Chiral Multifunctional Isoprene Units by Ring-Contraction of Riboside Oxiranes

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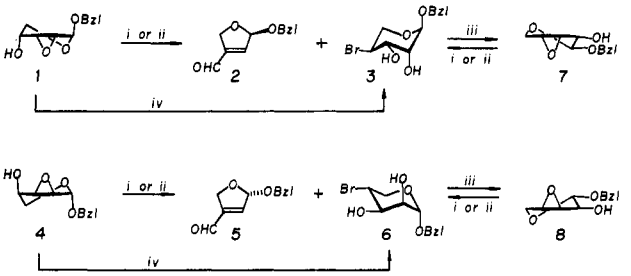
Lithium bromide induced ring-contraction of benzyl 2,3- and 3,4-anhydro-β-D(and L)-ribopyranoside (1 and 4) in HMPA/toluene or tetramethylurea (TMU)/toluene gave (*R*)(and *S*)-2-(benzyloxy)-2,5-dihydrofuran-4-carboxaldehyde (**2** and **5**) together with a small amount of benzyl 4-bromo-4-deoxy-β-L(and D)-lyxopyranoside (**3** and **6**). The latter compound was formed with lithium bromide in 1,1,1-trichloroethane. Benzyl 2,3- and 3,4-anhydro-2-deuterio-β-L-ribopyranoside (**4d** and **8d**) gave the deuterated aldehyde **5d**, which carried a vinylic deuterium atom, whereas benzyl 2,3-anhydro-4-deuterio-β-L-ribopyranoside (**4d'**) gave the nondeuterated aldehyde **5**. On the basis of these experiments, the mechanism of the ring-contraction was postulated.

The development of chiral synthons for use in enantioselective synthesis is of current interest. In a preliminary account of the present work, the aldehydes **2** and **5** were used as dienophiles in an enantiospecific Diels–Alder reaction with cyclopentadiene.[1] We also reported the stereospecific reduction of **1** and **4**, which gave the corresponding 3-deoxy compounds.[2] Lithium bromide/HMPA (or TMU)-induced ring-contraction of epoxycyclohexanols leads to cyclopentenecarboxaldehydes in high yield[3] and a mechanistic investigation of this reaction has been performed.[4] The ready availability of enantiomerically pure epoxy alcohols from sugars[5] led us to investigate the possibility of preparing chiral aldehydes by a route similar to that used for the cyclopentene aldehydes. To the best of our knowledge, no previous report has appeared on the preparation of chiral α,β-unsaturated aldehydes by ring-contraction of sugar derivatives, although the preparation of other branched sugar derivatives by ring-contraction of pyranosides has been reported.[6]

Lithium bromide/HMPA (or TMU)-induced ring-contraction of the benzyl 2,3-anhydro-β-D-ribopyranoside (**1**)[7] (or the L sugar **4**[2]) gave (*R*)-2-(benzyloxy)-2,5-dihydrofuran-4-carboxaldehyde (**2**) (or the *S* aldehyde **5**) in 34% yield, together with a small amount of benzyl 4-bromo-4-deoxy-β-D-lyxopyranoside (**3**) (or the L sugar **6**) and polymeric material (Scheme I).

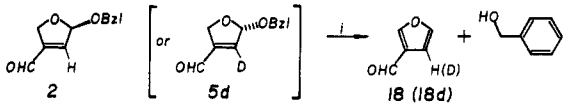
Although the yield in the reaction was quite modest, the fact that **2** and **5** are *chiral isoprene units* with unique structural characteristics and of potential for the enantiospecific synthesis of natural products makes this a procedure of merit, especially because of the easy preparation of the epoxy alcohols **1** and **4** (60% overall yield from arabinose[2,7]). Furthermore, **2** (or **5**) can be isolated by a simple filtration through silica gel because **2** moves much faster on the column than the byproducts (**3** and the polymeric material). In order to investigate the stability of **2**, it was resubmitted to the reaction conditions and recovered by normal workup. Chromatography gave pure

Scheme I[a]



[a] (i) LiBr, TMU, refluxing toluene, 8 min. (ii) LiBr, HMPA, toluene, 105 °C; 7 min. (iii) MeONa, MeOH. (iv) LiBr, refluxing Cl_3CCH_3, 70 min.

Scheme II[a]



[a] (i) H^+ resin, CH_2Cl_2, preparative gas chromatography.

