# Total Synthesis of Several Monodeoxy and Dideoxy-DL-hexopyranoses from 6,8-Dioxabicyclo[3.2.1]oct-2-ene and 6,8-Dioxabicyclo[3.2.1]oct-3-ene

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Reaction of osmic acid with 6,8-dioxabicyclo[3.2.1]oct-3-ene (**1**) gave 1,6-anhydro-4-deoxy-β-DL-*ribo*-hexopyranose (**3**, R = H) which was hydrolyzed to 4-deoxy-α,β-DL-*ribo*-hexopyranose (**4**, R = H). Conversion of **1** to 1,6:2,3-dianhydro-4-deoxy-β-DL-*ribo*-hexopyranose (**5**) followed by treatment of **5** with lithium aluminum hydride, gave 1,6-anhydro-3,4-dideoxy-β-DL-*erythro*-hexopyranose (**6**, R = H), and this in turn was hydrolyzed to 3,4-dideoxy-α,β-DL-*erythro*-hexopyranose (**7**, R = H).

Reaction of osmic acid with 6,8-dioxabicyclo[3.2.1]oct-2-ene (**2**) gave 1,6-anhydro-2-deoxy-β-DL-*ribo*-hexopyranose (**8**, R = H), which was hydrolyzed to 2-deoxy-DL-*ribo*-hexopyranose (**9**, R = H). Compound **2** was converted to 1,6:3,4-dianhydro-2-deoxy-β-DL-*ribo*-hexopyranose (**10**) which was hydrolyzed by aqueous base to 1,6-anhydro-2-deoxy-β-DL-*arabino*-hexopyranose (**12**) and this in turn was hydrolyzed by dilute hydrochloric acid to 2-deoxy-α,β-DL-*arabino*-hexopyranose (2-deoxy-DL-glucose) (**13**). The reaction of **10** with lithium aluminum hydride gave 1,6-anhydro-2,3-dideoxy-β-DL-*erythro*-hexopyranose (**14**).

Yields were good to excellent in each of the above reactions.

La réaction de l'acide osmique avec le dioxa-6,8 bicyclo[3.2.1] octène-3 (**1**) conduit à l'anhydro-1,6 désoxy-4 β-DL-*ribo*-hexapyranose (**3**, R = H) qui par hydrolyse fournit le désoxy-4 α,β-DL-*ribo*-hexapyranose (**4**, R = H). Le composé **1** peut être transformé successivement en dianhydro-1,6:2,3 désoxy-4 β-DL-*ribo*-hexapyranose (**5**), puis par traitement par $LiAlH_4$ en anhydro-1,6 didésoxy-3,4 β-DL-*erythro*-hexapyranose (**6**, R = H) et finalement, par hydrolyse, en didésoxy-3,4 α,β-DL-*erythro*-hexapyranose (**7**, R = H).

Par ailleurs l'action de l'acide osmique sur le dioxa-6,8 bicyclo[3.2.1] octène-2 (**2**) fournit l'anhydro-1,6 désoxy-2 β-DL-*ribo*-hexapyranose (**8**, R = H) qui conduit, par hydrolyse, au désoxy-2 DL-*ribo*-hexapyranose (**9**, R = H). On peut aussi transformer le composé **2** pour obtenir successivement le dianhydro-1,6:3,4 désoxy-2 β-DL-*ribo*-hexapyranose (**10**), puis par hydrolyse en milieu basique en anhydro-1,6 désoxy-2 β-DL-*arabino*-hexapyranose (**12**) et finalement par hydrolyse en milieu acide chlorhydrique dilué en désoxy-2 α,β-DL-*arabino*-hexapyranose (désoxy-2 DL-glucose) (**13**). La réaction de **10** avec $LiAlH_4$ fournit l'anhydro-1,6 didésoxy-2,3 β-DL-*erythro*-hexapyranose (**14**).

Dans chacune des réactions décrites ci-haut les rendements sont excellents.

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## Introduction

Recent reports from this laboratory have described the total synthesis of 1,6-anhydro-4-deoxy-β-DL-*xylo*-hexopyranose (1) and α,β-DL-chalcose (2) from 6,8-dioxabicyclo[3.2.1]oct-3-ene (**1**), a compound in turn readily prepared from acrolein dimer (1). We now report the preparation of several monodeoxy and dideoxy-hexopyranoses from the bicyclic olefin **1** and its isomer 6,8-dioxabicyclo[3.2.1]oct-2-ene (**2**), a compound recently described (3).

## Results and Discussion

The reactions performed with olefin **1**, and the products so obtained, are shown in Scheme 1. Those involving olefin **2** are portrayed in Scheme 2.

