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REACTIONS OF CARBOHYDRATE α-NITROEPOXIDES WITH DIMETHYLAMINE AND WITH METHYLMAGNESIUM IODIDE*

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ABSTRACT

Methyl 2,3-anhydro-4,6-*O*-benzylidene-3-*C*-nitro-β-D-allopyranoside (**1**), as well as its β-D-*manno* (**2**) and α-D-*manno* (**3**) isomers, reacted with dimethylamine to give the same, crystalline 3-(dimethylamino) adduct (**4**) of 1,5-anhydro-4,6-*O*-benzylidene-2-deoxy-2-(dimethylamino)-D-*erythro*-hex-1-en-3-ulose (**5**). The enulose **5** was obtained from **4** by the action of silica gel. Similarly, the β-D-*gulo* (**6**) and α-D-*talo* (**7**) stereoisomers of **1**–**3** afforded a 3-(dimethylamino) adduct (**8**) of the D-*threo* isomer (**9**) of **5**. Reaction of dimethylamine with 5,6-anhydro-1,2-*O*-isopropylidene-6-*C*-nitro-α-D-glucofuranose (**10**) yielded a mixture of two diastereoisomeric (possibly anomeric at C-6) 5-deoxy-5-(dimethylamino)-1,2-*O*-isopropylidene-α-D-hexodialdo-1,4:6,3-difuranoses (**11**). The β-glycoside **1** and the α-glycoside **3** reacted with methylmagnesium iodide to produce methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-3-(*N*-hydroxy-*N*-methylamino)-β- and -α-D-hexopyranosides (**12**) and (**13**), respectively; both products had the 1,2-*trans* configuration, but their configurations at the quaternary center C-3 have not been determined.

INTRODUCTION

In a preceding article[1] on chemical transformations of carbohydrate α-nitroepoxides, we showed that sodium borohydride causes reductive denitration of these compounds to give nitrogen-free, deoxy sugars. Attack by hydride ion occurred exclusively at the β-position of the α-nitro-oxirane moiety, and ring opening was followed by elimination of nitrite ion, to generate, presumably, an intermediary oxo derivative that underwent rapid reduction to the carbinol stage. The regiospecificity of the nucleophilic attack, resulting from the presence of the nitro group, was

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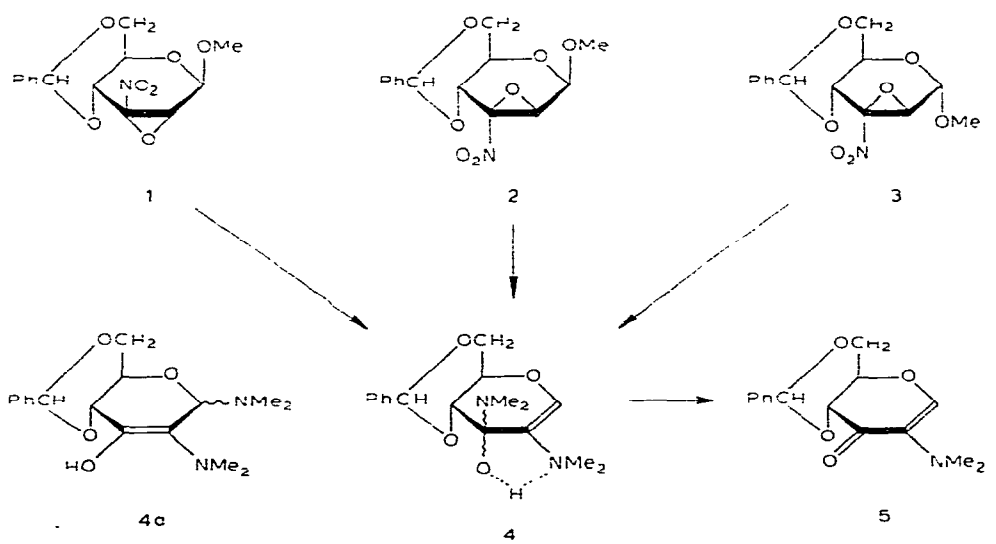
independent of the orientation of the oxirane ring, and thus provided an interesting contrast to similar reactions of analogous (but unsubstituted) epoxides. As is well known, epoxides of six-membered rings may incur ring-opening at either carbon atom, with regioselectivity governed by stereochemical features as expressed by the Fürst–Plattner rule. We now report on further reactions of carbohydrate α-nitroepoxides with each of two nucleophiles, namely, dimethylamine and methylmagnesium iodide. It will be demonstrated that both of these reagents also open the epoxide ring regiospecifically, regardless of the sugar configuration, but that they do so at different sites of the nitro-oxirane system.