2 in virtually quantitative yield, which clearly shows that **2** is stable under these reaction conditions. The polymer formation that accounts for nearly $^2/_3$ of the product must accordingly be the result of the reaction of some unstable intermediate (Scheme III). Treatment of **1** (or **4**) with lithium bromide in 1,1,1-trichloroethane (proton donor toward I or J in Scheme III) gave the bromolyxoside **3** (or **6**) without significant formation of the aldehyde **2** (or **5**). Addition of methanolic sodium methoxide to the crude reaction mixture followed by chromatography gave pure **7** (or **8**) in approximately 50% overall yield. Treatment of **7** (or **8**) with the lithium bromide/HMPA (or TMU) reagent gave approximately the same reaction mixture as with **1** (or **4**). The reason for this will be discussed below. In the synthesis of cyclopentene aldehydes from epoxycyclohexanols,[3,4] hexamethylphosphoric triamide (HMPA) in toluene was used as solubilizing agent for lithium bromide. Because of the carcinogenic nature of HMPA, we searched for a safe substitute. *N,N,N',N'*-Tetramethylurea (TMU) gave essentially the same product mixture as did HMPA in the present reaction. This also applies to the synthesis of cyclopentene aldehydes.[4]

The structure of the aldehyde **2** (or **5**) could not be determined with certainty by NMR methods since all proton–proton coupling constants are of the same relative magnitude, and all of the dihydrofuran ring protons show mutual spin–spin coupling. The number of possible structures for the aldehyde is however limited to two, since

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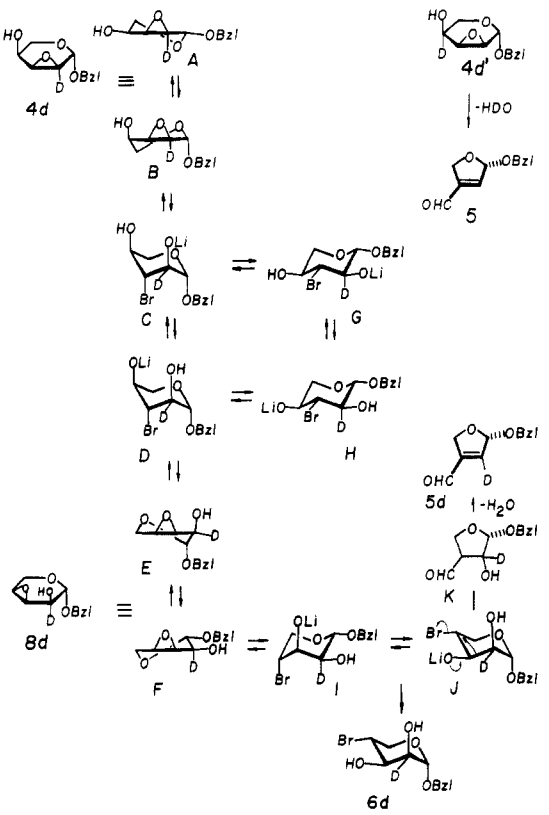
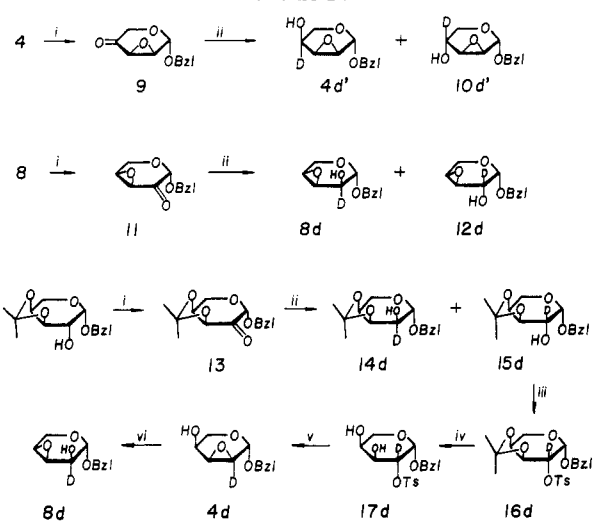
0022-3263/86/1951-3927$01.50/0

Scheme III



Scheme IV[a]



[a] (i) Me_2SO, $(COCl)_2$, CH_2Cl_2, −60 °C, 15 min, $(i\text{-}Pr)_2EtN$. (ii) $NaBD_4$, EtOH, 45 min. (iii) $H_3CC_6H_4SO_2Cl$, pyridine. (iv) $HClO_4$, H_2O. (v) MeONa, MeOH. (vi) LiBr, refluxing Cl_3CCH_3, 70 min, then MeONa, MeOH.

acid treatment of either enantiomer gave furan-3-carboxaldehyde (**18**) by 1,4-elimination of benzyl alcohol. Aldehyde **5d** gave the labeled furanaldehyde (**18d**) (Scheme II).