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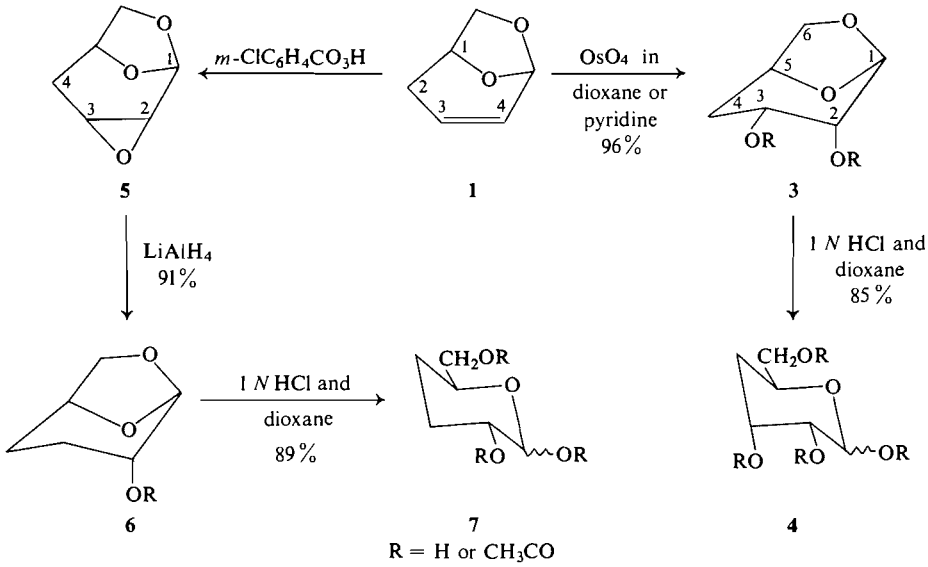
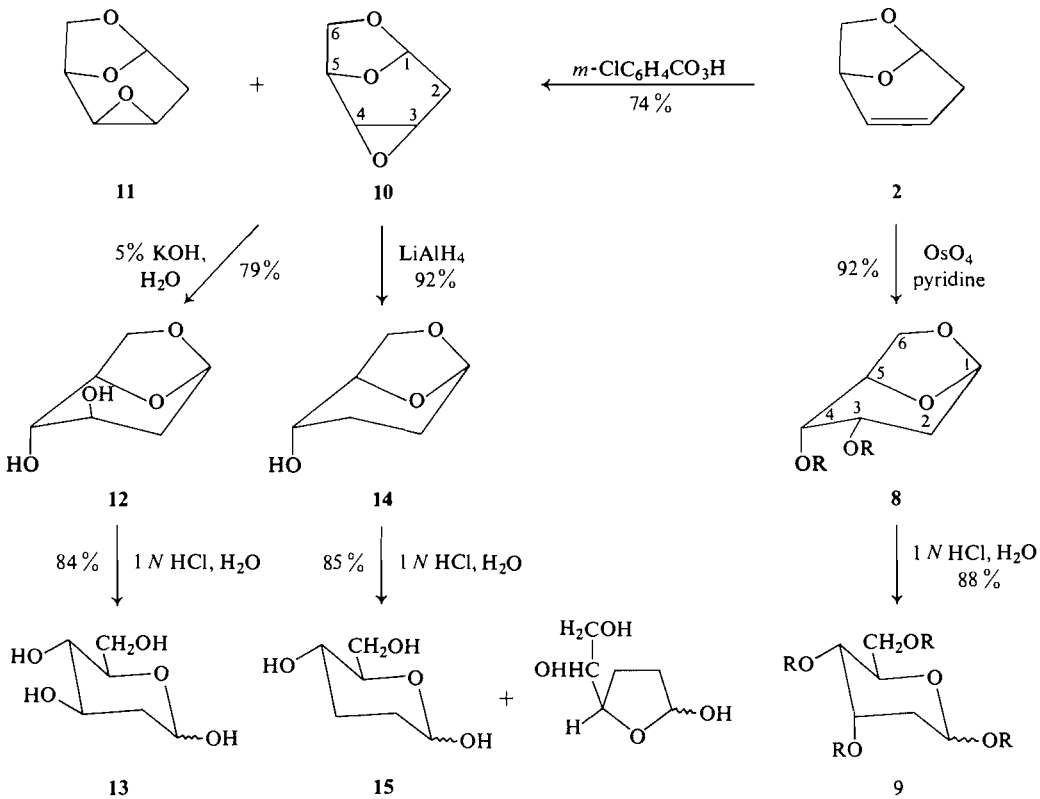
The reaction of **1** with osmic acid in dioxane or pyridine, following published directions (4–6), gave a nearly quantitative yield of crude material which showed only one spot on a t.l.c. Distillation provided pure 1,6-anhydro-4-deoxy-β-DL-*ribo*-hexopyranose (**3**, R = H) in 96% yield. The elemental analysis and the 100 MHz p.m.r. spectrum of **3** (R = H) as well as those of its diacetate **3** ($R = CH_3CO$) were in complete agreement with the structure shown by **3**. The previous observation (6) that the direction of attack by osmic acid on the double bond of such substituted cyclic olefins is strongly subject to steric influence also provides support for the structure **3**. Acid-catalyzed hydrolysis of **3** (R = H or $CH_3CO$) in aqueous dioxane gave 4-deoxy-α,β-DL-*ribo*-hexopyranose (**4**) (R = H) as a syrup in 85% yield. The 100 MHz p.m.r. spectrum of **4** (R = H) in $D_2O$, as well as that




SCHEME 1




SCHEME 2

of its tetraacetate (**4**, R = $CH_3CO$) in $CDCl_3$, showed that this substance possessed the configuration and conformation shown by **4**, and that it was present in $D_2O$ as a mixture of the α and β isomers in the ratio 1:3 respectively.

When 1,6:2,3-dianhydro-4-deoxy-β-DL-*ribo*-hexopyranose (**5**), prepared from **1** according to published directions (1, 2), was treated with lithium aluminum hydride in diethyl ether, the compound obtained in 91% yield was **6** (R = H). This was the product expected from preferential cleavage of the O—$C_3$ bond (7) as well as preferential formation of the chair structure obtained by cleavage of the oxirane ring so that the attacking agent and the leaving group are *trans* diaxially disposed (8–10). The 100 MHz p.m.r. spectra of both **6** (R = H) and its acetate **6** (R = $CH_3CO$) clearly showed that the product of lithium aluminum hydride reduction of **5** was indeed structure **6**. Acid-catalyzed hydrolysis of **6** (R = H) provided 3,4-dideoxy-α,β-DL-*erythro*-hexopyranose (**7**, R = H). The 100 MHz p.m.r. spectrum of **7** (R = H) as well as that of its triacetate (**7**, R = $CH_3CO$) completely supported the structure and conformation shown by **7**. The integrated areas of the two anomeric proton signals for **7** (R = H) of the spectrum in $D_2O$, showed that the α and β isomers were present in the ratio 1:4 respectively.

