s, 1H), 5.72−5.80 (m, 1H), 6.00−6.05 (m, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR (50 MHz) δ 29.7, 55.1, 65.6, 72.4, 73.2, 95.7, 125.3, 127.5, 128.3, 128.6, 138.3. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.56; H, 7.77.

Methyl 6-*O*-Benzyl-4-deoxy-α-L-*lyxo*-hexopiranoside (7a). To a solution of **6** (0.12 g; 0.52 mmol) in 1:1 *tert*-butyl alcohol/acetone (4.8 mL) cooled in ice bath was added an excess of a chilled 1:1 (w/w) solution of 4-methylmorpholine-*N*-oxide (0.14 g; 1.04 mmol) in water in one portion. After some minutes, a catalytic amount (2% mol) of OsO_4 was added to the reaction mixture, and stirring was continued for 28 h at room temperature. The reaction was quenched with saturated aqueous Na_2SO_3, and the mixture was extracted with Et_2O and washed with brine. The combined organic layers were dried (Na_2SO_4) and filtered, the solvent was evaporated, and the crude residue was purified on silica gel (hexane/acetone = 1/1) to give the diol **7a** (0.13 g) in 96% yield: mp 79−81 °C (from diethyl ether); $[\alpha]^{25}_D$ −20.9 (*c* 1.6, $CHCl_3$); IR (film) 1230, 1738, 1750 cm^{-1}, ^1H NMR (500 MHz) δ 1.64 (apparent q, 1H, $J_{4ax,3} = J_{4ax,4eq} = J_{4ax,5}$ = 12.0 Hz, H-4ax), 1.71−1.76 (m, 1H, H-4eq), 2.20−2.70 (m, 2 x OH), 3.38 (s, 3H, OCH_3), 3.53 (dd, 1H, $J_{6a,5}$ = 4.4, $J_{6a,6b}$ = 10.2 Hz, H-6a), 3.56 (dd, 1H, $J_{6b,5}$ = 5.4, $J_{6b,6a}$ =10.2 Hz, H-6b), 3.73 (brs, 1H, H-2), 3.88−3.93 (m, 1H, H-5), 3.94−4.00 (m, 1H, H-3), 4.58 (d, 1H, $J_{a,b}$ = 12.2 Hz, Bn-Ha), 4.62 (d, 1H, $J_{b,a}$ = 12.2 Hz, Bn-Hb), 4.79 (s, 1H, H-1), 7.27−7.39 (m, 5H, H-arom); ^{13}C NMR (50 MHz) δ 30.7 (C-4), 54.8 (OCH_3), 65.5, 67.3 and 68.8 (C-2, C-3 and C-5), 72.4 and 73.3 (C-6 and C−Bn), 101.3 (C-1), 127.5, 128.2 (C-arom), 137.8 (C-arom). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.72; H, 7.52.

Data for diacetate 7b: oily (98% yield); $[\alpha]^{25}_D$ −29.7 (*c* 0.4, $CHCl_3$); ^1H NMR (400 MHz) δ 1.77−1.96 (m, 2H), 2.03 (s, 3H), 2.16 (s, 3H), 3.41 (s, 3H), 3.55 (dd, 1H, *J* = 4.2, 10.3 Hz), 3.62 (dd, 1H, *J* = 5.7, 10.3 Hz), 4.03−4.12 (m, 1H), 4.58 (d,

1H, J = 12.1 Hz), 4.63 (d, 1H, J = 12.1 Hz), 4.77 (d, 1H, J = 1.7 Hz), 5.10−5.15 (m, 1H), 5.28 (ddd, 1H, J = 3.2, 5.1, 12.1 Hz), 7.26−7.40 (m, 5H); ^{13}C NMR (50 MHz) δ 20.9, 29.6 (2xC), 54.9, 66.7, 67.3, 67.9, 72.3, 73.3, 99.2, 127.4, 128.3, 131.7, 169.7, 170.0. Anal. Calcd for $C_{18}H_{24}O_7$: C, 61.35; H, 6.86. Found: C, 61.42; H, 6.88.