The enantiomeric purity of **2** and **5** was demonstrated by NMR, using the chiral shift reagent tris[(3-heptafluoropropyl)hydroxymethylene)-D-camphorato]europium(III). Well-resolved signals corresponding to **5** could not be detected in the spectrum of **2** and vice versa. The structure of **7** (or **8**) was determined by ^1H NMR double resonance experiments and was corroborated by the fact that the ^1H NMR spectrum of the ketone **11** (prepared by oxidation of **8**) revealed a singlet for the anomeric proton. The position of the bromine atom in **3** (or **6**) was also determined by NMR. The ^1H-4 signal was identified by double resonance and the ^{13}C-4 signal was obvious from the chemical shift (δ 49.8 ppm). A ^1H–^{13}C correlated 2D-experiment established the position of the bromine atom.

In order to get some idea about the mechanism of the reaction and to secure the structure of the aldehydes **2** and **5**, we prepared some specifically deuterated epoxy sugars (**4d**, **4d′**, **8d**, Scheme IV) for use as starting materials. It turned out that **4d** and **8d** (deuterium label on C-2) gave the aldehyde **5d** carrying a vinylic deuterium atom. On the other hand, **4d′** (deuterium label on C-4) gave **5** that had lost the deuterium label. These experiments, together with the facts that the 4-bromolyxoside **6** was formed from **4** as a byproduct, and that epoxide **8** functions equally well as starting material for the preparation of **5**, give certain indications about the reaction route. Nucleophilic attack on sugar epoxides is governed by the Fürst–Plattner rule,[5] so that the primary product (conformer) is formed with the new substituents in a 1,2-diaxial relationship. It is well-known that 2,3-oxirane ribosides (such as **4d** and **4d′**; Scheme III) react with bromide ion (and other nucleophiles) in position 3 of the sugar ring.[5]

Ring-contraction of the initially formed 3-bromo-3-deoxyxyloside alcoholate would give a mixture of two aldehydes by participation of the lithium alcoholate in either position 2 or 4 of the pyranosidic ring (cf. G and H; Scheme III). However, as shown by deuterium labeling, neither of these routes leds to isolable aldehydes. An aldehyde carrying a formyl deuterium would be the result of a rearrangement of **4d′** via a conformation corresponding to H in Scheme II. Instead, these alcoholates are probable intermediates en route to the 3,4-oxirane riboside **8d**, which in turn reacts with bromide ion in position 4. This is a well-known mode of reaction of 3,4-oxirane ribosides with nucleophiles.[5] The resulting 4-bromo-4-deoxylyxoside alcoholate (I) is, after a conformational flip to J, properly arranged for expulsion of bromide ion by the migrating ring carbon atom (C-2), thus forming K and then **5d** by elimination of water. In a side reaction, the water thus formed protonates I and/or J to give benzyl 4-bromo-4-deoxy-2-deuterio-α-L-lyxopyranoside (**6d**). When **8** was used as starting material (instead of **4**), virtually the same yield (34%) of the aldehyde **5** was obtained. This indicates that there are rapid equilibria among the compounds A–J (Scheme III). It should be noted that of all the intermediates C, D, G, H, I, and J, the latter should be the most stable one due to the axial orientation of the anomeric oxygen atom (anomeric effect[8]) and to the fact that two of the remaining three substituents are in equatorial positions. This is corroborated by the small $J_{1,2}$ value (1.55 Hz) of **6**, which is indicative of a $^4C_1$ conformation. Therefore, under these equilibrating conditions, both **4d** and **8d** are eventually transformed into J, which gets protonated to form **6d** or rearranges to K en route to **5d**.

The formation of **3** from **1** can help to explain some odd results in the literature.[9] Thus, when methyl 2,3-anhydro-β-D-ribopyranoside was treated with phenylacetylenelithium in the presence of lithium bromide, a bromo sugar was formed as a byproduct, together with the expected 3-phenylacetylene xyloside. The authors (unwillingly) concluded that the compound was methyl 2-bromo-2-deoxy-β-D-arabinopyranoside, formed by direct bromide ion attack on the epoxide ring. We suggest that the compound obtained is instead methyl 4-bromo-4-deoxy-α-L-lyxopyranoside and that it was formed by a

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route similar to that shown in Scheme III for the formation of J (and then **6d**) from **4d**.

The deuterium-labeled oxirane sugars (**4d, 8d, and 4d'**) were prepared as follows (Scheme IV). The 2,3-epoxy sugar **4** was oxidized [2,10] to give the epoxy ketone **9** (91%). Reduction of **9** with sodium borodeuteride gave a mixtuve of the epoxy sugars **10d'** and **4d'** (95%) in the ratio 7/3. Pure **10d'** and **4d'** were obtained by chromatography. Following the same procedure, **8** was oxidized[10] to give **11** (90%), which was then reduced to give **8d** and the expected *arabino* epimer **12d** in the ratio 1/5. Separation of **8d** and **12d** by chromatography was difficult, and an alternative route to pure **8d** (via **4d**) was developed. Benzyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside[7] was oxidized to give the ketone **13** (92%). Reduction of **13** with sodium borodeuteride in the presence of cerium chloride[11] gave a mixture of **14d** and **15d** in the ratio 3/2. In the absence of cerium chloride, the ratio was 6/1. Chromatography gave pure **15d**, which was transformed via **16d** and **17d** into **4d** as described[2,7] for the nondeuterated compound **4**. Rearrangement of **4d** with lithium bromide in 1,1,1-trichloroethane, followed by treatment with methanolic sodium methoxide and chromatographic purification, gave **8d** (40%).