Treatment of olefin **2** with osmic acid in pyridine gave 1,6-anhydro-2-deoxy-β-DL-*ribo*-hexopyranose (**8**, R = H) in 92% yield. Here again most if not all of the reaction with osmic acid had occurred from the least hindered side of the double bond of **2**. The structure was supported by its 100 MHz p.m.r. spectrum, since upon irradiation of the nucleus of the anomeric proton (H-1), a collapsed high field multiplet was obtained for the two protons on C-2 which contained a large coupling of ~10 Hz. A coupling of such magnitude can occur only if the H-3 proton and one of the C-2 protons are *trans* diaxially disposed. The elemental analysis and 100 MHz p.m.r. spectrum of the diacetate **8** (R = $CH_3CO$) also supported the structure designated by **8**. Hydrolysis of **8** (R = H) or its diacetate with 1 *N* aqueous hydrochloric acid gave 2-deoxy-DL-*ribo*-hexopyranose (**9**, R = H) in 88% yield. The 100 MHz p.m.r. spectrum of **9** (R = H) was identical to that of an authentic sample of 2-deoxy-D-*ribo*-hexopyranose (11, 12) kindly provided by Dr. K. V. Bhat. The elemental analysis and 100 MHz p.m.r. spectrum of the tetraacetate **9** (R = $CH_3CO$) agreed completely with the assigned structure.

Treatment of **2** with *m*-chloroperoxybenzoic acid gave a 74% yield of an oil whose analysis by g.l.c. showed only two symmetrical peaks in the area ratio of 49:1. The major compound, 1,6:3,4-dianhydro-2-deoxy-β-DL-*ribo*-hexopyranose (**10**), was readily separated in the pure state by g.l.c. The elemental analysis, and the i.r. and 100 MHz p.m.r. spectral data clearly supported structure **10**. The minor component, **11**, could not be obtained free of **10** because of the tailing from **10** during attempted g.l.c. separation. However, the mixture finally isolated was sufficiently enriched in **11** to obtain a 100 MHz p.m.r. spectrum which confirmed that the compound had the structure shown by **11**. The reaction of aqueous potassium hydroxide with **10** gave crystalline 1,6-anhydro-2-deoxy-β-DL-*arabino*-hexopyranose (**12**) in 79% yield. The 100 MHz p.m.r. spectrum agreed completely with the structure assigned and this structure was confirmed by hydrolysis of **12** with 1 *N* aqueous hydrochloric acid to 2-deoxy-α,β-DL-*arabino*-hexopyranose (**13**), whose 100 MHz p.m.r. spectrum in $D_2O$ was identical to that of authentic 2-deoxy-D-glucose.

Lithium aluminum hydride in ether reacted with the oxirane **10** to give, after sublimation, the solid 1,6-anhydro-2,3-dideoxy-β-DL-*erythro*-hexopyranose (**14**) as the only isolable product. Here again cleavage of the oxirane ring gave that product which was the chair form obtainable by opening of the three-membered ring so that the attacking and leaving groups are *trans* diaxially oriented (8–10). The 100 MHz p.m.r. spectrum's pattern of high field signals equivalent to four protons could be accounted for only if these protons were aliphatic and on two adjacent carbon atoms as shown by **14**.

Hydrolysis of **14** with 1 *N* hydrochloric acid gave a viscous syrup whose t.l.c. showed only one spot but the p.m.r. spectrum indicated it to be a mixture, presumably of pyranose and furanose structures. Several attempts to resolve this mixture were unsuccessful.

## Experimental

Melting points and boiling points are uncorrected. Elemental analyses were made by Mrs. Darlene

Mahlow and Miss A. Dunn in our microanalytical laboratory.

The i.r. absorption spectra were obtained by Mr. R. Swindlehurst of this Department using a Perkin–Elmer Model 421 spectrometer.

The 60 MHz p.m.r. spectra were made by Mr. R. Swindlehurst using a Varian A-60 instrument. The 100 MHz p.m.r. spectra and spin decoupling experiments were carried out by Mr. Glen Bigam and his associates. Tetramethylsilane was the internal reference. Signal assignments were made with the aid of double irradiation spin decoupling. The coupling constants were estimated from the signal spacings where this was possible, and accordingly are approximate values.

Column and t.l.c. was carried out using Silica Gel G (E. Merck and Co.) as absorbent. Solvents were removed by rotary evaporator under vacuum unless otherwise stated.

*6,8-Dioxabicyclo[3.2.1]oct-3-ene (**1**)*

Compound **1** was prepared according to the modification (2) of the published procedure (1).

*6,8-Dioxabicyclo[3.2.1]oct-2-ene (**2**)*

Compound **2** was prepared in good yield by using directions previously described (3).

*1,6-Anhydro-4-deoxy-β-DL-ribo-hexopyranose (**3**, R = H)*

Osmic acid (1.0 g, 3.93 mmol) in 5 ml of dry pyridine (4–6) was added slowly to a solution of 0.44 g (3.90 mmol) of **1** in 5 ml of pyridine at room temperature. The solution was then kept at room temperature and stirred for 15 h. The reaction mixture was treated with a solution of 1.8 g of sodium bisulfite in 20 ml of pyridine and 30 ml of water and the resulting mixture stirred for 1 h. The orange solution was extracted continuously for 24 h with 250 ml of chloroform. The chloroform extract was dried ($Na_2SO_4$), filtered, and freed from solvent at 45°. The syrupy residue showed only one spot on t.l.c. (solvent, 2% methanol in dichloromethane). The 60 MHz p.m.r. spectrum in deuteriochloroform showed only one anomeric proton signal and no signals in the olefinic proton region. The syrup was distilled at 120–121° at 0.05 mm to provide a low-melting colorless solid (~ 30°), yield, 0.55 g (96%); lit. m.p. of D isomer 105–107° (108–110° after sublimation) (13).