Epoxides 8 and 10. To a solution of **6** (0.18 g; 0.77 mmol) in CH_2Cl_2 was added *m*-CPBA (0.14 g; 0.80 mmol), at 0 °C, and the mixture was left at room temperature for 5 days. The solid was filtered off, and the organic layer was washed with 10% aqueous Na_2CO_3 and then brine until neutral. After drying (Na_2SO_4), the solvents were evaporated, and the crude residue was chromatographed on silica gel (hexane/acetone, 8:2), affording **8** (87.5 mg; 0.35 mmol) and **10** (60.0 mg; 0.24 mmol) in 77% overall yield.

Data for compound 8: oily; $[\alpha]^{25}_D$ −15.0 (*c* 0.6, $CHCl_3$); ^{1}H NMR (200 MHz) δ 1.82−1.92 (m, 2H), 2.98 (d, 1H, J = 3.9 Hz), 3.31−3.39 (m, 1H), 3.43 (dd, 1H, J = 4.3, 10.3 Hz), 3.47 (dd, 1H, J = 6.2, 10.3 Hz), 3.48 (s, 3H), 3.87−4.03 (m, 1H), 4.54 (d, 1H, J = 12.3 Hz), 4.60 (d, 1H, J = 12.3 Hz), 4.94 (s, 1H), 7.27−7.38 (m, 5H); ^{13}C NMR (125 MHz) δ 29.6, 50.8, 50.9, 55.4, 63.6, 72.0, 73.2, 95.6, 127.5, 128.3, 138.2. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.24; H, 7.27.

Data for compound 10: oily; $[\alpha]^{25}_D$ −20.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz) δ 1.89 (ddd, 1H, J = 1.3, 11.4, 14.5 Hz), 1.97 (dt, 1H, J = 2.3, 14.5 Hz), 3.34 (dd, 1H, J = 3.4, 4.3 Hz), 3.41−3.43 (m, 1H), 3.46 (dd, 1H, J = 5.4, 10.3 Hz), 3.47 (s, 3H), 3.53 (dd, 1H, J = 3.4, 10.3 Hz), 3.98−4.04 (m, 1H), 4.54 (d, 1H, J = 12.1 Hz), 4.60 (d, 1H, J = 12.1 Hz), 5.00 (d, 1H, J = 3.4), 7.27−7.38 (m, 5H); ^{13}C NMR (50 MHz) δ 29.6, 48.9, 49.5, 55.4, 63.0, 72.1, 73.2, 95.9, 127.5, 128.2, 138.2. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.04; H, 7.23.

Methyl 6-*O*-Benzyl-4-deoxy-α-L-*ara*-hexopiranoside (9). Typical Alkaline Hydrolysis Procedure. The epoxide **8** (60 mg; 0.24 mmol) suspended in 1 N NaOH was heated at 95 °C for 2 h. The reaction mixture was neutralized with glacial acetic acid, most of the water was evaporated, and the residue was extracted with $CHCl_3$ and washed with brine. The organic layer was dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel (hexane/acetone = 1/1) and gave pure **9** (58.6 mg, 93% yield): oily; $[\alpha]^{25}_D$ −29.3 (*c* 0.5, $CHCl_3$); IR (film) 3380 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.50−1.85 (m, 2 x OH), 1.63 (dt, 1H, $J_{4eq,3} = J_{4eq,5}$ = 2.8, $J_{4eq,4ax}$ = 14.3, Hz, H-4eq), 1.94−2.05 (m, 1H, H-4ax), 3.46 (s, 3H, OCH_3), 3.58 (d, 2H, $J_{6,5}$ = 3.8 Hz, H-6), 3.66 (brs, 1H, H-2), 3.90−3.95 (m, 1H, H-3), 4.15−4.22 (m, 1H, H-5), 4.58 (d, 1H, $J_{a,b}$ = 12.3 Hz, Bn-Ha), 4.62 (d, 1H, $J_{b,a}$ = 12.3 Hz, Bn-Hb), 4.77 (brs, 1H, H-1), 7.26−7.38 (m, 5H, H-arom); ^{13}C NMR (50 MHz) δ 29.9 (C-4), 55.9 (OCH_3), 63.9, 67.7 and 68.1 (C-2, C-3 and C-5), 72.9 and 73.7 (C-6 and C−Bn), 102.0 (C-1), 127.8, 127.9 and 128.6 (C-arom), 138.3 (C-arom). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.50; H, 7.48.