Experimental Section

All liquid chromatography purifications were performed in the gravity mode. Preparative gas chromatography purifications were performed with a modified Varian 600 gas chromatograph (15% SE-30 on Chromosorb A). Melting points (uncorrected) were determined on a Reichert microscope. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. NMR spectra were recorded with a Varian XL-300 spectrometer. Benzyl 2,3-anhydro-β-D(and L)-ribopyranoside (**1** and **4**) were prepared from D- and L-arabinose in approximately 60% overall yield.[2,7] The sodium borodeuteride (Merck) contained less than 2 mol % of hydrogen.

2(*R*)-(Benzyloxy)-2,5-dihydrofuran-4-carboxaldehyde (2) and Benzyl 4-Bromo-4-deoxy-α-L-lyxopyranoside (3). (a) Dry *N,N,N',N'*-tetramethylurea (TMU) (9.3 g, 80 mmol) and lithium bromide (7.0 g, 80 mmol) were dissolved in refluxing toluene 200 mL). Benzyl 2,3-anhydro-β-D-ribopyranoside[7] (**1**, 11.1 g, 50 mmol) in dry toluene (200 mL) was added rapidly under nitrogen. The mixture was refluxed for 8 min and cooled, and ether (200 mL) was added. The organic phase was separated from the heavy oil that was formed and filtered through SiO_2 (4 × 8 cm) using 200 mL of 2/1 toluene/ether. The filtrate was concentrated and the residue was chromatographed (SiO_2, 1/3 ethyl acetate/hexane) to give pure, crystalline **2** (3.5 g, 34%).

(b) Dry hexamethylphosphoric triamide (HMPA, 8.2 g, 46 mmol) and lithium bromide (4.03 g, 46 mmol) were dissolved in dry toluene (30 mL) and heated to 105 °C. Benzyl 2,3-anhydro-β-D-ribopyranoside[7] (**1**, 5.55 g, 25 mmol) in toluene (25 mL) was added (2 min) under nitrogen. The mixture was refluxed for 5 min, cooled, and poured into ether (300 mL). A heavy oil was formed and the ether phase was separated and washed with water (100 mL), and the water phase was extracted with ether (50 mL). The combined ethereal solutions were dried (sodium sulfate) and the ether was removed. The residue was chromatographed (SiO_2, 1/3 ethyl acetate/hexane) to give crystalline aldehyde **2** (1.3 g, 25%) and crystalline lyxopyranoside **3** (1.1 g, 14%).

(c) Benzyl 2,3-anhydro-β-D-ribopyranoside[7] (**1**, 153 mg, 0.69 mmol) in 1,1,1-trichloroethane (5 mL) was added to a refluxing mixture of 1,1,1-trichloroethane (10 mL) and lithium bromide (300 mg). The refluxing mixture was continuously dried by the use of a Soxhlet extractor that was filled with 5-Å molecules sieves (5 g). After 70 min at reflux, hydrochloric acid (10 mL, 0.1 M) was added. The water phase was extracted with chloroform (5 × 10 mL), and the combined organic phases were dried and concentrated. The residue (175 mg) was chromatographed (SiO_2, 1/1 ethyl acetate/hexane) to give the lyxopyranoside **3** (102 mg, 49%).

Aldehyde **2** had the following: mp 44–49 °C; $[\alpha]^{23}_D$ +89° (*c* 0.7, $CDCl_3$); ^1H NMR ($CDCl_3$, Me_4Si) δ 9.91 (s, 1 H, CHO), 7.35 (m, 5 H, C_6H_5), 6.69 (m, 1 H, $J_{2,3}$ = 1.2 Hz, $J_{3,5}$ = 2.1 Hz, $J_{3,5'}$ = 2.5 Hz, H-3), 6.08 (m, 1 H, $J_{2,3}$ = 1.2 Hz, $J_{2,5}$ = 1.2 Hz, $J_{2,5'}$ = 4.1 Hz, H-2), 4.93, 4.78 (m of AB q, each 1 H, J_{AB} = 14.0 Hz and couplings to H-2 and H-3, H-5,5'), 4.81, 4.62 (AB q, each 1 H, J_{AB} = 11.5 Hz, $CH_2C_6H_5$); ^{13}C NMR δ 187.1 (CHO), 145.9 (C-4), 140.4 (C-3), 137.3 (phenyl-C), 128.4, 128.0, 127.9 (phenyl-CH), 107.3 (C-2), 71.7, 69.8 (C-5 and $CH_2C_6H_5$). Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.6; H, 5.92. Found: C, 70.5; H, 5.93.