RESULTS AND DISCUSSION

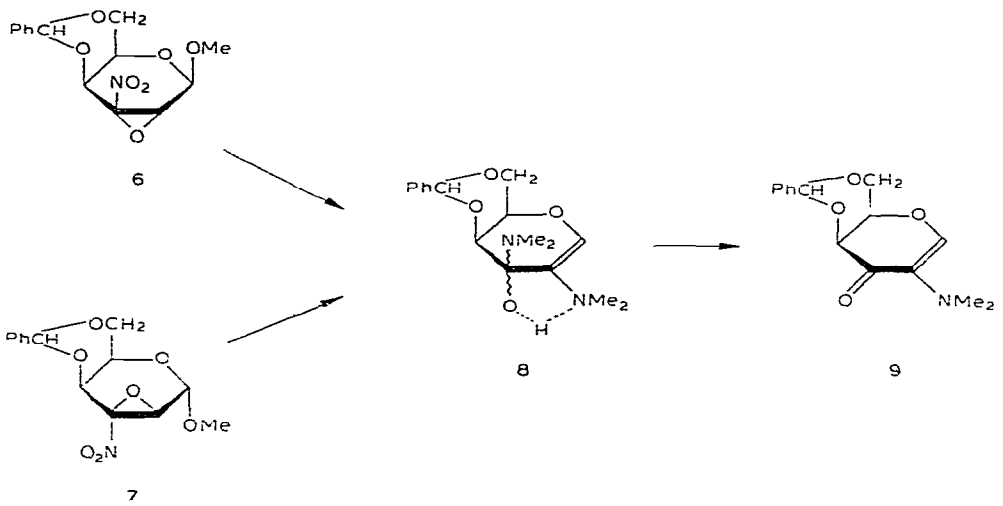
Reactions with dimethylamine

The three methyl 2,3-anhydro-4,6-*O*-benzylidene-3-*C*-nitrohexopyranosides[3,4] having the β-D-*allo* (**1**), β-D-*manno* (**2**), and α-D-*manno* (**3**) configurations each reacted at room temperature with aqueous, 25% dimethylamine to give the same product. According to t.l.c., the reactions of the β-glycosides **1** and **2** proceeded to completion within 1 to 2 h, whereas 48 h was required for the α-glycoside **3**. Only faint spots of unidentified side-products were detected on the chromatograms. The main product, obtained in ~55% yield after recrystallization, proved to be a 3-(dimethylamino) adduct (**4**) of 1,5-anhydro-4,6-*O*-benzylidene-2-deoxy-2-(dimethylamino)-D-*erythro*-



hex-1-en-3-ulose (**5**), a novel oxoglycal derivative. When a chloroform solution of **4** was passed through a column of silica gel, partial loss of dimethylamine occurred, and the enulose **5** was isolated crystalline in 49% yield .The stereoisomeric, epoxynitro glycosides having the β-D-*gulo* (**6**) and α-D-*talo* (**7**) configurations reacted with

dimethylamine in like fashion—the former, readily at room temperature, and the latter, rather more sluggishly within 48 h at 60°. The crystalline product obtained from either glycoside was found to be a 3-(dimethylamino) adduct (**8**) of the D-*threo* enulose **9** (the 4-epimer of **5**), although liberation of **9** and its isolation as described for **5** could not be achieved*. Finally, in view of the foregoing results, it was expected that **8** should also arise from the β anomer of **7**. This compound is not so readily accessible as the other isomers, and only one attempt was made to verify the prediction; unfortunately, the trial was frustrated by a lack of solubility which appeared to prevent reaction.

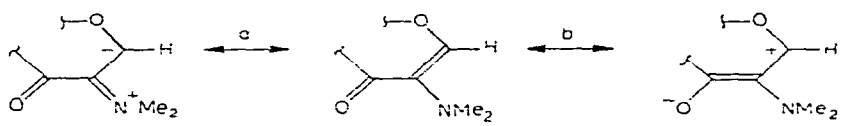


The constitution of the bis(dimethylamino) derivative **4** was deduced from elemental analysis and spectral data. The n.m.r. spectrum showed that the benzylidene acetal group had been retained, but that the glycosidic methoxyl group had been lost during the reaction, and that two dimethylamino groups were present (6-proton singlets at τ 6.87 and 7.40). Compound **4** exhibited strong infrared absorption in the region of O–H (or N–H) stretching vibrations (a double peak at 3360 and 3300 cm^{-1}) and a moderately strong band at 1635 cm^{-1} assignable to a C=C double bond, but it gave no carbonyl band. The possibility of an enol structure, such as **4a**, was excluded by the absence, from the n.m.r. spectrum, of an enolic proton signal in the lowfield region, scanned down to −10 τ. The signal of H-1 was found as a singlet at τ 2.49, which agrees with the glycal structure of **4**, although it might, at first sight, have been expected that this proton would be more shielded due to resonance of the olefinic bond with the lone electron pair of the 2-(dimethylamino) substituent. However, we suggest as an explanation that such resonance is absent because of involvement of the

*Surprisingly strong adsorption to silica gel took place, and no carbohydrate material was eluted, even with methanol.

lone pair in intramolecular hydrogen-bonding with the OH-3 group. The nitrogen atom would thereby acquire a positive charge and, hence, behave as an electron-withdrawing substituent that contributes to deshielding* of H-1. Evidence for a strongly chelated dimethylamino group in **4** was also present in the infrared spectrum. There was a very prominent peak at 1565 cm^{-1}, where tertiary amines normally do not absorb, that we consider was due to N–H bending vibrations, indicating considerable ammonium ion character of the group†. Furthermore, the i.r. spectra of **4** in a Nujol mull and in dilute chloroform solution did not differ in their essential features. Chelation existing between the 3-hydroxyl group and the 2-(dimethylamino) group would account for the stability of the geminal amino alcohol structure at C-3, the configuration of which could not be determined.