The epoxide **10** (40 mg; 0.16 mmol), treated under the same conditions for 20 h, afforded a mixture (0.14 mmol, 87% yield) of methyl pyranoside **9** (8.8 mg; 0.033 mmol) and methyl pyranoside **11** (28.4 mg; 0.106 mmol).

Data for methyl 6-*O*-benzyl-4-deoxy-α-L-*xylo*-hexopiranoside (11): oily; $[\alpha]^{25}_D$ −73.8 (*c* 0.5, $CHCl_3$); IR (film) 3375 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.50−1.80 (m, 3H, H-4ax and 2 x OH), 2.01 (ddd, 1H, $J_{4eq,5}$ = 2.0, $J_{4eq,3}$ = 4.8, $J_{4eq,4ax}$ = 10.7 Hz, H-4eq), 3.38−3.40 (m, 4H, H-2 and OCH_3), 3.51 (dd, 1H, $J_{6a,5}$ = 4.3, $J_{6a,6b}$ = 10.2 Hz, H-6a), 3.54 (dd, 1H, $J_{6b,5}$ = 6.3, $J_{6b,6a}$ = 10.2 Hz, H-6b), 3.85 (ddd, 1H, $J_{3,4eq}$ = 4.9, $J_{3,4ax}$ = 9.8, $J_{3,2}$ = 10.2 Hz, H-3), 3.94−4.00 (m, 1H, H-5), 4.59 (s, 2H, Bn-H), 4.83 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1), 7.27−7.40 (m, 5H, H-arom); ^{13}C NMR (100 MHz) ppm 29.6 (C-4), 55.3 (OCH_3), 67.4, 69.1 and 72.3 (C-2, C-3 and C-5), 73.4 and 74.4 (C-6 and Bn-C), 99.7 (C-1), 127.5, 127.6, 128.3 (C-arom), 138.2 (C-arom). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.78; H, 7.53.

Bromohydrin 12. To a solution of **6** (0.12 g; 0.52 mmol) in DMSO treated with water (0.02 g, 1.04 mmol), at 10 °C, was added NBS (0.18 g; 1.04 mmol) in one portion. After some minutes, a yellow color developed and the solution became quite warm. Stirring for 30 min was followed by quenching of the reaction mixture with saturated aqueous Na_2SO_3 and extraction with Et_2O. The organic layer was dried (Na_2SO_4) and filtered, the solvent was evaporated, and the crude residue was purified on silica gel (hexane/acetone = 6/4) to give the bromohydrin **12** (0.14 g, 85% yield): oily; $[\alpha]^{25}_D$ −41.9 (*c* 1.6, $CHCl_3$); ^{1}H NMR (500 MHz) δ 1.66 (dt, 1H, $J_{4eq,3} = J_{4eq,5}$ = 3.1, $J_{4eq,4ax}$ = 14.4, Hz, H-4eq), 2.28 (ddd, 1H, $J_{4ax,3}$ = 3.1, $J_{4ax,5}$ = 11.8, $J_{4ax,4eq}$ = 14.4, Hz, H-4ax), 3.43 (s, 3H, OCH_3), 3.56 (dd, 1H, $J_{6a,5}$ = 3.7, $J_{6a,6b}$ = 10.5 Hz, H-6a), 3.64 (dd, 1H, $J_{6b,5}$ = 6.0, $J_{6b,6a}$ = 10.5 Hz, H-6b) 4.02−4.05 (m, 1H, H-2), 4.13−4.18 (m, 1H, H-3), 4.22−4.28 (m, 1H, H-5), 4.61 (d, 1H, $J_{a,b}$ = 12.1 Hz, Bn-Ha), 4.64 (d, 1H, $J_{b,a}$ = 12.1 Hz, Bn-Hb), 4.98 (brs, 1H, H-1), 7.26−7.39 (m, 5H, H-arom); ^{13}C NMR (50 MHz) δ 29.9 (C-4), 46.0 (C-2), 56.0 (OCH_3), 60.6 and 68.9 (C-3 and C-5), 73.0 and 73.6 (C-6 and Bn-C), 102.0 (C-1), 127.8, 127.9 and 128.6 (C-arom$_r$), 138.1 (C-arom). Anal. Calcd for $C_{14}H_{19}O_5Br$: C, 50.77; H, 5.78. Found: C, 50.74; H, 5.75.