Bromolyxoside **3** was recrystallized from toluene: mp 139–141 °C; $[\alpha]^{23}_D$ +61° (*c* 0.9, $CDCl_3$); ^1H NMR ($CDCl_3$, Me_4Si) δ 7.36 (m, 5 H, C_6H_5), 4.96 (d, 1 H, $J_{1,2}$ = 1.6 Hz, H-1), 4.77, 4.52 (AB q, each 1 H, J_{AB} = 11.9 Hz, $CH_2C_6H_5$), 4.32–4.16 (m, 1 H, H-4), 4.10–3.98 (m, 2 H, H-2 and H-3), 3.94–3.90 (m, 2 H, H-5), 2.61, 2.42 (d, each 1 H, *J* = 3.9 and 3.0 Hz, OH); ^{13}C NMR δ 136.8 (phenyl-C), 128.6, 128.1, 128.0 (phenyl-CH), 98.9 (C-1), 71.8, 70.9 (C-2 and C-3), 69.4 ($CH_2C_6H_5$), 62.9 (C-5), 49.8 (C-4). Anal. Calcd for $C_{12}H_{15}BrO_4$: C, 47.5; H, 4.99. Found: C, 47.3; H, 4.96.

2(*S*)-(Benzyloxy)-2,5-dihydrofuran-4-carboxaldehyde (5) and Benzyl 4-Bromo-4-deoxy-α-D-lyxopyranoside (6). (a) Benzyl 2,3-anhydro-β-L-ribopyranoside (**4**)[2,7] was treated as described in method a above to give the pure aldehyde **5**.

(b) Compound **4** was treated as described in method c above to give the pure lyxopyranoside **6**.

Aldehyde **5** had the following: mp 43–49 °C; $[\alpha]^{23}_D$ −90° (*c* 0.8, $CDCl_3$).

Bromolyxoside **6** had the following: mp 139–142 °C; $[\alpha]^{23}_D$ −62° (*c* 0.8, $CDCl_3$).

Benzyl 3,4-Anhydro-β-D(and L)-ribopyranoside (7 and 8). Benzyl 4-bromo-4-deoxy-α-L(or D)-lyxopyranoside (**3** or **6**, 4.3 g, 14 mmol) was dissolved in methanol (100 mL). Methanolic sodium methoxide (1M, 18 mmol) was added at room temperature. After 1 h, the mixture was neutralized with hydrochloric acid (1 M), concentrated, and partitioned between ether and water. The ethereal solution was dried (sodium sulfate) and concentrated, and the residue was chromatographed (SiO_2, 1/3 ethyl acetate/hexane) to give **7** or **8** (2,84 g, 90%). Epoxide **7** had the following: mp 66–68 °C; $[\alpha]^{23}_D$ −166° (*c* 0.8, $CDCl_3$). **8** had the following: mp 68–70 °C; $[\alpha]^{23}_D$ +172° (*c* 2.7, $CDCl_3$); ^1H NMR ($CDCl_3$, Me_4Si) δ 7.35 (m, 5 H, C_6H_5), 4.74, 4.52 (AB q, each 1 H, J_{AB} = 11.8 Hz, $CH_2C_6H_5$), 4.60 (d, 1 H, $J_{1,2}$ = 1.9 Hz, H-1), 4.03 (dd, 1 H, J_{AB} = 13.4 Hz, $J_{4,5}$ = 1.0 Hz, H-5), 3.96 (d, 1 H, J_{AB} = 13.4 Hz, H-5'), 3.84 (ddd, 1 H, $J_{2,3}$ = 4.6 Hz, $J_{2\text{-OH}}$ = 10.1 Hz, H-2), 3.54 (t, 1 H, $J_{3,4}$ = 4.6 Hz, H-3), 3.37 (m, 1 H, H-4), 2.54 (d, 1 H, OH); ^{13}C NMR δ 136.9 (phenyl-C), 128.6, 128.1, 128.0 (phenyl-CH), 97.7 (C-1), 69.7 ($CH_2C_6H_5$), 64.5 (C-2), 57.8 (C-5), 51.8, 51.2 (C-2 and C-3). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.9; H, 6.35. Found: C, 64.5; H, 6.33.