The infrared spectrum of the 3-ulose **5** showed a strong and a moderately strong band, at 1710 and 1600 cm^{-1}, respectively, indicating an α,β-unsaturated ketone structure; it was devoid of hydroxyl absorption and of the band at 1565 cm^{-1} found in the i.r. spectrum of **4**. There was only one 6-proton singlet (τ 7.42), corresponding to a dimethylamino function, in the n.m.r. spectrum of **5**. The H-1 signal appeared as a sharp singlet at τ 3.04, *i.e.*, it was shifted upfield from its position in the spectrum of the adduct **4**, in agreement with absence of the chelation effect that was invoked for the latter. Resonance involving the 2-(dimethylamino) group according to *a* (Scheme 1) would be expected to shield H-1 even more, but this should



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Scheme 1

be offset by an opposite, and a more important, resonance contribution *b*. The conversion of **4** into **5** could be demonstrated in the following way. When a *small* drop of trifluoroacetic acid was added to the n.m.r. probe of **4** (in $CDCl_3$, after D_2O exchange), partial conversion took place, as seen by the appearance of the H-1 signal of **5** at the expense of that of **4**, and by corresponding changes in the high-field region of the *N*-Me resonances (in which additional signals due to liberated dimethylamine appeared). When the amount of acid added was increased, the conversion became complete, and the signals of **4** vanished. However, compound **5**, now fully protonated at its 2-(dimethylamino) group, incurred a downfield shift of its H-1 signal from τ 3.04

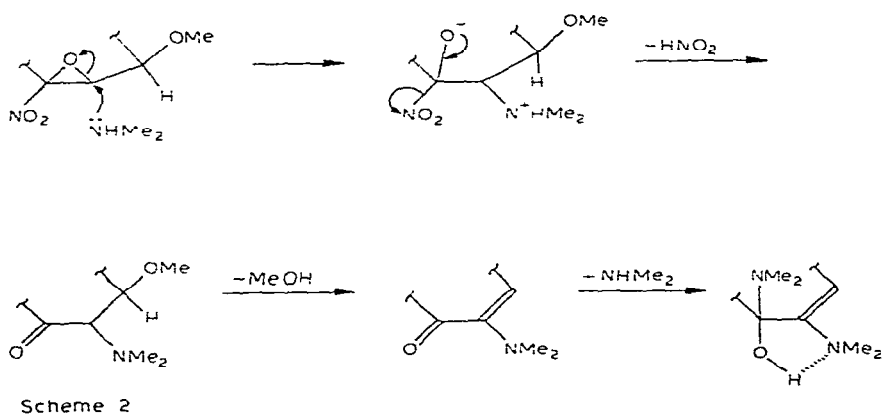
*The deshielding effect of a β-sulfonyl substituent[5] on the α-proton in vinyl ethers[6] is 0.95 p.p.m. Similarly, H-1 is strongly deshielded (τ 1.67) in tri-*O*-acetyl-2-*C*-nitro-D-glucal[7].

†Attribution of the peak to a nitro group, which would have absorbed at a similar frequency, was precluded by the microanalytical data. The spectrum contained, in addition, a weak but distinct band at 2790 cm^{-1} assignable to *N*-methyl, and a detailed, fingerprint pattern that undoubtedly included C–N vibrations.

to 1.86, and also a downfield shift of its *N*-Me_2 signal from τ 7.42 to 6.93. The similarities in chemical shifts of the 3-(dimethylamino) group of **4** and the 2-(dimethylamino) group of unprotonated **5** on the one hand, and of the chelated 2-(dimethylamino) group of **4** and the protonated group of **5** on the other, may be noted.

The bis(dimethylamino) derivative **8** displayed i.r.- and n.m.r.-spectroscopic features that were fully analogous to those of its isomer **4**, allowing the structural assignment as shown. One difference was that the H-1 signal could not be discerned in the n.m.r. spectrum of **8** in $CDCl_3$ solution, as it was obscured by the multiplet due to the phenyl-ring protons; however, in dimethyl sulfoxide-d_6 solution, where this multiplet was narrower (centered at τ 2.57), the H-1 signal was observable at τ 2.48. Addition of an excess of trifluoroacetic acid caused a spectral change similar to that described for **4**, with the H-1 signal moving downfield to τ 2.0. There can be little doubt that this indicated conversion into the protonated form of the 3-ulose **9**, although verification was not possible, because, as already mentioned, compound **9** was unavailable in isolated condition.

