Base Catalyzed Isomerization of Epoxides to Bicyclic Allylic Alcohols, Potential Intermediates for the Total Synthesis of the DL-Aldohexoses

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Treatment of the epoxide 2-deoxy-1,6:3,4-dianhydro-β-DL-*ribo*-hexopyranose (**3**) with *n*-butyllithium, and the epoxides 2-deoxy-1,6:3,4-dianhydro-β-DL-*lyxo*-hexopyranose (**5**) and 4-deoxy-1,6:2,3-dianhydro-β-DL-*lyxo*-hexopyranose (**7**) with lithium diethylamide has provided 1,6-anhydro-2,3-dideoxy-β-DL-*erythro*-hex-2-enopyranose (**4**), 1,6-anhydro-2,3-dideoxy-β-DL-*threo*-hex-2-enopyranose (**6**), and 1,6-anhydro-3,4-dideoxy-β-DL-*threo*-hex-3-enopyranose (**8**) in yields of 65, 50, and 20%, respectively. These allylic alcohols are potential intermediates for the synthesis of the various DL-aldohexoses.

La réaction de l'époxyde déoxy-2 dianhydro-1,6:3,4-β-DL-*ribo* hexopyrannose (**3**) avec le *n*-butyllithium de même que les réactions des époxydes déoxy-2 dianhydro-1,6:3,4 β-DL-hexopyrannose (**5**) et déoxy-4 dianhydro-1,6:2,3-β-DL-hexopyrannose (**7**) avec l'amidure diéthyl lithium ont conduit respectivement à l'anhydro-1,6 didéoxy-2,3-β-DL-*érythro*-hex-éno-2 pyrannose (**4**) anhydro-1,6 didéoxy-2,3-β-DL-*thréo*-hex-éno-3 pyrannose (**6**) et anhydro-1,6 didéoxy-3,4-β-DL-*thréo*-hex-éno-3 pyrannose (**8**) avec des rendements 65, 50 et 20%. Ces alcools allyliques sont des intermédiaires possibles pour les synthèses de divers aldohexose-DL.
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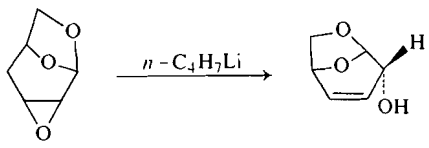
Introduction

Recent reports from this laboratory (1, 2*a*) have shown that *n*-butyllithium effected the conversion of 4-deoxy-1,6:2,3-dianhydro-β-DL-*ribo*-hexopyranose (**1**) to the allylic alcohol 1,6-anhydro-3,4-dideoxy-β-DL-*erythro*-hex-3-enopyranose (**2**). The latter could be converted to DL-glucose (1, 2*a*) and to DL-allose and DL-galactose (2*b*). We have now explored the feasibility of a



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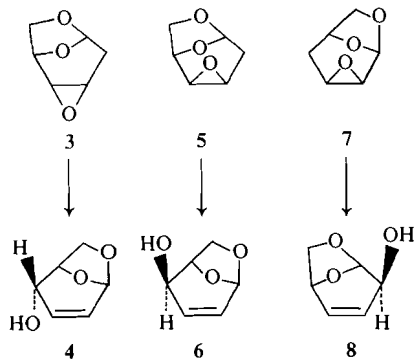
similar conversion of the isomeric epoxides **3**, **5**, **7** to the corresponding allylic alcohols **4**, **6**, **8**, compounds which could be used as intermediates for the preparation of most if not all of the eight isomeric DL-aldohexoses, as well as several mono- and dideoxy-DL-aldohexoses. This paper describes the results of our work on the preparation of these allylic alcohols.



