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METHYLATION OF NITRO SUGARS WITH DIAZOMETHANE, AND PREPARATION OF SOME NEW AMINO SUGAR METHYL ETHERS*†

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ABSTRACT

Diazomethane reacted with methyl 3,6-dideoxy-3-nitro-α-L-glucopyranoside (**1**) under catalysis by boron trifluoride to give the 2-*O*-methyl and the 2,4-di-*O*-methyl derivative (**2** and **3**). Similarly, the 4-acetate (**4**) of **1** afforded the 4-acetate (**5**) of **2**. Boron trifluoride-catalyzed acetylation of **2** at about −60° gave **5** whereas, at 0°, acetolysis took place producing 1,4-di-*O*-acetyl-3,6-dideoxy-2-*O*-methyl-3-nitro-α-L-glucopyranose (**6**). Diazomethane treatment of methyl 3,4,6-trideoxy-3-nitro-α-L-*erythro*- and -α-L-*threo*-hex-3-enopyranosides **7** and **8** furnished the corresponding 2-*O*-methyl derivatives **9** and **10**. With triphenylphosphine and carbon tetrachloride, **2** yielded methyl 4-chloro-3,4,6-trideoxy-2-*O*-methyl-3-nitro-α-L-galactopyranoside (**11**) which was dehydrochlorinated to **9**. Borohydride reduction of **9** gave methyl 3,4,6-trideoxy-2-*O*-methyl-3-nitro-α-L-*xylo*-hexopyranoside (**12**). Catalytic hydrogenation of **3** and **12** afforded the corresponding amino sugar hydrochlorides **13** and **15**. Treatment of **5** with ammonia gave a 4-amino-3-nitro glycoside (isolated as the hydrochloride **17**) hydrogenation of which led to methyl 3,4-diamino-3,4,6-trideoxy-2-*O*-methyl-α-L-glucopyranoside dihydrochloride (**19**). The *N*-acetyl derivatives (**14**, **16**, **18**, and **20**) of the four new amino sugars were prepared.

INTRODUCTION AND RESULTS

The possibility of methylating alcoholic hydroxyl groups by means of diazomethane was realized in carbohydrate chemistry many years ago when a limited number of methyl glycosides were synthesized with this reagent[2,3]. More recently, applications to the synthesis of some methyl ethers of nucleosides have been reported[4]. However, as a general reagent for the preparation of methyl ethers of sugars, particularly in cases where structural features militate against the employment of methylation methods that involve strongly basic reagents, diazomethane has found more widespread use[5] after the introduction[6] of catalysis by boron trifluoride. Stannous

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chloride has also been recommended as a catalyst[7]. In the course of our studies on nitro sugars, we became interested in the question whether the diazomethane–boron trifluoride reagent might be compatible with the presence of a nitro group. The literature[8] indicated that diazomethane by itself does not react with nitromethane or other nitroalkanes of low acidity ($pK_a^{nitro} > ca.$ 8), but that it reacts with those that are more acidic due to the presence of activating groups. The products are nitronic esters, which may subsequently undergo various further transformations. No report on the effect of added catalyst was found. We therefore undertook a model study[9] on the methylation of 2-nitrocyclohexane-1,3-diol, and encouraged by its success, proceeded to the present work.