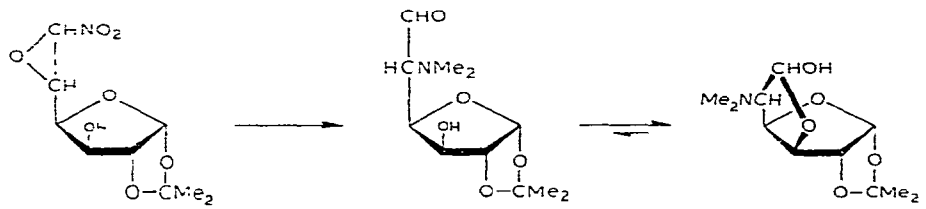
The formation of **4** and **8** is explained by attack of dimethylamine on C-2 of the respective epoxides, resulting in ring opening followed by ejection of nitrite ion from C-3, so as to produce an intermediate methyl 2-deoxy-2-(dimethylamino)-glycosid-3-ulose. This suffers β-elimination of methanol in the basic reaction-medium, to give the 1,2-unsaturated 3-ulose which, in turn, reacts with an excess of the amine to afford the adduct that is isolated (see Scheme 2). Kumazawa *et al.*[8] studied the related reaction of **1** and of the corresponding phenyl glycoside with ammonia. In their case, the assumed 2-amino-2-deoxy-glycosid-3-ulose intermediate did not eliminate the glycosidic group but, being a primary α-amino ketone, underwent dimeric condensation and oxidation to yield a pyrazine derivative.



Scheme 2

We also examined the action of dimethylamine upon 5,6-anhydro-1,2-*O*-isopropylidene-6-*C*-nitro-α-D-glucofuranose (**10**). This nitroepoxide appeared to be very reactive, and far-reaching decomposition or polymerization produced tar, rendering the isolation of a crystalline product rather difficult. Nevertheless, a crystalline

material was obtained in 10% yield, and spectral evidence suggested that the nitro group had been lost and one dimethylamino group introduced. The results of elemental analysis conformed to that calculated for a deoxy(dimethylamino)isopropylidenehexodialdose; a 5-deoxy-5-(dimethylamino)-1,2-*O*-isopropylidene-α-D-hexodialdo-1,4:6,3-difuranose (**11**) would be expected to arise through nucleophilic attack



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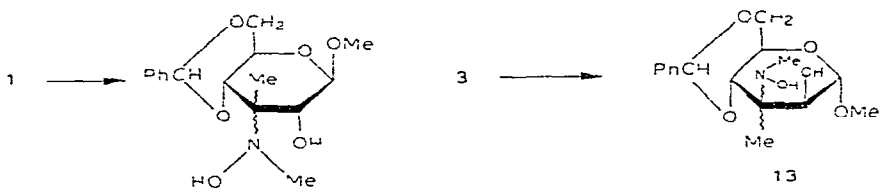
of the base upon C-5, elimination of nitrous acid, and internal hemiacetalation of the resulting aldehyde. Although the crystalline product gave a single spot in t.l.c., n.m.r. spectroscopy revealed that it consisted of two (presumably diastereoisomeric) components in the ratio of ~1:2. All signals that could be analyzed occurred in pairs having this intensity ratio, with the exception of the isopropylidene methyl signals, which were not duplicated. Thus, two 4-Hz doublets occurring at lowest field (τ 4.01 and 4.12) were attributable to H-1 of the isomers; they were coupled with two overlapping, unequal doublets for H-2 centered at τ 4.66. (In the n.m.r. spectrum of 1,2-*O*-isopropylidene-α-D-glucofuranose and its derivatives, H-2 usually gives a doublet due to coupling with H-1 only, as coupling with H-3 tends[9] to be close to zero.) Signals for H-5 were discerned as a narrow multiplet at τ 6.98 and a distinct quartet at τ 7.27, and the dimethylamino groups of the two components gave singlets at τ 7.60 and 7.66 having a combined intensity corresponding to six protons. It is not known whether the two components are C-6 anomers of C-5 epimers; the latter possibility cannot be excluded, even though attack of the nucleophile upon C-5 should be stereospecific, as a secondary epimerization might have ensued.

Reactions with methylmagnesium iodide

The chemistry of reactions between carbohydrate epoxides and Grignard reagents is a remarkably complicated matter. Branched-chain sugars may arise, but other products, such as halogenated, unsaturated, and reduced derivatives, are often formed mainly, or even exclusively, depending on the nature of the reactants and the reaction conditions, and normal as well as "anomalous" ring-openings (with respect to the Fürst–Plattner rule) have been observed[10]. Examples most pertinent to the present study are found in the work of Inch and Lewis[11], who made a detailed study of Grignard reactions with methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside and -mannopyranoside, *i.e.*, non-nitro analogs of the glycosides discussed here. Furthermore, the fate of the nitro group in our special case was deemed interesting.

Generally, aliphatic nitro compounds react with Grignard reagents to give, depending on the conditions, *N*-alkylnitronates, dialkyl nitroxides, or dialkyl(hydroxylamine)s[12].