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The oxide, **3**, previously synthesized (3), and the oxides **5** and **7**, both prepared by advantageous modifications of the procedure reported for the preparation of the D isomer of **7** (4), were first each subjected to treatment with *n*-butyllithium according to the directions which had been used for the conversion of **1** to **2** (1, 2*a*). This procedure was successful for **3**, giving **4** in 65% yield. However for both **5** and **7**, *n*-butyllithium was quite unsatisfactory since apparently

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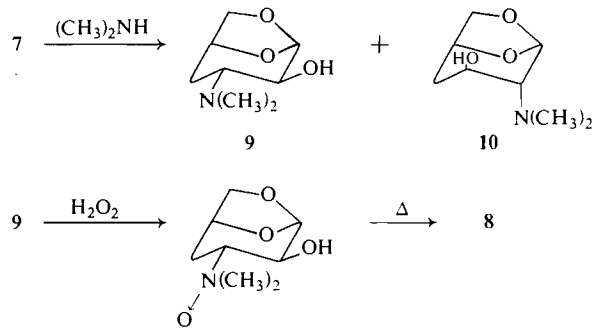

SCHEME 1

the attack by the *n*-butyl carbanion on the epoxide ring itself competed successfully, and little if any of the allylic alcohols **6** or **8** could be isolated. The reagent lithium diethylamide, however, provided **6** and **8** from **5** and **7** in yields of 50 and 20%, respectively.

The use of sodium hydride on benzene, toluene, or 1,2-dimethoxyethane solutions of the oxides or the application of the strong base 1,5-diazabicyclo[4.3.0]non-5-ene (5) was in each case quite unsuccessful.

Since pyrolysis of amine oxides has been used to prepare similar allylic alcohols in carbohydrate syntheses (6–8) we attempted a similar sequence of reactions on the epoxide **7** in order to obtain a better yield of **8**. Amination of **7** gave two products, **9** and **10**, isolable in yields of 60 and 30% respectively, based on **7** (Scheme 1). Conversion of the amine **9** to the amine oxide **11** (not isolated), followed by pyrolysis of the latter, gave **8** in 10% yield based on **9**. The bulk of **11** appeared to decompose to a charred mass. It is clear that the reaction of lithium diethylamide with **7** is preferred over the amination and pyrolysis route.

Experimental

All melting points and boiling points are uncorrected. Elemental analyses were made by Mrs. D. Mahlow of this department. The p.m.r. spectra and decoupling experiments were made with a Varian Associates HR 100 Spectrometer by Mr. Glen Bigam of this department. Tetramethylsilane was used as the internal standard. Observed couplings are reported.

The g.l.c. analyses were made with a Wilkins Autoprep Model A 700 using a column $\frac{1}{8}$ in. × 10 ft packed with a 1:1 mixture of butanediol succinate and silicone rubber SE 30 (F and M Scientific Corp., Avondale Pa.), total 20%, on Carbowax 4000 (W. H. Curtin and Co., Houston, Texas). Helium was the carrier gas at a flow rate of 60–90 ml/min.

The i.r. spectra were obtained with a Perkin-Elmer 421 Grating Spectrophotometer, by Mr. Robert Swindlehurst of this department.

Solvents were removed by rotary evaporator under water pump vacuum. Organic solutions were dried with magnesium sulfate.

Preparation of the Epoxides 3, 5, 7

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

This compound was prepared according to published directions (3).

2-Deoxy-1,6:3,4-dianhydro-β-DL-*lyxo-hexopyranose (5)*

Conversion of 7.16 g (0.4 ml) of the epoxide, **3**, to 1,6-anhydro-2-deoxy-β-DL-*arabino*-hexopyranose was accomplished by using the reported procedure (3), modified as follows to obtain a better yield of product in a much shorter time (1/2 day rather than 3 days). After the reaction mixture was neutralized to p*H* 8, the resulting aqueous solution was freed from water and the residue was dissolved in 100 ml of methanol. Precipitated sodium chloride was removed and the solution freed from methanol. The oily residue was dissolved in 100 ml of methanol again and the second precipitate of sodium chloride was removed. The methanol was distilled from the filtrate and the residue dissolved in 200 ml of chloroform. The solution was dried, freed from solid and solvent, and the residue purified by sublimation as previously described (3), giving a 90% yield of pure *1,6-anhydro-2-deoxy*-β-DL-*arabino-hexopyranose.*

