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UNEQUIVOCAL DETERMINATION OF THE CHIRALITY OF THE 1-HYDROXYETHYL GROUP IN BRANCHED-CHAIN SUGARS BY A COMBINATION OF SYNTHETIC PATHWAYS*

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ABSTRACT

A principle for the determination of the chirality of a 1-hydroxyethyl group introduced into a glycosidulose by a combination of synthetic pathways is illustrated with benzyl 2,3-di-*O*-benzyl-β-L-*threo*-pentopyranosid-4-ulose. The simultaneous inversion of the configurations of C-4 and C-4[1] of 4-*C*-(1-hydroxyethyl) derivatives is also shown.

INTRODUCTION

Branched-chain sugars having a two-carbon branch, such as D-aldgarose[2,3] in aldgamycin E, L-pillarose[4,5] in pillaromycin A, and L-γ-octose[6] in isochinocyclin A, have been synthesized through the introduction of a two-carbon unit into the appropriate glycosiduloses. However, in most cases, these syntheses proceeded without confirmation, during intermediary steps, of the chiralities at both the branching point and in the branch, and finished with a comparison of the diastereoisomers synthesized and the natural specimen. Although the determination of the chirality in a branching group is generally considered to be difficult, we now describe a principle for the chemical determination of the chirality of a 1-hydroxyethyl branch by a combination of a few synthetic pathways.

RESULTS AND DISCUSSION

In general, a two-carbon unit is introduced into an appropriate glycosidulose by reaction with vinylmagnesium bromide[3,4,6], 2-lithio-2-methyl-1,3-dithiane[2,5], or a suitable Wittig reagent[4]. In the case of vinyl[7] and 2-methyl-1,3-dithianyl[8] derivatives, the configurations of epimeric products were determined by comparison of the chemical shifts, in the ^{13}C-n.m.r. spectra, of the branching α-carbon atoms. If the (*E*) and (*Z*) configurations of the Wittig reaction-products (the ethylidene derivatives,

*Branched-chain Sugars, Part XXV. For Part XXIV, see ref. 1.

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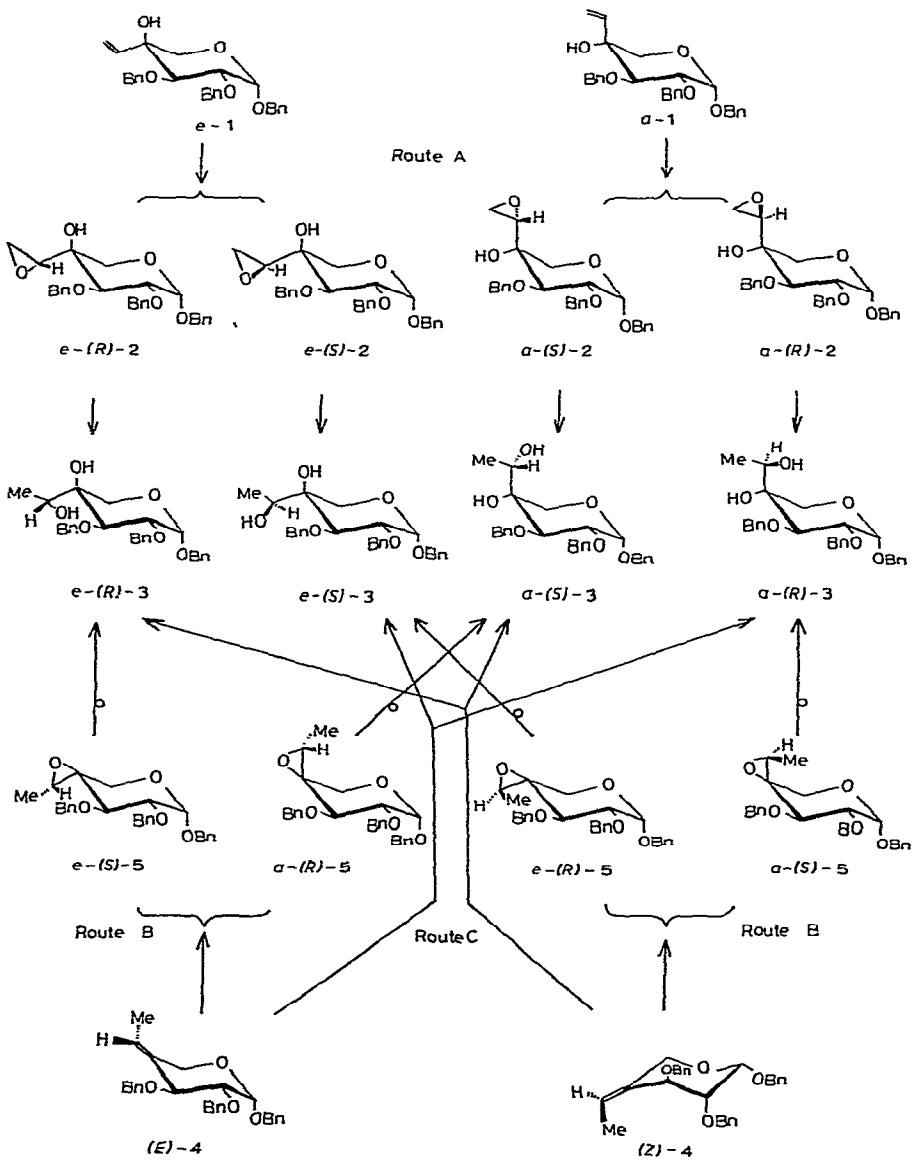
in this case) could be determined, the combination of two synthetic approaches from vinyl and ethylidene derivatives to 1-hydroxyethyl derivatives would disclose the chirality in the branch, as illustrated, with the corresponding derivatives from benzyl 2,3-di-*O*-benzyl-β-L-*threo*-pentopyranosid-4-ulose[9], in Scheme 1.