Both the β-D-*allo* (**1**) and the α-D-*manno* (**3**) glycosides reacted rapidly and completely with methylmagnesium iodide in ether solution, each giving (according to t.l.c.) one major product, isolable crystalline in 40–50% yield. The β-D-*gulo* (**6**) and α-D-*talo* (**7**) isomers, as well as the furanose **10**, reacted also, but difficulties in processing prevented the isolation and identification of products. The isomeric products **12** and **13** obtained from **1** and **3**, respectively, were revealed by analytical and spectral data to have arisen by loss of one oxygen atom, and incorporation of two methyl groups and two additional hydrogen atoms. Infrared spectra contained hydroxyl but no nitro bands. Detailed, structural information was derived from 250-MHz, n.m.r. spectra, obtained by courtesy of Dr. J. Defaye (Grenoble). The two newly introduced methyl groups of each isomer had chemical shifts indicative of *N*-CH_3 and *C*-CH_3 functions. There were two 1-proton signals, namely a singlet and a doublet, that were removable by deuterium exchange and were attributed to a di-*N*-substituted hydroxylamine and a secondary carbinol function. All the ring protons in both isomers could be accounted for; they were located at C-1, C-2, C-4, and C-5, as indicated by the coupling patterns and confirmed by spin decoupling. Therefore, C-3 had to be a quaternary center. In the n.m.r. spectrum of β-D-glycoside **12**, H-2 gave a quartet due to vicinal coupling with H-1 and OH-2: upon deuterium exchange, the quartet collapsed to a doublet showing $J_{1,2}$ 8 Hz, which proved the equatorial orientation of the hydroxyl group. In the n.m.r. spectrum of the α-D-glycoside **13**, H-2 produced a doublet caused by coupling with OH-2, and convertible



into a singlet by deuterium exchange, vicinal coupling with H-1 being close to zero. It was concluded that H-1 and H-2 are diequatorially positioned and that the hydroxyl group, therefore, is axial. The configurations of the quaternary carbon atoms (C-3) of the two isomers are not yet known. However, it is probably reasonable to assume that attack of the Grignard reagent upon C-3 of the nitroepoxides **1** and **3** (or of the respective *N*-hydroxyl-*N*-methylamino intermediates, if reductive methylation of the nitro group occurred first) took place from corresponding sides of the oxirane ring, so that the products have opposite C-3 configurations. Compounds **12** and **13**, then, would possess the β-D-*allo* and α-D-*manno*, or alternatively, the β-D-*gluco* and α-D-*altro*, configurations, respectively. The former situation should be the more likely. Compound **13** would be imparted the α-D-*manno* configuration by the favored

mode of diaxial ring-opening for **3**, which was experienced by the non-nitro analog of **3** when it reacted with alkylmagnesium chlorides[11], diethylmagnesium[11,13], or methyllithium[14]. In the epoxide **1**, diaxial opening to generate the *β*-D-*allo* configuration could be achieved through the $^1S_5$(D) conformation in the transition state.

EXPERIMENTAL

General methods. — Optical rotations were measured at ~25° with a Perkin–Elmer 141 automatic polarimeter. Thin-layer chromatography (t.l.c.) was performed on plates coated with MN-Silica Gel N-UV$_{254}$ (Macherey & Nagel Co., Germany) by use of ethyl acetate–petroleum ether (b.p. 60–80°) mixtures having the following proportions (v/v): 1:1 (solvent *A*), 2:3 (solvent *B*), or 1:1 (solvent *C*). The i.r. spectra were recorded with a Beckman IR-20 instrument, and absorption bands are characterized as b (broad), ms (medium strong), s (strong), or w (weak). Unless otherwise specified, the ^{1}H-n.m.r. data refer to 100-MHz spectra obtained for solutions in chloroform-*d*; the internal standard was tetramethylsilane.

3-(Dimethylamino) adduct (**4**) *of 1,5-anhydro-4,6-*O*-benzylidene-2-deoxy-2-(dimethylamino)*-D-erythro-*hex-1-en-3-ulose* (**5**). — *A. From* **1**. The nitroepoxide[3] **1** (400 mg) was stirred at room temperature in 25% aqueous dimethylamine solution (28 ml). After 75 min, the resulting, yellow solution was free from **1** and, according to t.l.c. (solvent *A*), contained one slow-moving, major product together with a trace of a slightly faster-moving by-product. The solution was diluted with some water and extracted with ether (2 × 25 ml). The extract was dried (K_2CO_3), partially decolorized with activated charcoal, and evaporated, to give a syrup (393 mg) that crystallized on scratching with a glass rod. Recrystallization from chloroform*–petroleum ether furnished **4** as fine, colorless prisms (227 mg, 55%), m.p. 131–133°, $[\alpha]_D$ −155.5° (*c* 0.4, chloroform) and −147.3° (*c* 1, ethanol); ν_{max}^{Nujol} 3360, 3300 (s, b, double peak), 2790 (w, *N*-Me), 1635 (ms, C=C), and 1565 cm^{-1} (s, probably associated with chelated NMe_2); $\nu_{max}^{CHCl_3}$ 3400 (s, b), 2790 (w), 1635 (ms), and 1565 cm^{-1} (s); n.m.r. data: τ 2.49 (s, 1 H, H-1), 2.6 (m, 5 H, Ph), 4.47 (s, 1 H, *Ph*-CH), 5.5–6.5 (m, unresolved, 5 H, H-4,5,6,6′, OH), and 6.87 and 7.40 (s, 6 H each, 2- and 3-NMe_2).

Anal. Calc. for $C_{19}H_{24}N_2O_4$ (320.4): C, 63.72; H, 7.55; N, 8.75; O, 19.97. Found: C, 63.92; H, 7.34; N, 8.56; O, 19.87.