The above *arabino*-hexopyranose was converted to a mixture of the mono- and ditosylated derivatives using the following modification of a reported tosylation procedure (9). A stirred mixture of 15.95 g (0.11 mol) of 1,6-anhydro-2-deoxy-β-DL-*arabino*-hexopyranose, 300 ml of dry pyridine, and 400 ml of dry acetone, cooled to 10° was treated with a total of 29.38 g (0.13 mol) of *p*-toluenesulfonyl chloride, added in small portions. When addition was complete, the mixture was allowed to stand for 5 days at 10–12° and then at room temperature for an additional 2 days. This temperature and time minimized the formation of the ditosylated product and allowed completion of reaction. The mixture was then reduced to $\frac{2}{3}$ its volume, and the residue was diluted with 400 ml of water and allowed to stand. The precipitate of ditosylated byproduct was removed. The mother liquor, on standing for 2 h in a refrigerator, deposited additional ditosylated product. The combined ditosylate, dissolved in chloroform, was washed thoroughly with cold 1% aqueous hydrochloric

acid (to remove pyridine) and then with water. The dried solution was freed from solid and solvent, and provided a colorless amorphous solid which was crystallized from ethanol to give 4 g (8%) of pure *1,6-anhydro-2-deoxy-3,4-di-O-p-toluenesulfonyl*-β-DL-*arabino-hexopyranose*, m.p. 146–148°.

Anal. Calcd. for $C_{20}H_{22}O_8S_2$: C, 52.85; H, 4.88; S, 14.1. Found: C, 52.80; H, 4.85; S, 13.81.

Both the i.r. and p.m.r. spectra agreed completely with the structure designated.

The mother liquor from the ditosyl compound above was extracted repeatedly with chloroform and the combined chloroform solutions were freed from solvent.The residue, again dissolved in 300 ml of chloroform, was washed carefully several times with cold 1% aqueous hydrochloric acid. After a final water wash, the solution was dried. Removal of the drying agent and solvent gave a residue which solidified on standing. This crude *1,6-anhydro-2-deoxy-4-O-p-toluenesulfonyl*-β-DL-*arabino-hexopyranose* (yield, 76%) melted at 58–60° but contained a small amount of pyridine (odor) probably as part of the crystalline structure. Attempts at further purification by repetition of the washing procedure produced a syrupy material which gave unsatisfactory elemental analyses. A similar observation has been reported for an analogous compound (9). However the crude material was quite satisfactory for the subsequent epoxide formation.

The 100 MHz p.m.r. spectrum of this crude material in $CDCl_3$ was surprisingly clean and clearly verified the structure. Signals occurred at δ 7.84 and 7.36 (two doublets as an AB quartet for 4H, aromatic), 5.55 (narrow multiplet for H-1, $w_{1/2} \sim 4$ Hz, $J_{1,5} < 0.5$ Hz, $J_{1,2endo} \sim 2$ Hz, $J_{1,2exo} < 0.5$ Hz); 4.48 (complex doublet for H-5); 4.42 (narrow multiplet for H-4, $w_{1/2} \sim 5.0$ Hz); 4.19 (doublet of narrow doublets for H-6_{endo}, $J_{6exo,6endo} \sim 7.5$ Hz, $J_{6endo,5} \sim 1$ Hz); 3.95–3.65 (complex multiplet for H-3); 3.62 (quartet for H-6_{exo}, $J_{6exo,5} \sim 5$ Hz); 3.28 (doublet for C_3—OH, $J_{3,OH} \sim 6$ Hz); 2.41 (singlet for CH_3); 2.08 (doublet of quartets for H-2_{endo}, $J_{1,2endo} \sim 2$ Hz, $J_{2endo,2exo} \sim 15$ Hz, $J_{2endo,3} \sim 6$ Hz); 1.82 (doublet for H-2_{exo}).

The crude monotosyl compound above (22.5 g) in 300 ml of chloroform was added with stirring to 100 ml of dry methanol, previously treated with 4 g of sodium metal. The solution was kept at room temperature and stirred for 12 h, then poured into cold water (200 ml). The organic layer was separated and the aqueous layer was extracted repeatedly with chloroform. The combined chloroform extracts and organic layer were dried, then freed from solid and solvent. The residue on distillation gave pure *2-deoxy-1,6:3,4-dianhydro*-β-DL-*lyxo-hexopyranose*, b.p. 45° at 0.3 mm. Yield, 8 g (83%).

Anal. Calcd. for $C_6H_8O_3$: C, 56.25; H, 6.29. Found: C, 56.32; H, 6.44.