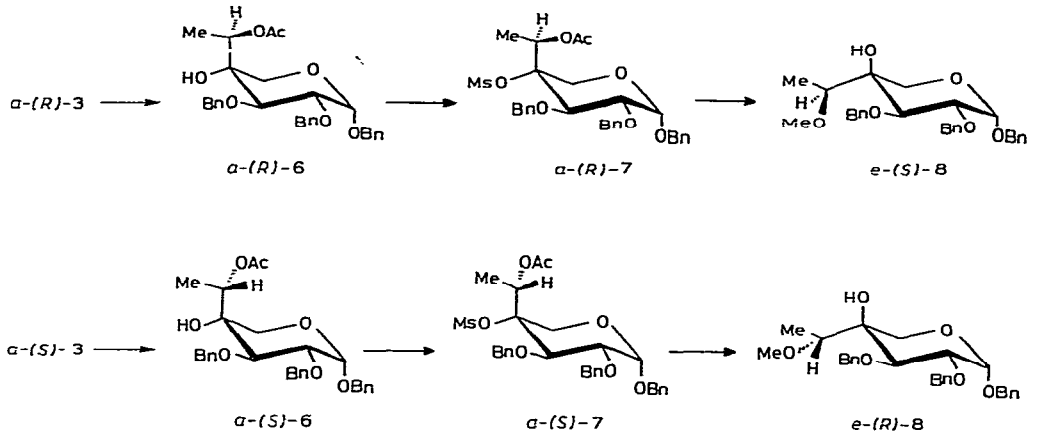
Scheme 1. The principle for the determination of the chirality of 1-hydroxyethyl groups by a combination of synthetic pathways.

Among four 1-hydroxyethyl derivatives (**3**), the equatorially (*e*) oriented (*R*) and (*S*) derivatives [*e*-(*R*)-**3** and *e*-(*S*)-**3**], obtainable from the equatorially oriented vinyl derivative (*e*-**1**) by Route A (successive epoxidation and reduction), should also be afforded by the (*E*)- and (*Z*)-vinyl derivatives [(*E*)-**4** and (*Z*)-**4** by Route B (successive epoxidation and alkaline ring-opening). Alternatively, they are directly obtainable by the osmium tetraoxide oxidation (Route C) of (*Z*)-**4** and (*E*)-**4**, respectively. Thus, the (*R*) and (*S*) configurations of *e*-**3** should be unequivocally determinable by a comparison of the products from routes A, B, and C. Analogous interrelations between these three routes will also be considered in the case of the axially (*a*) oriented (*S*) and (*R*) derivatives [*a*-(*S*)-**3** and *a*-(*R*)-**3**].

This principle was actually realized as follows. Epoxidation of benzyl 2,3-di-*O*-benzyl-4-*C*-vinyl-β-L-arabinopyranoside[7c] (*e*-**1**) with *m*-chloroperoxybenzoic acid gave the corresponding (*R*)- and (*S*)-epoxides [*e*-(*R*)-**2** and *e*-(*S*)-**2**] in 68% yield in the ratio of 1 : 14. Reduction of *e*-(*R*)-**2** and *e*-(*S*)-**2** with lithium aluminum hydride gave the corresponding 1-hydroxyethyl derivatives [*e*-(*R*)-**3** and *e*-(*S*)-**3**] in 70 and 86% yield, respectively. Similar epoxidation of benzyl 2,3-di-*O*-benzyl-4-*C*-vinyl-α-D-xylopyranoside[7c] (*a*-**1**) gave a mixture of the corresponding epoxides [*a*-(*S*)-**2** and *a*-(*R*)-**2**] in 91% yield; these could not be separated, but the ratio of the epimers was estimated to be 1.2 : 1, after conversion into the corresponding 4-*C*-(1-hydroxyethyl) derivatives [*a*-(*S*)-**3** and *a*-(*R*)-**3**]. Thus, four diastereoisomers of 4-*C*-(1-hydroxyethyl) derivatives were obtained.