B. From **2**. A mixture of compound[4] **2** (100 mg), aqueous 25% dimethylamine (7 ml), and 1,4-dioxane (2 ml) was stirred at room temperature. After 90 min, t.l.c. with solvent *B* indicated the presence of a large proportion of **4**, together with some residual **2**. To complete the reaction, another 2 ml of 1,4-dioxane was added, and stirring was continued for 30 min. The yellowish reaction-mixture was diluted with water, and extracted with ether (3 × 25 ml). The extract was washed twice with water, and the washings were re-extracted with ether, which was combined with the main

*It was found advantageous to use chloroform that had been briefly shaken with 1/10th of its volume of aqueous dimethylamine, and then dried over calcium chloride.

extract. Further processing of the ethereal solution as described under *A* gave 85 mg (82%) of crude, crystalline **4**, m.p. 122° (dec.). After recrystallization from chloroform–petroleum ether, the product (56 mg, 54%) melted at 129–131° and, according to the i.r. and n.m.r. spectra, was identical with **4** obtained from **1**.

C. From **3**. A mixture of the nitroepoxide[3] **3** (200 mg), chloroform (20 ml), and aqueous 25% dimethylamine (20 ml) was briefly warmed on a steam bath and then stirred magnetically for 48 h at room temperature. After phase separation, the chloroform layer was evaporated, to give a crystal-containing syrup which was triturated with ethyl acetate. A small amount of insoluble material (11 mg) was removed; it decomposed above 360° and was not identified. Evaporation of the ethyl acetate gave syrupy **4** (210 mg) which, in this instance, failed to crystallize, but was, according to t.l.c. (solvents *A* and *B*) and spectral data (i.r. and n.m.r.), identical with the product prepared from **1** or **2**.

1,5-Anhydro-4,6-O-benzylidene-2-deoxy-2-(dimethylamino)-D-erythro-*hex-1-en-3-ulose* (**5**). — The adduct **4** (155 mg) was dissolved in a small volume of chloroform and placed on a column that contained 10 g of Silica Gel 60 (70–239 mesh ASTM; E. Merck AG, Germany). The product eluted by means of solvent *B* crystallized on evaporation of the solvent, and weighed 66 mg (49.5%). Recrystallized from ethyl acetate–petroleum ether, it showed m.p. 132–133° (strongly depressed on admixture with **4**). $[\alpha]_D$ +204° (*c* 0.3, chloroform); ν_{max}^{Nujol} 2780 (w, *N*-Me), 1710 (s, C=O), and 1600 cm^{-1} (ms, C=C); n.m.r. data: τ 2.45–2.7 region (m, 5 H, Ph), 3.04 (s, 1 H, H-1), 4.47 (s, 1 H, *Ph*-CH), 5.45–6.15 (m, unresolved, 4 H, H-4,5,6,6'), and 7.42 (s, 6 H, NMe_2). On addition of CF_3CO_2H, the H-1 signal was shifted to τ 1.86, the Ph signal was somewhat narrowed, and the NMe_2 signal was shifted to τ 6.93.

Anal. Calc. for $C_{15}H_{17}NO_4$ (275.3): C, 65.44; H, 6.22; N, 5.09. Found: C, 65.25; H, 6.31; N, 4.97.

3-(Dimethylamino) adduct (**8**) *of 1,5-anhydro-4,6-O-benzylidene-2-deoxy-2-(dimethylamino)*-D-threo-*hex-1-en-3-ulose* (**9**). — *A. From* **6**. The nitroepoxide[3] **6** (150 mg) in 1,4-dioxane (6 ml) and 25% aqueous dimethylamine (2 ml) were allowed to react for 90 min at room temperature. T.l.c. with solvent *C* revealed almost complete replacement of **6** (R_F 0.4) by **8** (R_F 0.2). The reaction mixture was diluted with water, which caused a few milligrams of crystalline, unreacted **6** to precipitate. The filtrate therefrom was extracted with ether (3 × 25 ml), the extract was washed twice with water, and the water washings were re-extracted once with ether, which was then combined with the main extract. The dried (K_2CO_3) solution was evaporated, to give light-yellow needles, m.p. 124–127°. These were purified by treatment with activated charcoal in dimethylamine-containing chloroform, and recrystallized by careful addition of petroleum ether to the filtrate. There was obtained 62 mg (40%) of nearly colorless **8**, m.p. 134–136°, $[\alpha]_D$ +28.3° (*c* 0.4, chloroform): ν_{max}^{Nujol} 3350 (s, b), 2750–2600 (w), 1635 (ms, C=C), and 1570 cm^{-1} (s, probably chelated NMe_2); n.m.r. data: τ 2.4–2.7 region (m, 6 H, Ph and H-1), 4.39 (s, 1 H, *Ph*-CH), 5.44 (narrow d or s, 1 H, H-4, $J_{4,5}$ ~0 Hz), 5.80 (center of symmetrical d of q, 2 H, H-6,6', $J_{5,6}$ 1.5, $J_{5,6'}$ 2, $J_{6,6'}$ 12 Hz), 6.00 (narrow signal, 1 H, H-5, superposed on upfield lines of H-6),