The 100 MHz p.m.r. spectrum in $CDCl_3$ showed signals nearly identical to those reported for the same compound obtained as a minor product and contaminated with a small amount of the *ribo* isomer (3).

4-Deoxy-1,6:2,3-dianhydro-β-DL-*lyxo-hexopyranose (7)*

The epoxide 4-deoxy-1,6:2,3-dianhydro-β-DL-*ribo*-hexopyranose (10), (7.1 g, 0.4 mol) was converted to *1,6-anhydro-4-deoxy*-β-DL-*xylo-hexopyranose* following the modified procedure described above for the reaction of epoxide **3** to form 1,6-anhydro-2-deoxy-β-DL-*arabino*-hexopyranose. The *xylo* isomer, identical to that described previously (10), was obtained in a much shorter time and in ~90% yield.

The 1,6-anhydro-4-deoxy-β-DL-*xylo*-hexopyranose (3.6 g) was converted to a mixture of mono- and ditosylated derivatives according to the method used above for the *arabino* isomer, but with the following modification, required because of the different solubility and melting point properties. After the reacting mixture had stood for 5 days, it was diluted with water (100 ml) and then extracted thoroughly with chloroform. The combined chloroform extracts were washed carefully with cold 1% aqueous hydrochloric acid, then with water, and finally dried. Removal of the solid and solvent provided a crude product which showed only two spots on t.l.c. (chloroform – ethyl acetate, 2:1). Separation was carried out by chromatography on a silica gel column using chloroform – ethyl acetate, 2:1, as solvent. The first fraction gave a solid which when crystallized from dichloromethane–*n*-hexane produced 5.5 g (75%) of pure *1,6-anhydro-4-deoxy-2-O-p-toluenesulfonyl*-β-DL-*xylo-hexopyranose* as colorless needles, m.p. 123–124°.

Anal. Calcd. for $C_{13}H_{16}O_6S$: C, 52.0; H, 5.33; S, 10.66. Found: C, 51.97; H, 5.27; S, 11.04.

The 100 MHz p.m.r. spectrum in $CDCl_3$ showed signals at δ 7.82 and 7.34 (AB quartet for 4H, aromatic, $J \sim 8$ Hz); 5.27 (narrow multiplet for H-1, $w_{1/2} \sim 5$ Hz, $J_{1,2} \sim 1.0$ Hz); 4.68–4.50 (triplet for H-5, $J_{5,4exo} \sim 5$ Hz, $J_{5,4endo} \sim 1.0$ Hz, $J_{5,6endo} < 1.0$ Hz, $J_{5,6exo} \sim 5.0$ Hz); 4.25 (narrow multiplet for H-2, $w_{1/2} \sim 4.5$ Hz); 4.21 (doublet for H-6_{endo}, $J_{6endo,6exo} \sim 7.0$ Hz); 3.94 (multiplet for H-3, $J_{3,4exo} \sim 5.0$ Hz); 3.73 (triplet of doublets for H-6_{exo}, $J_{4,6exo} \sim 1.5$ Hz); 2.98 (singlet for OH, $w_{1/2} \sim 2.5$ Hz); 2.53 (singlet for CH_3); 2.31 (multiplet for H-4_{exo}, $J_{4exo,4endo} \sim 15.0$ Hz); 1.70 (doublet of narrow doublets for H-4_{endo}).

The second fraction, eluted with a 1:1 mixture of chloroform and ethyl acetate, gave *1,6-anhydro-4-deoxy-di-O-p-toluenesulfonyl*-β-DL-*xylo-hexopyranose*; colorless needles from dichloromethane-*n*-hexane; m.p. 46–47°; yield, 0.51 g (4.5%).

Anal. Calcd. for $C_{20}H_{22}O_8S_2$: C, 52.85; H, 4.88; S, 14.1. Found: C, 53.11; H, 4.97; S, 14.29.