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.31; H, 6.90. Found: C, 49.12; H, 7.06.

The i.r. spectrum in chloroform showed a band at 3560 with a shoulder at 3610 $cm^{-1}$ (OH).

The 100 MHz p.m.r. spectrum in deuteriochloroform showed signals at τ 4.51 for H-1 (doublet, $J_{1,2} \sim 2.5$ Hz); 5.98–6.40 (multiplet for H-2, -3, -6*exo*, and -6*endo*); 7.8–8.4 (multiplet for H-4*exo* and -4*endo*); 5.47 (broad singlet $w/2 = 10$ Hz for H-5); and 7.82 (singlet for OH). Irradiation of H-5 at τ 5.47 simplified the multiplet at 7.8–8.4 for H-4*exo* and -4*endo* to two quartets showing geminal coupling of ~ 14, $J_{3,4exo} \sim 10$, and $J_{3,4endo} \sim$ 6.5 Hz which can occur only if the C-3 proton is *endo* to the bicyclic structure.

When a mixture of 0.88 g of **1** and 2.0 g of osmic acid in 10 ml of dry dioxane was stirred at room temperature for 24 h as described in published directions (4–6), and then treated with dry hydrogen sulfide, followed by removal of the black precipitate, there was obtained after isolation and distillation as above, 1.0 g (87%) of the low melting (~ 30°) solid boiling at 120–123° at 0.05 mm. This was identical in every respect to **3** (R = H) described immediately above.

*1,6-Anhydro-2,3-di-O-acetyl-4-deoxy-β-DL-ribo-hexopyranose (**3**, R = $CH_3CO$)*

Compound **3** (R = H) (100 mg) was treated with acetic anhydride (5 ml) in pyridine (5 ml) at 60° for 0.5 h, and gave 130 mg (82.5%) of the crude diacetate **3** (R = $CH_3CO$). Distillation at 137–139° at 0.1 mm provided a viscous syrup.

Anal. Calcd. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.43; H, 5.93.

The i.r. spectrum in chloroform showed strong absorption at 1750 $cm^{-1}$ (C=O).

The 100 MHz p.m.r. spectrum in deuteriochloroform showed signals at τ 4.61 for H-1 (doublet, $J_{1,2} \sim 2.5$ Hz); 4.95 for H-2 (quartet showing some long range coupling (< 1.0 Hz) with H-4*endo*, $J_{2,3} \sim 4.5$ Hz); 4.75 for H-3 (multiplet $J_{3,4endo} \sim 6.5$, $J_{3,4exo} \sim 11$ Hz); 8.8 for H-4*exo* and -4*endo* (multiplet masked by acetyl protons); 5.39 for H-5 (multiplet, $J_{5,6endo} \sim 1.5$, $J_{5,6exo} \sim 5.0$ Hz); 6.08 for H-6*endo* (doublet of doublets, $J_{6exo,6endo} \sim$ 7.0 Hz); 6.28 for H-6*exo* (quartet of doublets, $J_{4,6exo} \sim$ 1.7 Hz long range coupling); 7.91 and 8.04 (each a singlet due to two $CH_3CO$).

*4-Deoxy-α,β-DL-ribo-hexopyranose (**4**, R = H)*

A mixture of 275 mg of **3** (R = H), 5 ml of dioxane, and 10 ml of 1 *N* aqueous hydrochloric acid was heated at ~ 80° for 5 h. The mixture was then cooled, neutralized with Amberlite IRA 400 ($OH^{\ominus}$), and filtered. The solvent was removed and the residue freeze-dried. The yellow syrup obtained was passed twice through a short column of Silica Gel G using a 1:1 mixture of methanol and chloroform as eluent. The solvent was removed and the residue distilled at 110–115° at 0.01 mm and gave 261 mg (85%) of a colorless viscous oil; lit. m.p. of D isomer 89–93° (13).

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 43.75; H, 7.92.

The 100 MHz p.m.r. spectrum in $D_2O$ obtained after the solution had stood for 24 h to permit completion of mutarotation, showed signals at τ 4.06 for H-1 of the α anomer (doublet, $J_{1,2} \sim 3.0$ Hz); 4.64 for H-1 of the β anomer (doublet, $J_{1,2} \sim 8.0$ Hz). Signal area ratio H-1α: H-1β was 1.0:3.0. Other signals were at τ 5.20–6.30 for H-2, -3, -5, and —$CH_2$— (complex multiplet); 7.40–7.92 for H-4*e* and -4*a* (multiplet); and 4.82 for OH (singlet).

*1,2,3,6-Tetra-O-acetyl-4-deoxy-α,β-DL-ribo-hexopyranose (**4**, R = $CH_3CO$)*

Treatment of 100 mg of **4** (R = H) with a mixture of 5 ml of acetic anhydride and 5 ml of pyridine at 60° for 0.5 h and then at room temperature overnight gave a syrup from which **4** (R = $CH_3CO$) was obtained as a colorless oil boiling at 141–143° at 0.1 mm; yield, 165 mg (79%).

Anal. Calcd. for $C_{14}H_{20}O_9$: C, 50.60; H, 6.07. Found: C, 50.68; H, 6.17.

The i.r. spectrum in chloroform showed strong absorption at 1755 $cm^{-1}$ (C=O).