Benzyl 2,3-Anhydro-β-L-erythropentopyranosid-4-ulose (9) and Benzyl 2,3-Anhydro-β-D-erythropentopyranosid-4-ulose. Dry dimethylsulfoxide (9.37 g, 120 mmol) in dry dichloromethane (25 mL) was added (5 min) to oxalyl chloride (6.98 g, 55 mmol) in dry dichloromethane (125 mL) at −60 °C under nitrogen, and the mixture was stirred for 10 min. Benzyl 2,3-anhydro-β-L(or D)-ribopyranoside (**4** or **1**, 11.1 g, 50 mmol) in dichloromethane (50 mL) was added, and the mixture was stirred for 15 min. Diisopropylethylamine (32.3 g, 250 mmol) was added (5 min) and the solution was left for 1 h to attain room temperature. Water (150 mL) was added and the dichloromethane phase was washed with hydrochloric acid (0.1 M), sodium hydrogen carbonate (0.1 M), and water and then dried (magnesium sulfate). The solvent was removed to give a crystalline material (12.1 g) that was subjected to column chromatography (SiO_2, 1/10 ethyl acetate/hexane) to give the desired uloses (10.0 g, 91%). Recrystallization from hexane/ethyl acetate gave pure material. Ulose **9** had the following: mp 53.5–55.5 °C; $[\alpha]^{23}_D$ +160° (*c* 1.0, $CDCl_3$). Benzyl 2,3-anhydro-β-D-erythropentopyranosid-4-ulose had the following: mp 53.0–55.0 °C; $[\alpha]^{23}_D$ −164° *c* 1.1, $CDCl_3$); ^1H NMR ($CDCl_3$, Me_4Si) δ 7.37 (m, 5 H, C_6H_5), 5.29 (d, 1 H, $J_{1,2}$ = 1.5 Hz, H-1), 4.81, 4.65 (AB q, each 1 H, J_{AB} = 11.7 Hz,

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$CH_2C_6H_5$), 4.16, 4.15 (AB q, each 1 H, J_{AB} = 18 Hz, H-5 and H-5′), 3.60 (dd, 1 H, $J_{2,3}$ = 4.1 Hz, H-2), 3.47 (d, 1 H, H-3); ^{13}C NMR δ 200.6 (C-4), 136.4 (phenyl-C), 128.7, 128.3, 128.1 (phenyl-CH), 92.9 (C-1), 70.6 ($CH_2C_6H_5$), 66.0 (C-5), 53.6, 53.3 (C-2 and C-3). Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.5; H, 5.49. Found: C, 65.7; H, 5.51.

Benzyl 2,3-Anhydro-4-deuterio-β-L-ribopyranoside (4d′) and Benzyl 2,3-Anhydro-4-deuterio-α-D-lyxopyranoside (10d′). The ketone **9** (3.30 g, 15 mmol) was dissolved in ethanol (40 mL), sodium borodeuteride (200 mg, 19 mmol) was added, and the mixture was stirred for 45 min. Acetone (ten drops) was added and the mixture was stirred for another 30 min. The solution was concentrated and the residue was partitioned between chloroform and water. The chloroform phase was dried (sodium sulfate) and concentrated, and the residue (3.23 g) was subjected to chromatography (SiO_2, 1/4 ethyl acetate/hexane) to give **4d′** (0.90 g, 27%) and **10d′** (2.1 g, 62%). Recrystallization from ethyl acetate/hexane gave the pure compounds. **4d′**: ^1H NMR ($CDCl_3$, Me_4Si) δ 7.36 (m, 5 H, C_6H_5), 5.04 (d, 1 H, $J_{1,2}$ = 0.7 Hz, H-1), 4.80, 4.58 (AB q, each 1 H, J_{AB} = 11.5 Hz, $CH_2C_6H_5$), 3.85, 3.44 (AB q, each 1 H, J_{AB} = 12.5 Hz, H-5, and H-5′), 3.54 (d, 1 H, $J_{2,3}$ = 3.7 Hz, H-3), 3.24 (dd, 1 H, H-2). **10d′**: mp 62.5–65.5 °C; $[\alpha]^{23}_D$ +105° (*c* 0.5, $CDCl_3$); ^1H NMR ($CDCl_3$, Me_4Si) δ 7.37 (m, 5 H, C_6H_5), 4.97 (d, 1 H, $J_{1,2}$ = 1.0 Hz, H-1), 4.85, 4.60 (AB q, each 1 H, J_{AB} = 12.0 Hz, $CH_2C_6H_5$), 3.66, 3.56 (AB q, each 1 H, J_{AB} = 11.5 Hz, H-5 and H-5′), 3.31 (d, 1 H, $J_{2,3}$ = 3.4 Hz, H-3), 3.19 (dd, 1 H, H-2).