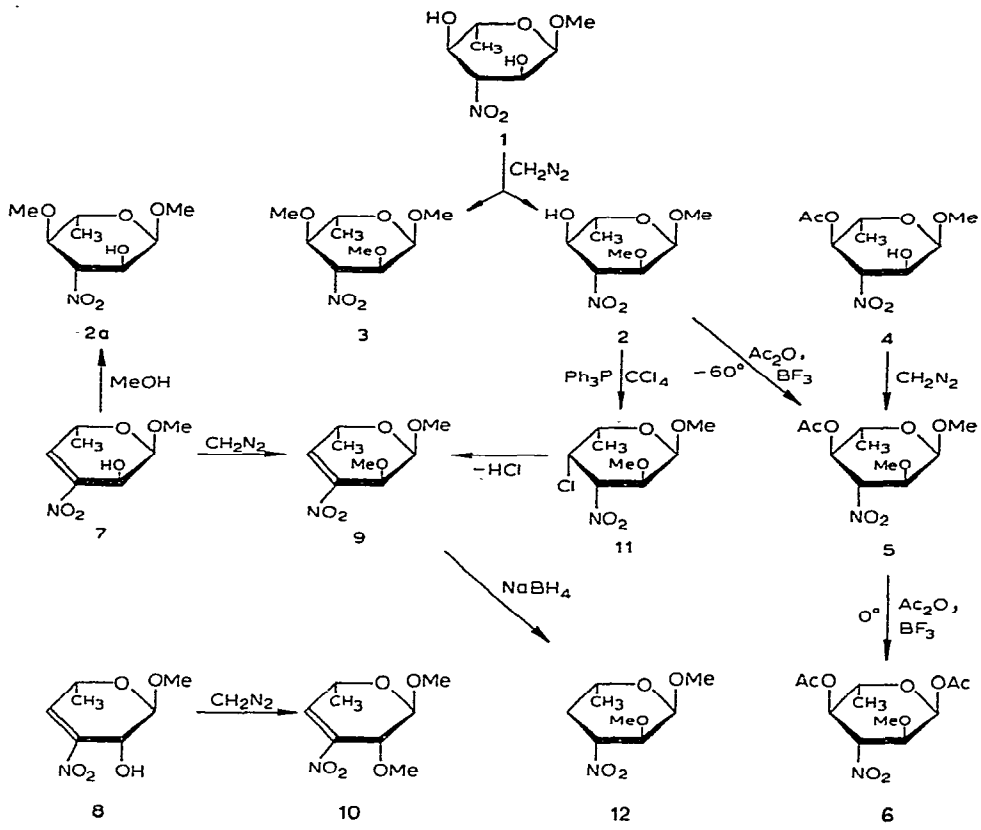
Methyl 3,6-dideoxy-3-nitro-α-L-glucopyranoside (**1**) was treated for 3 h with a large excess of diazomethane in the presence of boron trifluoride. Chromatographic separation of the reaction mixture furnished the 2-*O*-methyl derivative **2** and the 2,4-di-*O*-methyl derivative **3** in yields of 61 and 34%, respectively. A small amount of unchanged **1** was recovered, and no evidence for formation of the 4-*O*-methyl isomer (**2a**) of **2** was obtained. The structure of **2** was deduced from the n.m.r. spectrum of its acetate **5** and confirmed by an independent synthesis of the latter compound. (See the next paragraph). For structural comparison, the isomer **2a** was made by addition of methanol to the unsaturated glycoside **7**. Preferential methylation of the 2-hydroxyl group in nucleosides by diazomethane[4], and in various glycosides by other methylating agents[10], has been noted previously and has been attributed[10] to an acidity inductively enhanced by the neighboring acetal function.

The 4-*O*-acetyl derivative (**4**) of **1** provided a further example of facile *O*-methylation. Methyl 4-*O*-acetyl-3,6-dideoxy-2-*O*-methyl-3-nitro-α-L-glucopyranoside (**5**) was obtained in high yield. The same compound was produced almost quantitatively by acetylation (also boron trifluoride-catalyzed) of the methyl ether **2**, but only when the reaction was conducted for 10 min at about −60°. Performance at 0° with a somewhat extended reaction time caused acetolysis at C-1 to give 1,4-di-*O*-acetyl-3,6-dideoxy-2-*O*-methyl-3-nitro-α-L-glucopyranose (**6**). This is remarkable insofar as many glycosides, including in fact compound **1**, have previously been acetylated by this mild procedure[11–13] at 0° or even at room temperature without incurring such acetolysis*.