The 100 MHz p.m.r. spectrum in $CDCl_3$ showed signals at δ 7.80 and 7.40 (a doublet of quartets for 8H, aromatic); 5.27 (singlet for H-1, $w_{1/2} \sim 4$ Hz, $J_{1,2} \sim 1.0$ Hz); 4.74 (doublet of triplets for H-3, $J_{3,4exo} \sim 4.5$ Hz, $J_{3,4endo} \sim 1.5$ Hz, $J_{3,2} \sim 1.5$ Hz); 4.56 (multiplet for H-5, $J_{5,6exo} \sim 5.0$ Hz, $J_{5,6endo} \sim 1.0$ Hz, $J_{5,4exo} \sim 4.0$ Hz); 4.28 (narrow doublet for H-2, $w_{1/2} \sim 4.5$ Hz); 4.15 (doublet for H-6_{endo}, $J_{6endo,6exo} \sim 7$ Hz); 3.75 (two overlapping quartets for H-6_{exo}); 2.57 (singlet for two CH_3, overlapping signal for H-4_{exo}); 2.48 (doublet of triplets for H-4_{exo}, $J_{4exo,4endo} \sim 15.0$ Hz, $J_{4exo,6exo} \sim 1.5$ Hz); 1.95 (doublet for H-6_{endo}).

The monotosylated compound (7.8 g) from the first fraction was converted to the epoxide **7** by the same procedure used above to obtain epoxide **5** from the corresponding monotosylated compound. The pale yellow syrup obtained after removal of the chloroform solvent was purified by sublimation at 90–95° at 0.3–0.5 mm. There was obtained 3.0 g (94%) of **7** as colorless needles, m.p. 73–74° (lit. (4) m.p. for the D-enantiomer, 69–70°).

Anal. Calcd. for $C_6H_8O_3$: C, 56.25; H, 6.29. Found: C, 56.18; H, 6.11.

The 100 MHz p.m.r. spectrum of **7** in $CDCl_3$ showed signals at δ 5.70 (doublet for H-1, $J_{1,2} \sim 3.0$ Hz); 4.47 (complicated quartet for H-5, $J_{5,4exo} \sim 5.5$ Hz, $J_{5,6exo} \sim 3.5$ Hz, $J_{3,5} < 1.0$ Hz, $J_{4endo,5} < 1.0$ Hz); 3.75 (apparent singlet for H-6_{endo}, $w_{1/2} \sim 1.5$ Hz, $J_{6exo,6endo} \sim 0.0$ Hz); 3.73 (doublet for H-6_{exo}, $J_{6exo,5} \sim 3.5$ Hz); 3.42 (triplet for H-2, $J_{1,2} \sim 3$ Hz, $J_{2,3} \sim 4$ Hz); 3.20 (triplet for H-3, $J_{3,4exo} \sim 3.0$ Hz, $J_{2,3} \sim 4$ Hz, $J_{3,5} < 1.0$ Hz); 2.32 (doublet of quartets for H-4_{exo}, $J_{5,4exo} \sim 5.5$ Hz, $J_{4exo,4endo} \sim 16$ Hz, $J_{3,4exo} \sim 3$ Hz); 2.03 (doublet of narrow doublets for H-4_{endo}, $J_{5,4endo} < 1.0$ Hz).

*Preparation of the Allylic Alcohols **4**, **6**, and **8***

*1,6-Anhydro-2,3-dideoxy-*β-DL-*erythro-hex-2-enopyranose (**4**)*

A solution of 7.68 g (0.06 mol) of 2-deoxy-1,6:3,4-dianhydro-β-DL-*ribo*-hexopyranose (**3**) (3) in 50 ml of dry ether was treated with *n*-butyllithium (0.123 mol) according to published directions (2*a*), but with the following modification. The oil left after the removal of the solvent from the dried solution, was fractionally distilled to give 5 g (65%) of pure *1,6-anhydro-2,3-dideoxy-*β-DL-*erythro-hex-2-enopyranose (**4**)* b.p. 69° at 0.3 mm.

Anal. Calcd. for $C_6H_8O_3$: C, 56.25; H, 6.29. Found: C, 55.08; H, 6.39.