On the other hand, reaction of benzyl 2,3-di-*O*-benzyl-β-L-*threo*-pentopyranosid-4-ulose[9] with ethyltriphenylphosphonium bromide and butyllithium gave the corresponding 4-*C*-ethylidene derivatives [(*E*)-**4** and (*Z*)-**4**] in 21.8 and 24.4% yield, respectively. It was found that one isomer exists in the $^4C_1$ conformation ($J_{1,2}$ 3.0, $J_{2,3}$ 9.0 Hz), and the other in the $^1C_4$ conformation ($J_{1,2}$ 1.5, $J_{2,3}$ 4.0 Hz). Therefore, the former was unambiguously assigned to be (*E*), and the latter, (*Z*). A similar inversion of the conformation had been found in the oximation of methyl 2,3-di-*O*-benzyl-6-deoxy-α-D-*xylo*-hexopyranosid-4-ulose[10].

Now, epoxidation of (*E*)-**4** with *m*-chloroperoxybenzoic acid gave the corresponding *spiro* epoxides [*e*-(*S*)-**5** and *a*-(*R*)-**5**] in 97% yield in the ratio of 2.3 : 1. Ring opening of the epoxides, *e*-(*S*)-**5** and *a*-(*R*)-**5**, in sodium hydroxide and dimethyl sulfoxide was accompanied by inversion at C-4', to give *e*-(*R*)-**3** and *a*-(*S*)-**3** in 83 and 81% yield, respectively. Similar epoxidation of (*Z*)-**4** gave a mixture of the corresponding *spiro* epoxides [*e*-(*R*)-**5** and *a*-(*S*)-**5**] in 97% yield. However, they could not be separated, and consequently, the ratio was determined to be 1 : 1.5 after conversion into the corresponding 4-*C*-(1-hydroxyethyl) derivatives [*e*-(*S*)-**3** and *a*-(*R*)-**3**]. Moreover, oxidative *cis*-hydroxylation of (*E*)-**4** with osmium tetraoxide gave *e*-(*S*)-**3** and *a*-(*R*)-**3** in 93% yield in the ratio of 1 : 4.8. Similar oxidation of (*Z*)-**4** gave *e*-(*R*)-**3** and *a*-(*S*)-**3**, as expected. The foregoing facts clearly show that the chirality in a 1-hydroxyethyl branch introduced onto a hemiacetal ring can be chemically determined by a combination of synthetic pathways, even if the (*E*) and (*Z*) configurations of geometric isomers are ambiguous.



Scheme 2. The simultaneous inversion of the configurations of C-4 and C-4[1] of 4-*C*-(1-hydroxyethyl) derivatives.

In general, Route A mainly affords equatorially substituted derivatives[7c], whereas Route C gives a preponderance of axial compounds. Therefore, simultaneous inversion at the branching point and at C-4[1] of **3** was next examined.

Base-catalyzed acetylation of *a*-(*R*)-**3** and *a*-(*S*)-**3** with acetic anhydride afforded the corresponding 1-acetoxyethyl derivatives [*a*-(*R*)-**6** and *a*-(*S*)-**6**] in good yields. Mesylation of *a*-(*R*)-**6** and *a*-(*S*)-**6** with methanesulfonyl chloride in pyridine gave the 4-*O*-mesyl derivatives [*a*-(*R*)-**7** and *a*-(*S*)-**7**] in 48 and 46% yield, respectively. Treatment of *a*-(*R*)-**7** and *a*-(*S*)-**7** in dimethyl sulfoxide with sodium methoxide gave the expected products [*e*-(*S*)-**8** and *e*-(*R*)-**8**], respectively, *via* the intermediate, *spiro* epoxides, in good yields. The configuration of *e*-(*S*)-**8** was confirmed by an independent synthesis, *i.e.*, the *O*-methylation of *e*-(*R*)-**3**. (When the yield in the *O*-sulfonylation of the tertiary hydroxyl group has been improved, such inversions may provide a good approach for the stereoselective introduction of a 1-hydroxyethyl group.)