It was of interest, furthermore, to examine whether or not *O*-methylation can be accomplished in sugars that contain a nitroalkene grouping. It is known that nitroalkenes are capable of adding diazomethane in the 1,3-dipolar mode to give pyrazolines[16], and in concurrent work we have indeed achieved such additions using several fully blocked nitroolefinic glycosides[17]. However, it was found that free hydroxyl groups can be methylated without attack of diazomethane on the double bond if build-up of an excess of the reagent during the operation is avoided. Thus,

*Benzylidene acetal groupings were likewise unaffected[11] by acetic anhydride and boron trifluoride, although a case of cleavage of a trityl ether at 0° has been observed[14]. Compound **1** and a number of other glycosides have, however, been found[15] to suffer acetolysis under moderately forcing conditions (3 h at 40°).

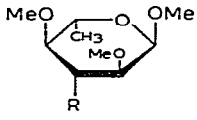
methyl 3,4,6-trideoxy-3-nitro-α-L-*erythro*-hex-3-enopyranoside (**7**) and its α-L-*threo* isomer **8** gave their 2-*O*-methyl derivatives **9** and **10**.



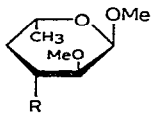
In order to devise a second route to **9**, dehydroacetoxylation of the acetate **5** was attempted. Surprisingly, trials using a variety of conditions were unsuccessful, although the nonmethylated analog **4** had been dehydroxyacetoxylated quite readily[18] to furnish **7**. However, an alternative approach to **9** did succeed. The ether **2** was treated with triphenylphosphine and carbon tetrachloride according to Lee and coworkers[19] to produce methyl 4-chloro-3,4,6-trideoxy-2-*O*-methyl-3-nitro-α-L-galactopyranoside (**11**), which readily underwent dehydrochlorination to give the olefin **9**. A similar, facile elimination of hydrogen iodide from a vicinal iodonitro sugar has been reported[20]. Reduction of **9** with sodium borohydride furnished methyl 3,4,6-trideoxy-2-*O*-methyl-3-nitro-α-L-*xylo*-hexopyranoside (**12**). The stereoselectivity of this reaction was in accordance with previous studies[21] that had established the predisposition of the nitro group, at position 3 of aldopyranosides, for assuming the equatorial orientation.

Some of the nitroglycoside methyl ethers just described were converted into amines. Platinum-catalyzed hydrogenation of **3** was unusually sluggish but never-

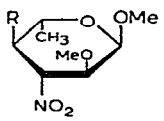
theless afforded a 62% yield of methyl 3-amino-3,6-dideoxy-2,4-di-*O*-methyl-α-L-glucopyranoside hydrochloride (**13**), which gave an *N*-acetyl derivative (**14**). The amino glycoside **13** has been reconverted[22] into **3** by oxidation with *m*-chloroperoxybenzoic acid. Hydrogenation of **12** and subsequent *N*-acetylation led to the amine **15** and its *N*-acetyl derivative **16**.



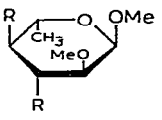
13 R = NH_3Cl
14 R = NHAc



15 R = NH_3Cl
16 R = NHAc



17 R = NH_3Cl
18 R = NHAc



19 R = NH_3Cl
20 R = NHAc

Treatment of the 4-acetate **5** with ammonia caused replacement[23] of the acetoxyl group by an amino group to give methyl 4-amino-3,4,6-trideoxy-2-*O*-methyl-3-nitro-α-L-glucopyranoside which was isolated as its crystalline hydrochloride (**17**) or *N*-acetyl derivative (**18**). Catalytic hydrogenation of **17** provided the corresponding 3,4-diamino glycoside, which was also characterized as crystalline dihydrochloride (**19**) and di-*N*-acetyl derivative (**20**). These reactions all gave excellent yields.

The configurations of all new compounds whose mode of formation might admit of stereochemical ambiguity were ascertained by n.m.r. spectra to be those indicated.