The 100 MHz spectrum in $CDCl_3$ agreed completely with the assigned structure and showed signals at δ6.02 (doublet of doublets for H-2, $J_{2,3} \sim 10$ Hz, $J_{1,2} \sim 3.5$ Hz); 5.82 (complicated doublet of doublets for H-3, $J_{3,4} \sim 4.0$ Hz, $J_{3,5} \sim 1.5$ Hz, $J_{1,3} \sim 1.0$ Hz); 5.51 (narrow doublet of doublets for H-1, $J_{1,2} \sim 3.5$ Hz, $J_{1,3} \sim 1.0$ Hz); 4.65 (multiplet for H-5, $J_{5,6exo} \sim 6.5$ Hz, $J_{5,6endo} \sim 2.0$ Hz, $J_{5,4endo} \sim 2.0$ Hz); 3.92 (doublet of doublets for H-6_{exo}, $J_{6exo,6endo} \sim 8.0$ Hz); 3.75–3.52 (multiplet for H-4); 3.43 (doublet of doublets for H-6_{endo}); 3.30–2.90 (broad signal for OH).

*1,6-Anhydro-2,3-dideoxy-*β-DL-*threo-hex-2-enopyranose (**6**)*

A solution of 1.28 g (0.01 mol) of 2-deoxy-1,6:3,4-dianhydro-β-DL-*lyxo*-hexopyranose (**5**) in 10 ml of dry benzene, was added all at once to a stirred solution of lithium diethylamide, previously prepared by the addition of 10.5 ml of 22.3% *n*-butyllithium to a solution of 2.25 g of diethylamine in a mixture of 10 ml of dry benzene and 10 ml of dry hexane (11). All operations were carried out under nitrogen. The stirred solution stood for 18 h at room temperature, and then was heated under reflux for 1 h. The solution was cooled and treated with 10 ml of water. The aqueous layer was extracted with methylene chloride (3 × 50 ml) and then continuously extracted with methylene chloride for 24 h to remove the somewhat water-soluble allylic alcohol. The combined extracts and organic layer were dried. Removal of the solid and solvent gave a brown oil which was fractionally distilled to provide 0.64 g (50%) of pure *1,6-anhydro-2,3-dideoxy-*β-DL-*threo-hex-2-enopyranose*, **6**, b.p. 65–60° at 0.05 mm.

Anal. Calcd. for $C_6H_8O_3$: C, 56.25; H, 6.25. Found: C, 56.13; H, 6.46.

The p.m.r. spectrum in $CDCl_3$ agreed with the proposed structure, showing signals at δ 5.87 (doublet of quartets for H-2, $J_{2,1} \sim 3$ Hz, $J_{2,3} \sim 10$ Hz, $J_{2,4} \sim 1.5$ Hz); 5.67 (double of multiplets for H-3, $J_{3,1} \sim 1.0$ Hz, $J_{3,4} \sim 2.0$ Hz, $J_{3,5} \sim 2.0$ Hz); 5.48 (doublet for H-1, $J_{1,2} \sim 3.0$ Hz, $J_{1,3} \sim 1.0$ Hz); 4.73 (multiplet for H-4, $J_{3,4} \approx J_{2,4} \approx J_{4,6exo} \sim 1.5$ Hz, $J_{4,5} \sim 5.0$ Hz); 4.48 (multiplet for H-5 $J_{5,3} \approx J_{5,6endo} \sim 2.0$ Hz); 4.18 (doublet of quartets for H-6_{endo}, $J_{6endo,6exo} \sim 8.0$ Hz, $J_{5,6endo} \sim 2.0$ Hz, $J_{1,6endo} \sim 0.5$ Hz); 3.86 (doublet of quartets for H-6_{exo}, $J_{6exo,4} \sim 1.5$ Hz, $J_{6exo,5} \sim 6.0$ Hz); 3.34 (singlet for OH, $w_{1/2} \sim 3$ Hz).

*1,6-Anhydro-3,4-dideoxy-*β-DL-*threo-hex-3-enopyranose (**8**)*

This compound was prepared by the following two methods.

Procedure A

The epoxide 4-deoxy-1,6:2,3-dianhydro-β-DL-*lyxo*-hexopyranose (**7**) (1.28 g, 0.01 mol) was converted to **8** by the same procedure used to obtain **6** above. After a second distillation to remove traces of contaminating epoxide **7**, 0.26 g (20%) of *1,6-anhydro-3,4-dideoxy-*β-DL-*threo-hex-3-enopyranose (**8**)* was obtained boiling at 43–44° at 0.1 mm. This was about 98% pure. An analytical sample was prepared by preparative g.l.c. on a column packed with butanediol succinate and S.E. 30, operating at 160 °C with a helium gas flow rate of 60 ml/min.