EXPERIMENTAL

General methods. — Melting points are uncorrected. Solutions were evaporated under diminished pressure at a bath temperature not exceeding 45°. Specific rotations were measured in a 0.5-dm tube with a Carl Zeiss LEP-Al polarimeter, with chloroform as the solvent, unless otherwise stated. I.r. spectra were recorded with a Hitachi Model EPI-G2 spectrometer. N.m.r. spectra were recorded with a JEOL PS-100-MHz spectrometer for solutions in chloroform-*d* with tetramethylsilane as the internal standard, unless otherwise stated.

*Benzyl 2,3-di-*O*-benzyl-4-*C*-*[(E)- *and* -(Z)-*ethylidene*]-β-*L*-*threo*-pentopyranoside* [(E)-**4** *and* (Z)-**4**]. — To a solution of ethyltriphenylphosphonium bromide

(8.00 g, 21 mmol) in ether (80 mL) in a three-necked, round-bottomed flask equipped with a Dimroth condenser, a stirrer, and a dropping funnel was added a hexane solution of butyllithium (10%, 20.4 mL) with stirring, under an argon atmosphere. After stirring for 1 h, benzyl 2,3-di-*O*-benzyl-β-L-*threo*-pentopyranosid-4-ulose (5.86 g, 14 mmol) in ether was added dropwise to the orange-colored solution, with stirring. After 1 h, the mixture was poured into water, and the resulting solution was extracted with ether. The extract was processed in the usual way, and separation of the products on a column of silica gel with 20:1 hexane–ethyl gave (*E*)-**4** (1.35 g, 22.4%) and (*Z*)-**4** (1.51 g, 25.0%) as syrups.

(*E*)-**4**: $[\alpha]_D$ +225° (*c* 1.2); n.m.r.: δ 7.5–7.1 (m, 15 H, 3 Ph), 5.79 (bq, 1 H, $J_{4^1,4^2}$ 7.0 Hz, CH-4^1), 5.1–5.4 (m, 6 H, 3 CH_2Ph), 4.93 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1), 4.35 (bd, 1 H, $J_{2,3}$ 9.0 Hz, H-3), 4.26 and 4.18 (ABq, 2 H, *J* 13.0 Hz, H-5*e*,5*a*), 3.53 (dd, 1 H, H-2), and 1.65 (bd, 3 H, Me-4^2); and long-range couplings of $J_{5a,4^2}$, $J_{5a,4^1}$, $J_{3,4^2}$, and $J_{3,4^1}$ of <0.8 Hz were observed.

Anal. Calc. for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 77.80; H, 7.22.

(*Z*)-**4**: $[\alpha]_D$ +134° (*c* 2.1); n.m.r.: δ 7.4–7.1 (m, 15 H, 3 Ph), 5.78 (bq, 1 H, $J_{4^1,4^2}$ 7.0 Hz, CH-4^1), 5.1–4.2 (m, 6 H, 3 CH_2Ph), 4.79 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.35 (dd, 1 H, $J_{2,3}$ 4.0 Hz, H-3), 4.31 and 4.06 (ABq, 2 H, J 12.6 Hz, H-5*e*,5*a*), 3.53 (dd, 1 H, H-3), and 1.64 (bd, 3 H, Me-4^2); and long-range couplings, as in the case of (*E*)-**4**, were observed.

Anal. Calc. for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 77.96; H, 7.36.

Route A

Benzyl 2,3-di-O-*benzyl-4*-C-[(R)- *and* -(S)-*oxiran-2-yl*]-β-L-*arabinopyranoside* [e-(R)-**2** *and* e-(S)-**2**]. — A solution of benzyl 2,3-di-*O*-benzyl-4-*C*-vinyl-β-L-arabinopyranoside[7c] (*e*-**1**) (1.3 g, 2.9 mmol) and *m*-chloroperoxybenzoic acid (1.55 g, 9 mmol) in 1,2-dichloroethane (10 mL) was boiled under reflux for 2 h, and cooled. The mixture was diluted with 1,2-dichloroethane, washed successively with aqueous sodium sulfite (10%), sodium hydroxide (6%), and water, dried (magnesium sulfate), and evaporated to a syrup. Separation of the syrup on a column of silica gel with 10:1 hexane–ethyl acetate gave *e*-(*R*)-**2** (60 mg, 4.5%) and *e*-(*S*)-**2** (850 mg, 63%) in the ratio of 1:14.

e-(*R*)-**2**: syrup, $[\alpha]_D$ +97.1° (*c* 1.0); n.m.r.: δ 7.6–7.0 (m, 15 H, 3 Ph), 4.90 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.98–4.44 (m, 6 H, 3 CH_2Ph), 4.03 (d, 1 H, $J_{2,3}$ 9.8 Hz, H-3), 3.86 (dd, 1 H, H-3), 3.80 and 3.41 (ABq, 2 H, *J* 12.8 Hz, H-5*e*,5*a*), 2.88, 2.63, and 2.56 (each dd, 3 H, *J* 5.5, 4.0, and 2.8 Hz, H-4^1,4^2).