and 6.83 and 7.38 (s, 6 H each, NMe_2). The OH proton gave broad resonance in the region of τ 5.5–6.0, as manifested by an elevation in the base line (removed by deuterium exchange) and by total intensity integration of the region. A 60-MHz spectrum of **8** in Me_2SO-d_6 showed a narrow multiplet for the phenyl protons at τ 2 57, beside which the H-1 singlet was visible at τ 2 48. One NMe_2 signal occurred at τ 6 84, but the other (expected near τ 7 4) was obscured by Me_2SO. Addition of an excess of CF_3CO_2H (for conversion of **8** into **9**) caused shift of the H-1 signal to τ 2.00, and narrowing of the Ph signal to a sharp singlet at τ 2.60; an NMe_2 signal appeared at τ 6.95.

Anal. Calc. for $C_{17}H_{24}N_2O_4$ (320.4): C, 63.72; H, 7.55: N, 8.75. Found: C, 63.68; H, 7.41: N, 8.89.

B. From **7**. A mixture of compound[3] **7** (100 mg), chloroform (5 ml), and aqueous 25% dimethylamine (1 ml) was magnetically stirred in a water bath at 60°, and additional portions (5 × 2 ml) of dimethylamine were added in the course of 12 h. Heating was then continued for another 36 h, after which, t.l.c. (solvent *C*) showed the reaction to be complete. The mixture was diluted with water, and the aqueous phase was extracted twice with chloroform which was combined with the organic phase and washed twice with water, dried ($MgSO_4$), and evaporated. The syrupy residue (57 mg, 55%) was crystallized, and recrystallized, from chloroform–petroleum ether to give 20 mg of pure **8**, m.p. 135–136°, undepressed upon admixture with **8** prepared from **6**. The identity of the two preparations was borne out by their i.r. and n.m.r. spectra.

5-Deoxy-5-(dimethylamino)-1,2-O-isopropylidene-α-D-hexodialdo-1,4:6,3-difuranose (**11**). — To a solution of the epoxide[1,2] **10** (300 mg) in ethanol (10 ml) was added aqueous 25% dimethylamine (4 ml). After 1 h, the yellow mixture was diluted with water, and extracted three times with ether. The extract was washed once with water, treated with activated charcoal, dried (K_2CO_3), and evaporated, to yield a dark oil (228 mg). Trituration of the oil with hexane led to partial crystallization. Tarry material was removed mechanically as far as possible. The crude, crystalline product was dissolved in chloroform, treated with charcoal, recovered by evaporation of the solution, and recrystallized from hexane to give 30 mg (10%) of pure **10**, m.p. 142–144°, $[\alpha]_D$ −10° (*c* 0.5, chloroform); ν_{max}^{Nujol} 3300–2500 cm^{-1} (b, OH), no bands in the 2000–1500 cm^{-1} region. The product gave a single spot in t.l.c. (solvent *A*), but exhibited two sets of n.m.r. signals in an intensity ratio of ~2:1; data for the major component: τ 4.12 (d, 2/3 H, $J_{1,2}$ 4 Hz, H-1), 7.27 (q, 2/3 H, *J* 2.5 and 4.5 Hz, H-5), and 7.59 (s, 6 × 2/3 H, NMe_2); data for the minor component: τ 4.01 (d, 1/3 H, $J_{1,2}$ 4 Hz, H-1), 6.98 (narrow m, 1/3 H, H-5), and 7.66 (s, 6 × 1/3 H, NMe_2). The H-2 and H-3 signals of the components overlapped near τ 4.7 and 5.1, respectively. An unresolved, 3 H multiplet in the region τ 5.2–5.5 was assigned to H-4, H-6, and OH, and the CMe_2 resonances coincided at τ 8.52 and 8.68 (s, 2 × 3 H).

Anal. Calc. for $C_{11}H_{19}NO_5$ (245.3): C, 53.86; H, 7.81; N, 5.71. Found: C, 53.79; H, 7.94: N, 5.88.