The 100 MHz p.m.r. spectrum in deuteriochloroform showed signals at $\tau$ 3.80 for H-1 of the $\alpha$ anomer (doublet, $J_{1,2} \sim 4.0$ Hz); 4.01 for H-1 of the $\beta$ anomer (doublet, $J_{1,2} \sim 8.5$ Hz). Signal area ratio $\alpha$:$\beta \sim 1.0$:3.0. Other signals were at $\tau$ 5.19 for H-2 of the $\beta$ anomer (quartet, $J_{2,3} \sim 3.0$ Hz); 4.98 for H-2 of the $\alpha$ anomer (triplet, $J_{2,3} \sim J_{1,2} \sim 4.0$ Hz); 4.40–4.70 for H-3 of $\alpha$ and $\beta$ anomers (multiplet); 7.8–8.3 for H-4*e* and -4*a* masked by the four $CH_3$—CO (multiplet); 5.60–5.95 for H-5 and —$CH_2$— (multiplet); 7.90, 7.92, 7.94, and 8.02 (four singlets, each $CH_3CO$).

*1,6-Anhydro-3,4-dideoxy-*β*-*DL*-erythro-hexopyranose (**6**, R = H)*

A solution of 1.28 g (0.01 mol) of 1,6:2,3-dianhydro-4-deoxy-β-DL-*ribo*-hexopyranose (**5**) (1, 2) in 20 ml of dry ether was added slowly, dropwise, to a stirred solution of lithium aluminum hydride (0.88 g, 0.01 mol) in 25 ml of dry ether at room temperature. This was stirred for 12 h at room temperature. The aluminum complex was then decomposed by gradual addition of 15 ml of ether saturated with water, then further addition of 1 ml of 15% aqueous sodium hydroxide. The granular precipitate was separated by gravity filtration and the colorless solid was washed with ether (3 × 20 ml). The combined ether solutions from the washings and filtrate were dried ($Na_2SO_4$) and freed from solvent at 40° under vacuum (50 mm). The residual solid was sublimed under vacuum (50–55° at 0.01 mm) and provided **6** (R = H) as colorless needles; m.p. 81–82°; yield, 1.18 g (~91%).

Anal. Calcd. for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.25; H, 7.80.

The i.r. spectrum in chloroform showed absorption at 3517 $cm^{-1}$ (OH).

The 100 MHz p.m.r. spectrum in deuteriochloroform showed signals at $\tau$ 4.67 for H-1 (narrow triplet, $w/2 \sim 4$, $J_{1,2} \sim 1.0$, $J_{1,3} \sim 1.0$ Hz due to long range coupling); 6.40 for H-2 (multiplet, $w/2 \sim 7$; $J_{2,3} \sim 2.0$ Hz); 7.60–8.20 for H-3*exo* and -3*endo* (multiplet); 8.20–8.70 for H-4*exo* and -4*endo* (multiplet $J_{4endo,5} \sim 2.0$; $J_{4exo,6exo} \sim 1.2$ Hz due to long range coupling); 5.50 for H-5 (multiplet, $w/2 \sim 10$, $J_{5,6endo} \sim 1.5$, $J_{5,6exo} \sim 5.0$ Hz); 6.00–6.13 for H-6*endo* (doublet of doublets, $J_{6exo,6endo} \sim 7.0$ Hz); 6.13–6.30 for H-6*exo* (multiplet); $\tau$ 7.41 for OH (singlet).

*2-O-Acetyl-1,6-anhydro-3,4-dideoxy-*β*-*DL*-erythro-hexopyranose (**6**, R = $CH_3CO$)*

The reaction of 300 mg of **6** (R = H) with acetic anhydride (5 ml) in pyridine (5 ml) for 1 h at 60° gave the crude monoacetate as a pale yellow liquid. Distillation provided a colorless oil boiling at 55–59° at 0.01 mm; yield, 370 mg (93%).

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 55.66; H, 6.96.

The i.r. spectrum in chloroform showed a strong absorption band at 1725 $cm^{-1}$ (C=O).

The 100 MHz p.m.r. spectrum in deuteriochloroform showed signals at $\tau$ 4.61 for H-1 (narrow quartet, $J_{1,2} \sim 2.0$, $J_{1,3} \sim 1.0$ Hz); 5.30–5.53 for H-2 and -5 (overlapping multiplets, $J_{2,3} \sim 2.0$, $J_{5,6exo} \sim 5.0$, $J_{5,6endo} \sim 1.0$ Hz); $\tau$ 8.0–8.35 for H-4*exo* and -4*endo* (multiplet, $J_{4endo,5} \sim 2.0$, $J_{4exo,6exo} \sim 1.2$ Hz long range coupling); 8.35–8.70 for H-3*exo* and -3*endo* (multiplet); 6.07 for H-6*endo* (doublet of doublets, $J_{6exo,6endo} \sim 7.0$ Hz), 6.12–6.30 for H-6*exo* (multiplet); 7.96 for $CH_3CO$ (singlet).

*3,4-Dideoxy-*α,β-DL*-erythro-hexopyranose (**7**, R = H)*

A solution of 500 mg of **6** (R = H) in a mixture of 10 ml of 1 *N* aqueous hydrochloric acid and 5 ml of dioxane was heated at 80° for 5 h in an oil bath. The mixture was cooled and then neutralized with Amberlite IRA 400 ($OH^{\ominus}$) and filtered. The solvent was removed and the residue freeze-dried to give a pale yellow syrup. This was purified by column chromatography using a 3:2 mixture (by volume) of chloroform and methanol as eluent. The first fraction (50 ml) gave a gum which was discarded. The second fraction (150 ml) provided a syrup which was distilled at 130–135° at 0.4 mm to give **7** (R = H) as a viscous colorless oil; yield, 505 mg (89%).