Epoxide 10 from Bromohydrin 12. To a suspension of NaH (13.5 mg, 0.54 mmol) in THF was slowly added a solution of bromohydrin **12** (0.12 g, 0.36 mmol), in the same solvent. The mixture was stirred at room temperature for 3 h, quenched with water, and extracted with CH_2Cl_2. The combined organic layers were washed with water until neutral, dried (Na_2SO_4), and evaporated to afford a crude residue that, after purification on silica gel (hexane/acetone = 6/4), gave the epoxide **10** (70.2 mg, 78% yield), identical by spectral data and physical properties with **10** obtained from the epoxidation of **6** with MCPBA.

Data for the Enantiomers of the Above Cited Products. Starting from the coupling product **3a**, all of the enantiomers of the products **4**−**11** were obtained. Their ^{1}H NMR and ^{13}C NMR spectra were superimposable to those already reported. **Enantiomer of 4**: oily, $[\alpha]^{25}_D$ +19.0 (*c* 2.5, $CHCl_3$). Anal. Calcd for $C_{17}H_{20}O_4S_2$: C, 57.93; H, 5.72. Found: C, 57.81; H 5.74. **Enantiomer of 5**: oily, $[\alpha]^{25}_D$ −41.5 (*c* 1.5, $CHCl_3$). Anal. Calcd for $C_{16}H_{20}O_3S_2$: C, 59.23; H, 6.21. Found: C, 59.11; H 6.23. **Enantiomer of C-1 epimer of 5**: oily, $[\alpha]^{25}_D$ −15.0 (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{16}H_{20}O_3S_2$: C, 59.23; H, 6.21. Found: C, 59.13; H 6.20. **Enantiomer of 6**: $[\alpha]^{25}_D$ −25.2 (*c* 1.5, $CHCl_3$). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.90; H, 7.77. **Enantiomer of 7a**: oily, $[\alpha]^{25}_D$ +18.0 (*c* 1.8, $CHCl_3$). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.75; H, 7.48. **Enantiomer of diacetate 7b**: oily,$[\alpha]^{25}_D$ +31.1 (*c* 1.5, $CHCl_3$). Anal. Calcd for $C_{18}H_{24}O_7$: C, 61.35; H, 6.86. Found: C, 61.45; H, 6.84. **Enantiomer of compound 8**: oily, $[\alpha]^{25}_D$ +18.5 (*c* 1.9, $CHCl_3$). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.06; H, 7.23. **Enantiomer of compound 10**: oily; $[\alpha]^{25}_D$ +21.5 (*c* 1.3, $CHCl_3$). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.10; H, 7.27. **Enantiomer of compound 9**: oily; $[\alpha]^{25}_D$ +31.0 (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.52; H, 7.53. **Enantiomer of compound 11**: oily; $[\alpha]^{25}_D$ +75.0 (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.78; H, 7.52.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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