Anal. Calc. for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.57; H, 6.47.

e-(*S*)-**2**: syrup, $[\alpha]_D$ +71.6° (*c* 1.0); n.m.r.: δ 7.5–7.1 (m, 15 H, 3 Ph), 4.90 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1), 5.02–4.44 (m, 6 H, (CH_2Ph), 3.98 (d, 1 H, $J_{2,3}$ 9.8 Hz, H-3), 3.86 (dd, 1 H, H-2), 3.79 and 3.51 (ABq, 2 H, *J* 12.1 Hz, H-5*e*,5*a*), 2.79 and 2.59 (d and t, 3 H, *J* 4.4 and 8.0 Hz, H-4^1,4^2), and 2.42 (bs, 1 H, OH).

Anal. Calc. for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.21; H, 6.60.

Benzyl 2,3-di-O-*benzyl-4*-C-[(S)- *and* -(R)-*oxiran-2-yl*]-α-D-*xylopyranoside*

[a-(S)-**2** *and* a-(R)-**2**]. — Epoxidation of benzyl 2,3-di-*O*-benzyl-4-*C*-vinyl-α-D-xylopyranoside[7c] (*a*-**1**) as just described gave a mixture of *a*-(S)-**2** and *a*-(*R*)-**2**, as a syrup, in 91% yield. Because they could not be separated, the ratio was estimated to be 1.2:1 after conversion into *a*-(*S*)-**3** and *a*-(*R*)-**3**.

*Benzyl 2,3-di-*O*-benzyl-*4-C-[(R)- *and* -(S)-(*1-hydroxyethyl*)]-β-L-*arabinopyranoside* [e-(R)-**3** *and* e-(R)-**3**]. — A suspension of *e*-(*R*)-**2** (30 mg, 65 μmol) and lithium aluminum hydride (84 μmol) in anhydrous oxolane was stirred for 2 h at room temperature, small amounts of ethyl acetate and water were added (to decompose the excess of the hydride), and the mixture was filtered. The filtrate was evaporated, and the residual syrup was extracted with chloroform. The extract was processed in the usual way, and purification of the product by preparative t.l.c. with 3:1 hexane–ethyl acetate gave pure *e*-(*R*)-**3** as a syrup (22 mg) in 73% yield: $[\alpha]_D$ +121.9° (*c* 0.5); n.m.r.: δ 7.6–7.2 (m, 15 H, 3 Ph), 5.08–4.42 (m, 6 H, 3 CH_2Ph), 4.90 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 4.01 (d, 1 H, $J_{2,3}$ 9.0 Hz, H-3), 3.90 (dd, 1 H, H-2), 3.70 and 3.54 (ABq, 2 H, *J* 12.0 Hz, H-5*e*,5*a*), 3.90 (q, 1 H, $J_{4^1,4^2}$ 7.0 Hz, H-4^1), 2.90 (bs, 2 H, OH), and 1.02 (d, 3 H, Me-4^2).

Anal. Calc. for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 71.84; H, 6.96.

In a similar way, *e*-(*S*)-**2** was converted into *e*-(*S*)-**3** as a syrup in 86% yield; $[\alpha]_D$ +184.5° (*c* 2.7); n.m.r.: δ 7.6–7.1 (m, 15 H, 3 Ph), 5.10–4.42 (m, 6 H, 3 CH_2Ph), 4.89 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.26 (d, 1 H, $J_{2,3}$ 9.8 Hz, H-3), 3.93 (dd, 1 H, H-2), 3.94 and 3.46 (ABq, 2 H, *J* 12.2 Hz, H-5*e*,5*a*), 3.66 (q, 1 H, $J_{4^1,4^2}$ 7.0 Hz, H-4^1), 2.76 (bs, 2 H, OH), and 1.15 (d, 3 H, Me-4^2).

Anal. Calc. for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94; Found: C, 72.22; H, 7.03.