Anal. Calcd. for $C_6H_{12}O_4$: C, 48.64; H, 8.16. Found: C, 48.46; H, 7.73.

The 100 MHz p.m.r. spectrum in deuterium oxide, obtained after the solution has stood for 24 h to complete mutarotation, showed signals at $\tau$ 4.59 for H-1 of the $\alpha$ anomer (doublet, $J_{1,2} \sim 3.5$ Hz); 5.22 for H-1 of the $\beta$ anomer (doublet, $J_{1,2} \sim 8.0$ Hz). Signal area ratio H-1$\alpha$:H-1$\beta$ was 1.0:4.0. Other signals appeared at $\tau$ 6.31 for H-2 of $\beta$ anomer (multiplet); 7.75–8.40 for two H-3 and two -4 (complex multiplet); 5.05 for OH (singlet); 6.15 for —$CH_2$— and H-5 (multiplet).

*3,4-Dideoxy-*α,β-DL*-erythro-hexopyranose Triacetate (**7**, R = $CH_3CO$)*

Treatment of 150 mg of **7** (R = H) with a mixture of 5 ml of acetic anhydride and 5 ml of pyridine at 60° for 30 min and then at room temperature overnight gave a syrup which distilled at 95–97° at 0.2 mm to give **7** (R = $CH_3CO$) as a viscous oil; yield, 265 mg (90%).

Anal. Calcd. for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62. Found: C, 52.81; H, 6.50.

The i.r. spectrum in chloroform showed strong absorption at 1735 $cm^{-1}$ (C=O).

The 100 MHz p.m.r. spectrum in deuteriochloroform showed signals at $\tau$ 3.79 for H-1 of $\alpha$ anomer (doublet $J_{1,2} \sim 3.5$ Hz); 4.34 for H-1 of $\beta$ anomer (doublet, $J_{1,2} \sim 8.0$ Hz). Signal area ratio H-1$\alpha$:H-1$\beta \sim 1$:3. Other signals appeared at $\tau$ 4.90–5.40 for H-2 (broad multiplet); 7.50–8.70 for two H-3 and two -4 (multiplets); 7.87, 7.90, and 7.93 each a singlet for $CH_3CO$.

*1,6-Anhydro-2-deoxy-*β*-*DL*-ribo-hexopyranose (**8**, R = H)*

The reaction of osmic acid with **2** (3) was carried out essentially as described above for the reaction of osmic acid with **1** to form **3** (R = H). From 0.44 g (0.0039 mol) of **2**, treated with 1.0 g (0.0039 mol) of osmic acid was obtained a colorless syrup which was sublimed at 80° at 1.0 mm to provide 0.52 g (92%) of **8** (R = H) melting at 28–31°; lit. m.p. for D isomer, 98–99° (14). The t.l.c. analysis (3% methanol in chloroform) showed only one spot. A satisfactory elemental analysis could not be obtained, carbon being generally low. The diacetate **8** (R = $CH_3CO$) gave satisfactory analysis (see below).

The i.r. spectrum (neat) showed a broad band at 3300–3500 $cm^{-1}$ (OH).

The 100 MHz p.m.r. spectrum in $CDCl_3$ showed signals at $\tau$ 4.55 for H-1 (broad singlet $w/2 \sim 5$ Hz); 5.46 for H-5 (multiplet $w/2 \sim 11$ Hz); 5.94–6.50 for H-3,

-4, -6*exo*, -6*endo* (overlapping multiplets); 6.30 for two OH (singlet); 8.00 for H-2*endo* (quartet $J_{2exo,2endo} \sim 14$, $J_{2endo,3} \sim 6.5$ Hz); 8.42 for H-2*exo* (quartet, $J_{2exo,3} \sim 10$ Hz).

*3,4-Di-O-acetyl-1,6-anhydro-2-deoxy*-β-DL-*ribo-hexopyranose (**8**, R = $CH_3CO$)*

A mixture of 12 ml of acetic anhydride, 10 ml of pyridine, and 1.05 g (0.0072 mol) of **8** (R = H) was stirred at room temperature for 72 h. The excess of acetic anhydride and pyridine was removed and the residual brown oil was neutralized with 10 ml of 6 *N* ammonium hydroxide. The mixture was then extracted with chloroform (6 × 15 ml) and the solution dried ($MgSO_4$). Removal of solvent gave a light brown syrup which formed crystals from hexane. Yield of **8** (R = $CH_3CO$), 1.24 g (93%), m.p. 80–81°.

Anal. Calcd. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.19; H, 5.95.

The i.r. spectrum in chloroform showed a strong band at 1755 $cm^{-1}$ (C=O).

The 100 MHz p.m.r. spectrum in $CDCl_3$ showed signals at τ 4.37 for H-1 (narrow multiplet, $w/2 \sim 5$ Hz); 4.50–5.00 for H-3 and -4 (multiplet); 5.30–5.40 for H-5 (multiplet); 6.05 for H-6*endo* (quartet, $J_{6endo,6exo} \sim 7.5$, $J_{5,6endo} \sim 1.5$ Hz); 6.23 for H-6*exo* (quartet, $J_{5,6exo} \sim 5$ Hz); 7.70–8.20 for H-2*exo* and -2*endo* (multiplet); 7.82 and 7.96, each a singlet for $CH_3CO$.