Anal. Calcd. for $C_6H_8O_3$: C, 56.25; H, 6.25. Found: C, 55.94; H, 6.10.

The 100 MHz p.m.r. spectrum in $CDCl_3$ verified the assigned structure, showing signals at δ 6.14 (doublet of doublets for H-4, $J_{4,5} \sim 4.0$ Hz, $J_{4,3} \sim 10.0$ Hz, $J_{4,2} \sim 1.0$ Hz); 5.72 (doublet of triplets for H-3, $J_{3,1} \sim J_{3,2} \sim 2.0$ Hz, $J_{3,5} < 1.0$ Hz); 5.53 (narrow multiplet for H-1, $w_{1/2} \sim 6.5$ Hz, $J_{1,2} \sim 3.5$ Hz, $J_{1,3} \sim 2.0$ Hz); 4.66 (triplet for H-5, $J_{4,5} \sim 4.0$ Hz, $J_{5,6exo} \sim 4.0$ Hz); 4.33 (narrow multiplet for H-2, $w_{1/2} \sim 6.5$ Hz, $J_{2,1} \sim 3.5$ Hz, $J_{2,3} \sim 2.0$ Hz, $J_{2,4} < 1.0$ Hz); 3.85 (doublet for H-6_{endo}, $J_{6endo,6exo} \sim 6.5$ Hz, $J_{6endo,5} < 1.0$ Hz); 3.73 (doublet of doublets for H-6_{exo}); 2.31 (singlet for OH, $w_{1/2} \sim 2.5$ Hz).

Procedure B

A mixture of 2.56 g (0.02 mol) of 4-deoxy-1,6:2,3-dianhydro-β-DL-*lyxo*-hexopyranose and 20 ml of 20% dimethylamine in water was allowed to stand for 72 h at room temperature. The water and excess dimethylamine were then removed. The residue solidified on standing. The 100 MHz p.m.r. spectrum of this crude material showed two signals in the anomeric proton region, of area ratio ~1:2, indicative of two products. The two substances were separated by repeated crystallization using dry ether as solvent and provided the two amines **9** and **10**. Compound **9** was purified by sublimation at 0.1 mm, bath temperature 80–90°. There was obtained 2.1 g (60% based on **7**) of pure *1,6-anhydro-3,4-dideoxy-3-dimethylamino-*β-DL-*arabino-hexopyranose*, **9**, melting at 108–109°.

Anal. Calcd. for $C_8H_{15}O_3N$: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.27; H, 8.76; N, 7.86.

The 100 MHz p.m.r. spectrum in $CDCl_3$–acetone-d_6 showed signals at δ 5.23 (narrow doublet for H-1, $J_{1,2} \sim 2.0$ Hz); 4.66–4.48 (multiplet for H-5); 3.78 (doublet for H-6_{endo}, $J_{6endo,5} \sim 1$ Hz, $J_{6endo,6exo} \sim 7.0$ Hz); 3.65 (doublet of doublets for H-$6_{exo,5} \sim 5.0$ Hz); 6.57 (doublet of doublets for H-2, $J_{2,3} \sim 9.0$ Hz); 3.00–2.50 (multiplet for H-3, $J_{3,4eq} \approx J_{3,4ax} \sim 8$ Hz); 2.27 (singlet for $(CH_3)_2N$); 1.50–1.90 (multiplet for H-4_{exo} and H-4_{endo}, $J_{4eq,5} \approx J_{4ax,5} \sim 2$ Hz).

The second product was purified by distillation and gave 1.0 g (30%) of pure *1,6-anhydro-2,4-dideoxy-2-dimethylamino*-β-DL-*xylo-hexopyranose*, ***10***, b.p. 45–47° at 0.15 mm, m.p. 94–95°.

Anal. Calcd. for $C_8H_{15}O_3N$: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.40; H, 8.94; N, 7.85.