EXPERIMENTAL

General methods. — Melting points were determined in capillaries with a Gallenkamp apparatus equipped with a calibrated thermometer. Evaporations were normally carried out under diminished pressure at 35° (bath temperature). Reactions were routinely monitored by t.l.c., which was performed with layers of Silica Gel G (E. Merck A. G., Darmstadt, Germany) as the absorbent and 1% ceric sulfate in 10% sulfuric acid as the indicator. Silica Gel 7734 (Merck) was used for column separations. Chromatographic solvent mixtures (*v/v*) were: *A*, carbon tetrachloride–ethanol (92:8); *B*, the same (4:1); *C*, benzene–ethyl acetate (9:1); *D*, the same (4:1). Petroleum ether refers to the fraction boiling at 30–60°. I.r. data were obtained with a Beckman IR-20 spectrophotometer and refer to Nujol mulls unless otherwise indicated. Only selected bands of particular relevance are reported; more details are listed elsewhere[18a]. Optical rotations were measured at room temperature (~22°) with a Perkin–Elmer Model 141 automatic polarimeter. Unless otherwise stated, n.m.r. spectra were recorded on a Varian HA-100 instrument by using chloroform-*d* solutions with tetramethylsilane as the internal standard.

Methyl 3,6-dideoxy-2,4-di-O-methyl-3-nitro-α-L-glucopyranoside (**3**). — A solution of the nitro glycoside[24] **1** (2.0 g) in anhydrous ether (50 ml) was stirred for 10 min in a Dry Ice bath. An ethereal solution of diazomethane (generated from 40 g of *N*-nitrosomethylurea) and ethereal boron trifluoride (3 ml) were then added

dropwise in alternating sequence during the course of 3 h. The additions were carried out at such a rate as to always maintain the presence of a moderate excess of diazomethane. Precipitated polymethylene was filtered off and washed well with ether, and the filtrate was evaporated to give a pale-yellow syrup that by t.l.c. (solvent *A*) showed a small amount of residual **1** and two faster-moving products. Chromatography with solvent *A* on a column of silica gel (250 g) gave, from early fractions, the dimethyl ether **3** as a homogeneous oil (783 mg, 34%) whose i.r. spectrum lacked hydroxyl absorption and showed nitroalkane bands at 1555 and 1360 cm^{-1}. The oil solidified slowly on standing in the open air giving crystals having m.p. 54–55°, $[\alpha]_D$ −141.3° (*c* 1.6, chloroform); n.m.r. data: τ 5.15 (d, $J_{1,2}$ 3 Hz, H-1), 5.23 (t, $J_{2,3}$ and $J_{3,4}$ 10 Hz, H-3), 6.20 (q, H-2), 6.32–6.78 (m, H-4 and 5), 6.60, 6.64 (s, 9H, OMe), 8.71 (d, 3H, $J_{5,6}$ 6 Hz, *C*-Me).

Anal. Calc. for $C_9H_{17}NO_6$ (235.2): C, 45.95; H, 7.28; OCH_3, 39.57. Found: C, 46.51; H, 7.17, OCH_3, 39.33.

*Methyl 3,6-dideoxy-2-*O*-methyl-3-nitro-α-*L*-glucopyranoside* (**2**). — Further elution of the column mentioned in the preceding section furnished the monomethyl ether **2**, which crystallized on evaporation of the solvent; yield 1.314 g (61.5%). Recrystallized from carbon tetrachloride–petroleum ether, the flaky crystals had m.p. 87.5–88.5°, $[\alpha]_D$ −160.3° (*c* 1.3, chloroform); ν_{max} 3430 (OH) and 1550 cm^{-1} (NO_2); n.m.r. data: τ 5.12 (d, $J_{1,2}$ 3.5–4 Hz, H-1), 5.26 (t, $J_{2,3}$ and $J_{3,4}$ 10–11 Hz, H-3), 6.19 (q, H-2), 6.18–6.46 (m, 2H, H-4 and 5), 6.58, 6.62 (s, 6H, OMe), 7.5 (1H, broad, removed by D_2O exchange, OH), 8.71 (d, 3H, $J_{5,6}$ 6 Hz, *C*-Me).