*2-Deoxy*-DL-*ribo-hexopyranose (**9**, R = H)*

A solution of 0.3 g (0.0021 mol) of **8** (R = H) in 15 ml of 1 *N* hydrochloric acid was stirred at 55° for 12 h. The solution was then diluted with 100 ml of water and neutralized with Amberlite IRA-400 resin ($OH^{\ominus}$). The resin was removed by filtration and washed with water. The water was removed from the filtrate and washings at reduced pressure to give a colorless syrup. Crystallization from absolute ethanol gave 0.29 g (88%) of solid **9** (R = H), melting at 138–140°; lit. m.p. of 2-deoxy-D-*ribo*-hexopyranose, 140–142° (12).

The 100 MHz p.m.r. spectrum in $D_2O$ was identical to that of authentic 2-deoxy-D-*ribo*-hexopyranose (12). The two quartets for H-1 at τ 4.00 and 4.40 showed that the α and β anomers were present in the approximate ratio of 1:2 as shown by the integrated areas.

*2-Deoxy*-DL-*ribo-hexopyranose Tetraacetate (**9**, R = $CH_3CO$)*

Acetylation was accomplished by the same procedure as that used to prepare **8** (R = $CH_3CO$) above. From 0.1 g (0.0006 mol) of **9** (R = H) there was obtained 0.17 g (88%) of **9** (R = $CH_3CO$), a syrup, after sublimation of the crude viscous oil at 95° at 0.75 mm. Attempts to crystallize this were unsuccessful. A t.l.c. analysis using 4% methanol in chloroform showed only one spot.

Anal. Calcd. for $C_{14}H_{19}O_9$: C, 50.76; H, 5.78. Found: C, 50.49; H, 6.08.

The i.r. spectrum (neat) showed a strong band at 1775 $cm^{-1}$ (C=O).

The 100 MHz p.m.r. spectrum in $CDCl_3$ showed two anomeric proton signals, at τ 3.64 for H-1 of the α anomer (quartet), $J_{1,2e \text{ or } a} \sim 3.0$, $J_{1,2a \text{ or } e} \sim 5.0$ Hz) and at 3.99 for H-1 of the β anomer (quartet, $J_{1,2a} \sim 7.5$, $J_{1,2e} \sim 3.5$ Hz).

*2-Deoxy-1,6:3,4-dianhydro*-β-DL-*ribo-hexopyranose (**10**)*

To a stirred solution of 11.2 g (0.01 mol) of **2** in 200 ml of methylene chloride kept at room temperature, was added 21.5 g (0.10 mol) of 87% *m*-chloroperoxybenzoic acid. The resulting mixture was stirred at room temperature for an additional 24 h then filtered to remove precipitated *m*-chlorobenzoic acid. The precipitate was washed with 50 ml of methylene chloride. The combined washings and filtrate were washed with water, then with saturated aqueous sodium carbonate (2 × 50 ml). The aqueous washings were extracted with methylene chloride. The combined methylene chloride solutions were dried ($MgSO_4$) and freed from solvent to provide a light amber oil which was distilled at 55–56° at 1.0 mm to give 9.5 g (74%) of 2-deoxy-1,6:3,4-dianhydro-β-DL-*ribo*-hexopyranose (**10**) containing the *lyxo* isomer **11** to the extent of 2%. The g.l.c. analysis of this distillate with a column of 20% butanediol succinate on Gas-Chrom P at 185°, showed two distinct symmetrical peaks in the area ratio 49:1. A 12′ × 1/4″ preparative g.l.c. column of 20% butanediol succinate on Gas-Chrom P, 60–80 mesh, separated the major component **10**. Reinjection of this separated material showed only one peak.

The minor component **11** could not be freed from the isomer **10** because of tailing from the major peak but was obtained as a mixture of **10** and **11** in the ratio 1:2 respectively as measured by the areas of the signals of the H-5 protons in the 100 MHz p.m.r. spectrum and by the g.l.c. analysis.

Anal. Calcd. for $C_6H_8O_3$ for **10**: C, 56.25; H, 6.29. Found: C, 56.38; H, 6.56.

The i.r. spectrum of **10** (neat) showed no absorption band in the double bond region.

The 100 MHz p.m.r. spectrum of **10** in $CDCl_3$ showed signals at τ 4.65 for H-1 (narrow multiplet, $J_{1,2exo} \sim J_{1,2endo} \sim 1$, $J_{1,3} \sim 1.5$ Hz for long range coupling); 5.35 for H-5 (doublet of narrow quartets, $J_{5,6exo} \sim 4.5$, $J_{5,6endo} \sim 1$, $J_{4,5} \sim 1.5$ Hz); 5.95 for H-6*endo* (quartet, $J_{6exo,6endo} \sim 8$ Hz); 6.27 for H-6*exo* (quartet); 6.85–7.05 for H-3 and -4 (narrow multiplet); 7.87 for H-2*exo* (quartet, $J_{2exo,2endo} \sim 16$, $J_{1,2exo} \sim 2.7$ Hz); 8.20 for H-2*endo* (quartet of triplets, $J_{2endo,3} \sim 3.5$, $J_{1,2endo} \sim 1$ Hz).

*2-Deoxy-1,6:3,4-dianhydro*-β-DL-*lyxo-hexopyranose (**11**)*

The 100 MHz p.m.r. spectrum of this mixture showed the signals found for isomer **10** above. In addition the following signals were perceived. τ 4.60 for H-1 overlapping H-1 of isomer **10** (narrow multiplet $w/2 \sim 6$ Hz); 5.20 for H-5 (triplet $J_{5,6exo} \sim 5$, $J_{4,5} \sim 5$, $J_{5,6endo} < 1$ Hz); 5.97 for H-6*endo* (doublet, $J_{6endo,6exo} \sim 6.5$ Hz); 6.37–6.58 for H-6*exo* and -4 (multiplet); 6.80–7.20 for H-3 overlapping H-3 and -4 of the isomer **10** (multiplet); 7.28–8.23 for H-2*exo* and -2*endo* overlapping the signals for these protons of the isomer **10** (multiplet).