The 100 MHz p.m.r. spectrum in $CDCl_3$–acetone-d_6 showed signals at 5.47 (singlet for H-1, $w_{1/2} \sim 3$ Hz, $J_{1,2} \approx J_{1,3} < 1$ Hz); 4.51 (complicated triplet for H-5, $J_{5,6endo} < 0.5$ Hz, $J_{5,6exo} \sim 5.0$ Hz, $J_{5,4ax} \sim 5$ Hz, $J_{5,4eq} \sim 1$–2 Hz); 4.04 (doublet for H-6_{endo}, $J_{6endo,6exo} \sim 6.5$ Hz); 3.97–3.80 (multiplet for H-3, $J_{3,2} \sim 2$ Hz, $J_{3,4eq} \sim 3$ Hz, $J_{3,4ax} \sim 6.0$ Hz, $J_{3,5} \sim 1$ Hz); 3.55 (multiplet for H-6_{exo}, $J_{6exo,4ax} \sim 2$ Hz); 2.50–2.28 (multiplet for overlapping signals for H-2 and $(CH_3)_2N$); 2.28–2.05 (multiplet for H-4_{ax}, $J_{4ax,4eq} \sim 15$ Hz).

A quantity (1.0 g) of the amine **9** was treated with 10 ml of 30% hydrogen peroxide and the mixture was allowed to stand at room temperature for 2½ weeks. The length of time was necessary to ensure completion of the slow reaction. The bulk of the excess hydrogen peroxide was removed carefully by rotary evaporator at room temperature under vacuum, and the residual peroxide removed under 0.1 mm vacuum at a bath temperature not exceeding 40° to avoid decomposition. The crude glassy *N*-oxide was then subjected directly to pyrolysis under vacuum (0.1 mm) using an oil bath heated at first to 130–140° at which temperature pyrolysis begins and the product **8** distills, and then finally to 170° at which temperature pyrolysis is considered to be complete and the residue is black. The distillate was dissolved in chloroform and dried. The solid and solvent were removed and the residue was distilled and purified following the directions in procedure A above. Yield of pure **8**, based on the amine **9** is 10%.

Pyrolysis of the quaternary ammonium salt obtained by the reaction of **9** with methyl iodide gave only the epoxide **7**.

1,6-Anhydro-3,4-dideoxy-2-O-methyl-β-DL-*threo-hexopyranose*

The allylic alcohol **8** was methylated according to reported procedure (12). The product, obtained in good yield, boiled at 42° at 0.1 mm; η_D^{25} 1.4759.

Anal. Calcd. for $C_7H_{10}O_3$: C, 59.14; H, 7.09. Found: C, 58.98; H, 7.26.

1,6-Anhydro-2,3-dideoxy-4-O-methyl-β-DL-*threo-hexopyranose*

The allylic alcohol **6** was methylated by the procedure noted immediately above; b.p. 35° at 0.1 mm; η_D^{25} 1.4695.

Anal. Calcd. for $C_7H_{10}O_3$: C, 59.14; H, 7.09. Found: C, 58.55; H, 7.39.

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1. U. P. SINGH and R. K. BROWN. Can. J. Chem. **48**, 1791 (1970).
2. U. P. SINGH and R. K. BROWN. Can. J. Chem. (*a*) **49**, 3342; (*b*) **49**, 1179 (1971).
3. T. P. MURRAY, U. P. SINGH, and R. K. BROWN. Can. J. Chem. **49**, 2132 (1971).
4. M. CERNÝ and J. PACÁK. Coll. Czech. Chem. Commun. **27**, 94 (1962).
5. H. OEDIGER, H-J. KABBE, F. MÖLLER, and K. EITER. Chem. Ber. **99**, 2012 (1966).
6. W. D. CELMER. J. Am. Chem. Soc. **87**, 1797 (1965).
7. P. H. JONES and E. K. ROWLEY. J. Org. Chem. **33**, 665 (1968).
8. A. BANASZEK and A. ZAMOJSKI. Carbohydr. Res. **25**, 453 (1972).
9. M. CERNÝ, L. KALVODA, and J. PACÁK. Coll. Czech. Chem. Commun. **33**, 1143 (1968).
10. F. SWEET and R. K. BROWN. Can. J. Chem. **46**, 2289 (1968).
11. J. K. CRANDALL. J. Org. Chem. **29**, 2830 (1964).
12. R. M. SRIVASTAVA and R. K. BROWN. Can. J. Chem. **48**, 2334 (1970).