Benzyl 3,4-Anhydro-β-L-erythropentopyranosid-2-ulose (11) and Benzyl 3,4-Anhydro-β-D-erythropentopyranosid-2-ulose. Benzyl 3,4-anhydro-β-L(or D)-ribopyranoside (**8** or **7**, 0.56 g, 2.5 mmol) was oxidized with dimethyl sulfoxide, as described in the preparation of **9**. The crude products were subjected to chromatography (SiO_2, 1/4 ethyl acetate/hexane) to give pure **11** (oil, 0.51 g, 90%), which had $[\alpha]^{24}_D$ +52° (*c* 1.5, $CDCl_3$), and benzyl 3,4-anhydro-β-D-erythropentopyranosid-2-ulose: $[\alpha]^{23}_D$ −52° (*c* 1.7, $CDCl_3$); ^1H NMR ($CDCl_3$, Me_4Si) δ 7.36 (m, 5 H, C_6H_5), 4.82 (s, 1 H, H-1), 4.76, 4.63 (AB q, each 1 H, J_{AB} = 11.7 Hz, $CH_2C_6H_5$), 4.22, 4.09 (AB q, each 1 H, J_{AB} = 13.3 Hz, H-5 and H-5′), 3.59 (d, br, 1 H, $J_{3,4}$ = 4.0 Hz, H-4), 3.43 (d, 1 H, H-3); ^{13}C NMR δ 195.4 (C-2), 136.2 (phenyl-C), 128.6, 128.3 , 128.2 (phenyl-CH), 95.2 (C-1), 70.3 ($CH_2C_6H_5$), 56.1 (C-5), 51.7, 51.5 (C-3 and C-4). Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.5; H, 5.49. Found: C, 65.1; H, 5.62.

Benzyl 3,4-Anhydro-2-deuterio-β-L-arabinopyranoside (12d). Reduction of **11** (91 mg, 0.4 mmol) with sodium borodeuteride, as described for the preparation of **4d′** and **10d′**, followed by chromatography (SiO_2, 1/3 ethyl acetate/hexane) gave **12d** containing approximately 20% of **8d**. Pure **12d** (53 mg, 60%) was obtained after recrystallization from 1/2 ethyl acetate/hexane. **12d**: mp 90.5–93.5 °C; $[\alpha]^{23}_D$ +138° (*c* 0.4, $CDCl_3$); ^1H NMR ($CDCl_3$, Me_4Si) δ 7.35 (m, 5 H, C_6H_5), 4.81, 4.56 (AB q, each 1 H, J_{AB} = 12 Hz, $CH_2C_6H_5$), 4.79 (s, 1 H, H-1), 4.04, 3.99 (AB q, each 1 H, J_{AB} = 13.4 Hz, H-5 and H-5′), 3.27 (complex d, 1 H, $J_{3,4}$ = 4.3 Hz, H-3), 3.23 (complex d, 1 H, H-4).

Benzyl 3,4-*O*-Isopropylidene-β-L-erythropentopyranosid-2-ulose (13). Benzyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside[7] was oxidized with dimethyl sulfoxide, as described for the preparation of **9**. The crude product was chromatographed (SiO_2, 1/4 ethyl acetate/hexane) to give **13** as an oil (92%). The corresponding D sugar has been prepared.[12] **13**: $[\alpha]^{23}_D$ +144° (*c* 1.3, $CDCl_3$); ^1H NMR ($CDCl_3$, Me_4Si) δ 7.36 (m, 5 H, C_6H_5), 4.91 (s, 1 H, H-1), 4.80, 4.61 (AB q, each 1 H, J_{AB} = 11.5 Hz, $CH_2C_6H_5$), 4.73 (d, 1 H, $J_{3,4}$ = 5.6 Hz, H-3), 4.53 (ddd, 1 H, $J_{4,5}$ = 2.2 Hz, $J_{4,5'}$ = 1.0 Hz H-4), 4.30, 4.10 (AB q, each 1 H, J_{AB} = 13.3 Hz, H-5 and H-5′), 1.46, 1.39 (s, each 3 H, CH_3).

Benzyl 2-Deuterio-3,4-*O*-isopropylidene-β-L-ribopyranoside (14d) and Benzyl 2-Deuterio-3,4-*O*-isopropylidene-β-L-arabinopyranoside (15d). Cerium(III) chloride hexahydrate (3.9 g, 11 mmol) and **13** (2.78 g, 10 mmol) were dissolved in methanol (30 mL). Sodium borodeuteride (430 mg, 10 mmol) was added rapidly (vigorous gas evolution) and the mixture was stirred for 30 min at 35 °C. The methanol was evaporated and the residue was partitioned between ethyl acetate and water. Drying (sodium sulfate) and concentration gave a residue that was chromatographed (SiO_2, 1/3 ethyl acetate/hexane) to give **15d** (0.94 g, 35%), **14**: (1.49 g, 55%), and unreacted **13** (0.16 g, 6%). Recrystallization from ethyl acetate/hexane gave pure **14d** and **15d**. **14d**: mp 75.0–78.5 °C; $[\alpha]^{23}_D$ +125° (*c* 0.7, $CDCl_3$); ^1H NMR ($CDCl_3$, Me_4Si) δ 7.35 (m, 5 H, C_6H_5), 4.85 (s, 1 H, H-1), 4.83, 4.57 (AB q, each 1 H, J_{AB} = 11.7 Hz, $CH_2C_6H_5$), 4.50 (d, 1 H, $J_{3,4}$ = 6.5 Hz, H-3), 4.28 (ddd, 1 H, $J_{4,5}$ = 3.4 Hz, $J_{4,5'}$ = 3.0 Hz, H-4), 3.87, 3.74 (d AB q, each 1 H, J_{AB} = 13.0 Hz, H-5 and H-5′), 1.55, 1.37 (q, each 3 H, J = 0.5 Hz, CH_3). **15d** had physical and spectroscopic data in accord with the unlabeled material.[2,7]