*1,6-Anhydro-2-deoxy*-β-DL-*arabino-hexopyranose (**12**)*

A mixture of 1.46 g (0.014 mol) of **10** in 5% aqueous potassium hydroxide was stirred and heated under reflux for 24 h. It was then cooled, neutralized with dilute hydrochloric acid to p*H* 8, saturated with sodium chloride, and then extracted continuously for 65 h with chloroform. The chloroform extract was dried ($MgSO_4$), filtered, and freed from solvent to provide a syrup.

This was sublimed at 78–85° at 0.2 mm to give 1.6 g (79%) of the diol **12** as colorless needles melting at 98–101°. The t.l.c. of this material (on silica gel with 20% methanol in chloroform) showed only one spot; lit. m.p. of D isomer 156–153° (14).

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.31; H, 6.89. Found: C, 49.38; H, 6.81.

The i.r. spectrum in $CHCl_3$ showed a broad band at 3420 and a narrower band at 3580 $cm^{-1}$ (OH).

The 100 MHz p.m.r. spectrum in $CDCl_3$ showed signals at $\tau$ 4.40 for H-1 (narrow multiplet $w/2 \sim 4$ Hz); $\tau$ 5.48 for H-5 (multiplet, $J_{5,6exo} \sim 6$ Hz); 5.61 for H-6*endo* (doublet of doublets, $J_{6endo,6exo} \sim 7$, $J_{5,6endo} \sim 1$ Hz); 6.05–6.35 for H-3, -4, and -6*exo* (multiplet); 7.02 for two OH (broad singlet $w/2 \sim 6$ Hz); 7.81 for H-2*exo* (doublet of quartets, $J_{2exo,2endo} \sim 14$; $J_{2exo,3} \sim 5$, $J_{1,2exo} \sim 2$ Hz); 8.17 for H-2*endo* (complicated doublet).

*2-Deoxy-*α,β-DL-*arabino-hexopyranose (13)*

A stirred solution of 1.12 g (0.0077 mol) of **12** in 50 ml of 1 *N* hydrochloric acid was heated at 55° for 12 h. The mixture was then diluted to 200 ml with distilled water and neutralized with Amberlite IRA-400 ($OH^{\ominus}$). The resulting water solution was treated with animal charcoal and the excess water removed under reduced pressure to afford 1.06 g (84%) of **13**. The t.l.c. analysis (50% methanol in chloroform) showed a single spot with slight tailing. Therefore, the sugar was chromatographed over a short column of Silica Gel G (eluting with 50% methanol in chloroform) to afford a colorless syrup which crystallized as white needles from methanol–ether (m.p. 125–126°). The p.m.r. is identical with that of an authentic sample of the D isomer.

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 44.04; H, 7.32.

*1,6-Anhydro-2,3-dideoxy-*β-DL-*erythro-hexopyranose (14)*

A solution of the oxirane **10** (0.73 g, 0.0057 mol) in 25 ml of dry ether was added dropwise with stirring, over a 45 min period, to a slurry of 0.23 g (0.006 mol) of lithium aluminum hydride in 35 ml of dry ether. The resulting mixture was then stirred for 20 h and subsequently treated slowly with 15 ml of ether saturated with water, then with 1 ml of 15% aqueous sodium hydroxide. The colorless precipitate was removed by filtration and washed with ether (3 × 10 ml). The combined ether washings and filtrate were dried ($MgSO_4$). Removal of the drying agent and solvent gave a hygroscopic solid which was sublimed at 60° at 0.3 mm to afford 0.68 g (92%) of **14**, melting at 79–81°.

Anal. Calcd. for $C_6H_{10}O_3$: C, 55.37; H, 7.75. Found: C, 55.07; H, 7.62.

The i.r. spectrum in chloroform showed a band at 3580 $cm^{-1}$ (OH).

The 100 MHz p.m.r. spectrum in deuteriochloroform showed signals at $\tau$ 4.48 for H-1 (broad singlet $w/2 \sim 4$ Hz, $J_{1,2endo} \sim 1.5$, $J_{1,6exo} \sim 1$ Hz); 5.53 for H-5 (narrow multiplet $w/2 \sim 10$ Hz); 6.04–6.30 for H-6*exo* and -6*endo* (multiplets); 6.33 for H-4 (narrow multiplet $w/2 \sim 8$ Hz); 6.65 for one OH (singlet); 7.78–8.60 for H-3*exo*, -3*endo*, -2*exo*, -2*endo* (multiplets).

*Hydrolysis of 14*

A solution of 0.37 g (0.00285 mol) of **14** in a mixture of 10 ml of water and 10 ml of 1 *N* hydrochloric acid was kept at 55° for 24 h and then diluted with 50 ml of water. The acid was neutralized with Amberlite IRA-400 ($OH^{\ominus}$). The water was removed from the filtrate under reduced pressure. The residual syrup was chromatographed through a short column of silica gel (eluent, 20% methanol in chloroform) and gave 0.36 (85%) of a viscous syrup. The t.l.c. analysis (20% methanol in chloroform) showed a single spot.

Anal. Calcd. for $C_6H_{12}O_4$: C, 48.63; H, 8.10. Found: C, 47.90; H, 8.12.

The i.r. spectrum (neat) had a broad band at 3390 $cm^{-1}$ (OH).

The 100 MHz p.m.r. spectrum in DMSO-$d_6$ showed a broad unresolved signal over the range $\tau$ 8.00–8.80 for the two methylene aliphatic groups, and broad unresolved multiplets over the range $\tau$ 4.90–5.50 in the anomeric proton region.

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