*Benzyl 2,3-di-*O*-benzyl-4-*C-[(S)- *and* -(R)-(*1-hydroxyethyl*)]-α-D-*xylopyranoside* [a-(S)-**3** *and* a-(R)-**3**]. — Reduction of a mixture (150 mg) of *a*-(*S*)-**2** and *a*-(*R*)-**2** with $LiAlH_4$ as before, and separation of the products by preparative t.l.c. with 3:1 hexane–ethyl acetate, gave *a*-(*S*)-**3** (34 mg, 22.6%) and *a*-(*R*)-**3** (28 mg, 18.6%) as syrups.

a-(*S*)-**3**: $[\alpha]_D$ +121° (*c* 0.91); n.m.r.: δ 7.5–7.0 (m, 15 H, 3 Ph), 5.04–4.24 (m, 6 H, 3 CH_2Ph), 4.76 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.01 (dd, 1 H, $J_{5e,5a}$ 12.0, $J_{3,5e}$ 1.1 Hz, H-5*e*), 3.76 (d, 1 H, H-5*a*), 3.72 (dd, 1 H, $J_{2,3}$ 4.8 Hz, H-2), 3.70 (q, 1 H, $J_{4^1,4^2}$ 6.8 Hz, H-4^1), 3.59 (dd, 1 H, H-3), 2.35 (bs, 1 H, OH), and 1.12 (d, 1 H, Me-4^2).

Anal. Calc. for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 72.50; H, 6.96.

a-(*R*)-**3**: $[\alpha]_D$ +192° (*c* 1.4); n.m.r.: δ 7.5–7.1 (m, 15 H, 3 Ph), 4.92–4.48 (m, 6 H, 3 CH_2Ph), 4.79 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1), 4.05 (q, 1 H, $J_{4^1,4^2}$ 7.0 Hz, H-4^1), 3.97 (d, 1 H, $J_{2,3}$ 8.8 Hz, H-3), 3.72 and 3.55 (ABq, 2 H, *J* 12.8 Hz, H-5*e*,5*a*), 3.68 (dd, 1 H, H-2), and 1.16 (d, 3 H, Me-4^2).

Anal. Calc. for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 71.84; H, 6.94.

Route B

*Benzyl 4,4^1-anhydro-2,3-di-*O*-benzyl-4-*C-[(S)-(*1-hydroxyethyl*)]-β-L-*arabinopyranoside* [e-(S)-**5**] *and* -*4*-C-[(R)-(*1-hydroxyethyl*)]-α-D-*xylopyranoside* [a-(R)-**5**]. — A solution of (*E*)-**4** (200 mg, 0.46 mmol) and *m*-chloroperoxybenzoic acid (120 mg,

0.69 mmol) in 1,2-dichloroethane (8 mL) was stirred overnight at room temperature, and then washed successively with 10% sodium sulfite (twice), saturated sodium hydrogencarbonate, and water. The usual processing of the extract, and separation of the products by preparative t.l.c. with 3:1 hexane–ethyl acetate, gave *e*-(*S*)-**5** and *a*-(*R*)-**5** in 67.5 (140 mg) and 28.9% (60 mg) yield, respectively.

e-(*S*)-**5**: m.p. 84–85°, $[\alpha]_D$ +174.7° (*c* 0.67); n.m.r.: δ 7.5–7.2 (m, 15 H, 3 Ph), 5.00–4.46 (m, 6 H, 3 CH_2Ph), 4.94 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1), 4.06 (d, 1 H, $J_{2,3}$ 9.4 Hz, H-3), 3.77 (dd, 1 H, H-2), 4.02 and 3.42 (ABq, 2 H, *J* 12.6 Hz, H-5*e*,5*a*), 3.22 (q, 1 H, $J_{4^1,4^2}$ 6.9 Hz, H-4^1), and 1.20 (d, 3 H, Me-4^2).

Anal. Calc. for $C_{28}H_{30}O_5$: C, 75.31; H, 6.77. Found: C, 75.13; H, 6.71.

a-(*R*)-**5**: syrup; $[\alpha]_D$ +266° (*c* 2.6); n.m.r.: δ 7.5–7.0 (m, 15 H, 3 Ph), 5.07–4.40 (m, 6 H, 3 CH_2Ph), 4.85 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.21 (d, 1 H, $J_{2,3}$ 10.0 Hz, H-3), 4.21 (dd, 1 H, H-2), 4.01 and 3.30 (ABq, 2 H, *J* 12.0 Hz, H-5*e*,5*a*), 3.57 (q, 1 H, $J_{4^1,4^2}$ 6.0 Hz, H-4^1), and 1.30 (d, 3 H, Me-4^2).

Anal. Calc. for $C_{28}H_{30}O_5$: C, 75.31; H, 6.77. Found: C, 75.10; H, 6.75.