Methyl 4,6-O-benzylidene-3-deoxy-3-C-methyl-3-(N-hydroxy-N-methylamino)-β-D-hexopyranoside (**12**). — To an ethereal solution of methylmagnesium iodide, freshly prepared from magnesium (300 mg) and methyl iodide (4 ml), was added a suspension of compound[3] **1** (200 mg) in absolute ether (4 ml). An exothermic reaction occurred, and this was complete after 30 min, as indicated by t.l.c. (solvent *C*), which showed complete consumption of **1** and formation of a more-slowly migrating product. The mixture was stirred with an aqueous solution of ammonium chloride until effervescence ceased. The organic phase and several chloroform extracts of the aqueous phase were combined, dried ($CaCl_2$), and evaporated, to give a partially crystallizing syrup (180 mg). By crystallization from chloroform–petroleum ether, 97 mg (50%) of **12** could be isolated; m.p. 158–160°, unchanged on recrystallization; $[\alpha]_D$ −50.7° (*c* 0.3, chloroform); ν_{max}^{Nujol} 3440–3420 cm^{-1} (s, OH). The mother liquor gave a further 20 mg of crystalline **12**. N.m.r. data (250 MHz, $CDCl_3$): τ 2.55 (m, 5 H, Ph), 4.58 (s, 1 H, *Ph*CH), 5.01 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 5.61 (a, 1 H, $J_{5,6e}$ 5, $J_{6a,6e}$ 10.3 Hz, H-6$_e$), 5.81 (sextet, 1 H, $J_{4,5}$ 9.7, $J_{5,6a}$ 10, $J_{5,6e}$ 5 Hz, H-5), 6.33 (t, 1 H, *J* 10.3 Hz, H-6*a*), 6.38 (s, 3 H, OMe), 6.53 (d, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 6.62 (d, 1 H, $J_{1,2}$ 8 Hz, H-2), 7.16 (s, 3 H, NMe), and 8.55 (s, 3 H, CMe); irradiation: of H-1 produced a singlet for H-2; of H-4, a quartet for H-5; of H-6*e* (or H-6*a*), corresponding multiplicity changes for H-5 and H-6*a* (or H-6*e*); in Me_2SO-d_6 (250 MHz): τ 1.70 (s, 1 H, exchangeable with D_2O, *N*-OH), 2.57 (s, 5 H, Ph), 4.51 (s, 1 H, *Ph*CH), 2.79 (d, 1 H, *J* 8 Hz, exchangeable, OH-2), 5.09 (d, 1 H, *J* 8 Hz, H-1), 5.76 (q, 1 H, H-6*e*), 5.93 (sextet, 1 H, H-5), 6.35–6.5 (m, 2 H, H-6*a*, H-4), 6.58 (s, 3 H, OMe), 6.83 (t, 1 H, *J* 8 Hz, collapses to d on D_2O exchange, H-2), 7.33 (s, 3 H, NMe), and 8.74 (s, 3 H, CMe).

Anal. Calc. for $C_{16}H_{23}NO_6$ (325.4): C, 59.06; H, 7.13; N, 4.31. Found: C, 58.90; H, 7.01; N, 4.16; mol. wt., 325 (mass spectrum).

Methyl 4,6-O-benzylidene-3-deoxy-3-C-methyl-3-(N-hydroxy-N-methylamino)-α-D-hexopyranoside (**13**). — The procedure described for the preparation of **12** was applied to the nitroepoxide[4] **3** (200 mg). After reaction for 15 min, when t.l.c. (solvent *C*) showed the formation of one major product together with a trace of a faster-moving by-product, the mixture was processed, to furnish a partly crystalline material (180 mg). This was chromatographed on a column of silica gel (10 g) with 1:3 ethyl acetate–petroleum ether as the eluant. The fast-moving by-product was obtained from early fractions as a syrup (28 mg) that could not be crystallized and was not characterized. Subsequent fractions yielded crystalline **13** (110 mg, m.p. 159–162°) which, on recrystallization from ethyl acetate–petroleum ether, was obtained as colorless plates (81 mg, 42%), m.p. 163–165°, unchanged on further recrystallization; $[\alpha]_D$ +62.5° (*c* 0.3, chloroform); ν_{max}^{Nujol} 3470, and 3440 cm^{-1} (s, sharp, OH), with no bands in the 2500–1500-cm^{-1} region; n.m.r. data (250 MHz, $CDCl_3$): τ 2.55 (m, 5 H, Ph), 4.4 (broad peak, exchangeable with D_2O, OH), 4.54 (s, 1 H, *Ph*CH), 5.35 (s, 1 H, H-1), 5.48 (sextet, 1 H, $J_{4,5}$ 9.7, $J_{5,6a}$ 10, $J_{5,6e}$ 5 Hz, H-5), 5.70 (q, 1 H, $J_{5,6e}$ 5, $J_{6a,6e}$ 10.5 Hz, H-6*e*), 5.83 (s, somewhat broadened, sharp after D_2O exchange, H-2), 6.14 (d, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 6.28 (t, 1 H, *J* 10.5 Hz, H-6*a*), 6.51

(s, 3 H, OMe), 7.21 (s, 3 H, NMe), and 8.69 (s, 3 H, CMe), irradiation of H-4 transformed the H-5 sextet into a quartet; in Me_2SO-d_6 (250 MHz): τ 2.6 (narrow m, 5 H, Ph), 3.45 (s, 1 H, exchangeable with D_2O, *N*-OH), 4.48 (s, 1 H, *Ph*CH), 4.53 (d, 1 H, *J* 6 Hz, exchangeable, OH-2), 5.49 (s, 1 H, H-1), 5.8 (m, 2 H, H-5,6*e*), 6.04 (d, 1 H, *J* 6 Hz, collapsed to s on D_2O exchange, H-2), 6.12 (d, 1 H, H-4), 6.39 (t, 1 H, H-6*a*), 6.66 (s, 3 H, OMe), 7.35 (s, 3 H, NMe), and 8.87 (s, 3 H, CMe).

Anal. Calc. for $C_{16}H_{23}NO_6$ (325.4): C, 59.06; H, 7.13; N, 4.31. Found: C, 59.32; H, 7.18; N, 4.23; mol. wt. 325 (mass spectrum).

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