Benzyl 2,3-Anhydro-2-deuterio-β-L-ribopyranoside (4d). Compound **15d** was transformed via **16d** and **17d** as described for the unlabeled material[7] to **4d**, which had the following: ^1H NMR ($CDCl_3$, Me_4Si) δ 7.37 (m, 5 H, C_6H_5), 5.04 (s, 1 H, H-1), 4.80, 4.58 (AB q, each 1 H, J_{AB} = 11.4 Hz, $CH_2C_6H_5$), 3.95–3.87 (br, m, 1 H, H-4), 3.85, 3.45 (m, AB q, each 1 H, J_{AB} = 12.5 Hz, H-5 and H-5′), 3.54 (d, 1 H, $J_{3,4}$ = 5.0 Hz, H-3), 2.68 (d, 1 H, $J_{4\text{-OH}}$ = 11.0 Hz, OH).

Benzyl 3,4-Anhydro-2-deuterio-β-L-ribopyranoside (8d). Compound **4d** was reacted with lithium bromide in 1,1,1-trichloroethane, followed by treatment with methanolic sodium methoxide, as described above for the preparation of **7** and **8**. The labeled epoxide **8d** had the following: ^1H NMR ($CDCl_3$, Me_4Si) δ 7.35 (m, 5 H, C_6H_5), 4.73, 4.51 (AB q, each 1 H, J_{AB} = 11.6 Hz, $CH_2C_6H_5$), 4.59 (s, 1 H, H-1), 4.03 (dd, 1 H, J_{AB} = 13.4 Hz, $J_{4,5}$ = 1.0 Hz, H-5), 3.96 (d, 1 H, J_{AB} = 13.4 Hz, H-5′), 3.53 (d, 1 H, $J_{3,4}$ = 4.2 Hz, H-3), 3.37 (m, 1 H, H-4).

Lithium bromide treatment of the epoxy sugars 8, 8d, 4d, and 4d′ was performed as described for the preparation of **2**, method a.

The unlabeled compound **8** gave the aldehyde **5** (34% yield).

The labeled compound **8d** gave **2(*S*)-(benzyloxy)-3-deuterio-2,5-dihydrofuran-4-carboxaldehyde (5d),** with the following ^1H NMR data ($CDCl_3$, Me_4Si): δ 9.91 (s, 1 H, CHO), 7.35 (m, 5 H, C_6H_5), 6.08 (dd, 1 H, $J_{2,5}$ = 1.2 Hz, $J_{2,5'}$ = 4.1 Hz, H-2), 4.93, 4.78 (m of AB q, each 1 H, J_{AB} = 14.0 Hz and couplings to H-2; H-5 and H-5′), 4.81, 4.62 (AB q, each 1 H, J_{AB} = 11.5 Hz, $CH_2C_6H_5$).

The labeled compound **4d** gave the labeled aldehyde **5d**.

The labeled compound **4d′** gave the unlabeled aldehyde **5**.

Furan-3-carboxaldehyde (18). Aldehyde **2** or **5** (10 mg) was dissolved in dichloromethane (0.5 mL) and Duolit resin (H^+ form, 5 mg) was added. The mixture was stirred for 1 h, filtered, neutralized (sodium hydrogen carbonate), and subjected to preparative gas chromatography to give benzyl alcohol and furan-3-carboxaldehyde[13] (**18**) with the following NMR data ($CDCl_3$, Me_4Si): ^1H δ 9.96 (s, 1 H, CHO), 8.07 (s, 1 H, H-2), 7.49 (s, 1 H, H-5), 6.81 (s, 1 H, H-4); ^{13}C δ 184.5 (CHO), 151.4 (C-5), 144.8 (C-2), 143.2 (C-3), 106.8 (C-4).

4-Deuteriofuran-3-carboxaldehyde (18d). Aldehyde **5d** was treated as above to give **18d** which had the following ^1H NMR data ($CDCl_3$, Me_4Si): δ 9.96 (s, 1 H, CHO), 8.07 (s, 1 H, H-2), 7.49 (s, 1 H, H-5).

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