Benzyl 4,4^1*-anhydro-2,3-di*-O-*benzyl-4*-C-[(R)-(*1-hydroxyethyl*)]-*β*-L-*arabino-pyranoside* [e-(R)-**5**] *and -4*-C-[(S)-(*1-hydroxyethyl*)]-*α*-D-*xylopyranoside* [a-(S)-**5**]. — Epoxidation of (*Z*)-**4** as before gave a mixture of *e*-(*R*)-**5** and *a*-(*S*)-**5** as a syrup in 96.7% yield. However, these could not be separated, and the ratio was determined to be 1:1.5 after conversion into *e*-(*S*)-**3** and *a*-(*R*)-**3**.

Ring-opening of 4,4^1*-anhydro derivatives.* — A solution of *e*-(*S*)-**5** (140 mg, 0.31 mmol) in Me_2SO (5 mL) and 2M aqueous sodium hydroxide (1 mL) was refluxed for 2 days, cooled, and extracted with ether. The usual processing of the extract, and purification of the product by preparative t.l.c. with 4:1 benzene–acetone, gave pure *e*-(*R*)-**3** (120 mg, 82.4%). Similarly, *a*-(*S*)-**3** was obtained in 80.6% yield from *a*-(*R*)-**5**.

Treatment of a mixture of *e*-(*R*)-**5** and *a*-(*S*)-**5** (140 mg, 0.31 mmol) in the same way, and separation of the products by preparative t.l.c. with 4:1 benzene–acetone, gave *e*-(*S*)-**3** and *a*-(*R*)-**3** in 35% (51 mg) and 23% (34 mg) yield, respectively.

Route C

Oxidation of (E)-**4** *and* (Z)-**4** *with osmium tetraoxide.* — To a solution of 4-methylmorpholine *N*-oxide dihydrate (65.8 mg, 0.43 mmol) and osmium tetraoxide (5 mg) in *tert*-butanol (1 mL) and 5:2 acetone–water (7 mL) was added dropwise a solution of (*E*)-**4** (170 mg, 0.39 mmol) in acetone, and the mixture was stirred overnight at room temperature. Hydrogen sulfide was bubbled through the mixture, and the black precipitate formed was filtered off, the filtrate evaporated, and the residue extracted with chloroform. The usual processing of the extract, and purification of the product by preparative t.l.c. with 3:1 hexane–ethyl acetate, gave *e*-(*S*)-**3** and *a*-(*R*)-**3** in 77.4% (142 mg) and 16.4% (30 mg) yield, respectively.

Similar treatment of (*Z*)-**4** gave *e*-(*R*)-**3** and *a*-(*S*)-**3** in 15 and 26% yield, respectively.

Inversion of configuration of C-4 and C-4[1]

Benzyl 4-C-[(R)- *and* -(S)-(*1-acetoxyethyl*)]-*2,3-di*-O-*benzyl*-α-D-*xylopyranoside* [a-(R)-**6** *and* a-(S)-**6**]. — Base-catalyzed acetylation of *a*-(*R*)-**2** (0.8 g, 1.7 mmol) with acetic anhydride and pyridine gave the corresponding 4^1-acetate [*a*-(*R*)-**6**] as a syrup (0.75 g, 86%) yield, $[\alpha]_D$ +159° (*c* 2.4).

Anal. Calc. for $C_{30}H_{34}O_7$: C, 71.13; H, 6.77. Found: C, 70.91; H, 6.42.

Similar acetylation of *a*-(*S*)-**2** gave *a*-(*S*)-**6** as a syrup in 79% yield, $[\alpha]_D$ +176.7° (*c* 4.8).

Anal. Calc. for $C_{30}H_{34}O_7$: C, 71.13; H, 6.77. Found: C, 71.36; H, 6.81.

Benzyl 4-C-[(R)- *and* -(S)-(*1-acetoxyethyl*)]-*2,3-di*-O-*benzyl-4*-O-(*methylsulfonyl*)-α-D-*xylopyranoside* [a-(R)-**7** *and* a-(S)-**7**]. — A solution of *a*-(*R*)-**6** (1 g, 1.97 mmol) and methanesulfonyl chloride (2 g, 17.5 mmol) in pyridine (4 mL) was kept for 1 week at room temperature, poured into ice–water, and the solution extracted with chloroform. The usual processing of the extract, and purification of the product by preparative t.l.c. with 10:1 hexane–ethyl acetate, gave pure syrupy *a*-(*R*)-**7** (560 mg, 48.5% yield); $[\alpha]_D$ +55° (*c* 1.7); n.m.r.: δ 7.50–6.90 (m, 15 H, 3 Ph), 5.58 (q, 1 H, $J_{4^1,4^2}$ 6.7 Hz, H-4^1), 4.88–4.38 (m, 6 H, 3 CH_2Ph), 4.74 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.46 (d, 1 H, $J_{2,3}$ 9.0 Hz, H-3), 4.45 and 4.02 (ABq, 2 H, *J* 11.7 Hz, H-5*e*,5*a*), 3.84 (dd, 1 H, H-3), 2.90 (s, 3 H, OMe), 1.85 (s, 3 H, OAc), and 1.34 (d, 3 H, Me-4^2).

Anal. Calc. for $C_{31}H_{36}O_9S$: C, 63.68; H, 6.21; S, 5.48. Found: C, 63.29; H, 6.11; S, 5.26.

Similarly, *a*-(*S*)-**7** was obtained from *a*-(*S*)-**6** in 46% yield; m.p. 103–106°, $[\alpha]_D$ +52° (*c* 2.0); n.m.r.: δ 7.50–7.00 (m, 15 H, 3 Ph), 5.38 (q, 1 H, $J_{4^1,4^2}$ 7.2 Hz, H-4^1), 4.90–4.36 (m, 6 H, 3 CH_2Ph), 4.74 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.41 (d, 1 H, $J_{2,3}$ 8.2 Hz, H-3), 4.49 and 4.01 (ABq, 2 H, *J* 12.0, H-5*e*,5*a*), 3.65 (dd, 1 H, H-3), 2.96 (s, 3 H, OMs), 2.04 (s, 3 H, OAc), and 1.42 (d, 3 H, Me-4^2).

Anal. Calc. for $C_{31}H_{36}O_9S$: C, 63.68; H, 6.21; S, 5.48. Found: C, 63.42; H, 6.05; S, 5.35.

Benzyl 2,3-di-O-*benzyl-4*-C-[(S)- *and* -(R)-(*1-methoxyethyl*)-β-L-*arabinopyranoside* [e-(S)-**8** *and* e-(R)-**8**]. — A solution of *a*-(*R*)-**7** (0.2 g, 0.34 mmol) in methanol containing sodium (50 mg) and Me_2SO (10 mL) was heated overnight at 80°, cooled, and evaporated, and the residue was extracted with ether. The usual processing of the extract, and purification of the product by preparative t.l.c. with 3:1 hexane–ethyl acetate, gave pure *e*-(*S*)-**8** as a syrup (134 mg; yield, 81.8%) $[\alpha]_D$ +94.8° (*c* 1.0); n.m.r.: δ 7.5–7.0 (m, 15 H, 3 Ph), 5.10–4.44 (m, 6 H, 3 CH_2Ph), 4.94 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.32 (d, 1 H, $J_{2,3}$ 9.8 Hz, H-3), 3.91 and 3.53 (ABq, 2 H, *J* 12.0 Hz, H-5*e*,5*a*), 3.86 (dd, 1 H, H-2), 3.43 (q, 1 H, $J_{4^1,4^2}$ 6.4 Hz, H-4^1), 3.28 (s, 3 H, OMe), and 1.15 (d, 3 H, Me-4^2).

Anal. Calc. for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found: C, 72.41; H, 7.09.

In a similar way, *e*-(*R*)-**8** was obtained from *a*-(*S*)-**7**, in 73% yield, as a syrup, $[\alpha]_D$ +155.9° (*c* 3.9); n.m.r.: δ 7.6–7.2 (m, 15 H, 3 Ph), 5.07–4.47 (m, 6 H, 3 CH_2Ph), 4.88 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 4.04 (d, 1 H, $J_{2,3}$ 9.5 Hz), 3.92 (dd, 1 H, H-3), 3.78

and 3.46 (ABq, 2 H, J 12.1 Hz, H-5*e*,5*a*), 3.42 (q, 1 H, $J_{4^1,4^2}$ 7.2 Hz, H-4^1), 3.34 (s, 3 H, OMe), and 0.98 (d, 3 H, Me-4^2).

Anal. Calc. for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found: C, 72.33; H, 7.31.

The structure of *e*-(*S*)-**8** was ascertained by an independent synthesis, as follows. To a solution of *e*-(*S*)-**3** (160 mg, 0.34 mmol) in *N*,*N*-dimethylformamide were successively added sodium hydride (24 mg, 0.34 mmol) and methyl iodide (48 mg, 0.34 mmol), and the mixture was stirred for 1 h at room temperature, poured into water, and extracted with chloroform. The usual processing of the extract, and separation of the products by preparative t.l.c. with 4:1 benzene–acetone gave *e*(*S*)-**8** (65 mg; yield, 38.8%) which was identical with that already obtained.

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