Anal. Calc. for $C_8H_{15}NO_6$ (221.2): C, 43.43; H, 6.84; N, 6.33. Found: C, 43.50; H, 6.95; N, 6.14.

By continued elution of the column, 108 mg of **1** was recovered.

*Methyl 3,6-dideoxy-4-*O*-methyl-3-nitro-α-*L*-glucopyranoside* (**2a**). — A solution of methyl 3,4,6-trideoxy-3-nitro-α-L-*erythro*-hex-3-enopyranoside[18] (**7**, 100 mg) in anhydrous methanol (20 ml) was gently refluxed overnight. Removal of the solvent and recrystallization of the solid residue from ether–petroleum ether furnished **2a** (108 mg, 92.5%) as long needles, m.p. 113–113.5°, $[\alpha]_D$ −183.5° (*c* 0.8, chloroform); ν_{max} 3440 (OH) and 1550 cm^{-1} (NO_2); n.m.r. data: τ 5.27 (d, $J_{1,2}$ 3.8 Hz, H-1), 5.89 (q, $J_{2,3}$ and $J_{3,4}$ 9.5–10.3 Hz, H-3), 5.94 (octet, collapsing to quartet upon deuterium exchange, H-2), 6.2–6.8 (m, 2H, H-4 and 5), 6.59, 6.63 (s, 6H, OMe), 7.68 (d, 1H, $J_{2,OH}$ 11.5 Hz, O-H, disappearing on deuterium exchange), 8.71 (d, 3H, $J_{5,6}$ 6Hz, *C*-Me).

Anal. Calc. for $C_8H_{15}NO_6$ (221.2): C, 43.43; H, 6.84; N, 6.33. Found: C, 43.58; H, 6.69; N, 6.42.

*Methyl 4-*O*-acetyl-3,6-dideoxy-2-*O*-methyl-3-nitro-α-*L*-glucopyranoside* (**5**). — *A. By acetylation of* **2**. Compound **2** (350 mg) in acetic anhydride (5 ml) was chilled with Dry Ice, and 3 drops of boron trifluoride etherate were added with stirring. After 10 min the mixture was poured into ice–water and processed, after the decomposition of the anhydride, by evaporation followed by evaporation of ethanol from the residue. The residue was triturated with water, filtered off, and dried. The product

(433 mg, 99.5%) was recrystallized from ether–petroleum ether to give long needles, m.p. 78.5–79.5°, $[\alpha]_D$ −149.5° (*c* 1, chloroform); ν_{max} 1747 (ester CO) and 1550 cm^{-1} (NO_2) with no hydroxyl absorption; n.m.r. data: τ 4.82 (t, $J_{3,4}$ and $J_{4,5}$ 10 Hz, H-4), 5.07 (d, $J_{1,2}$ 3.5 Hz, H-1), 5.15 (t, $J_{2,3}$ 10 Hz, H-3), 6.08 (q, 3.5 and 10 Hz, H-2), 6.19 (m, H-5), 6.55, 6.59 (s, 6H, OMe), 7.97 (s, 3H, OAc), 8.82 (d, 3H, $J_{5,6}$ 6 Hz, *C*-Me).

Anal. Calc. for $C_{10}H_{17}NO_7$ (263.2): C, 45.62; H, 6.51; N, 5.32. Found: C, 45.55; H, 6.55; N, 5.14.

B. By methylation of **4**. A solution in anhydrous ether (3 ml) of 40 mg of methyl 4-*O*-acetyl-3,6-dideoxy-3-nitro-α-L-glucopyranoside[18] (**4**, m.p. 112–113°, $[\alpha]_D$ −178.5° in chloroform) was treated with ethereal diazomethane (from 2 g of *N*-nitrosomethylurea) and boron trifluoride according to the procedure described for the methylation of **1**. The product was crystallized from carbon tetrachloride–petroleum ether, and the crystals (35 mg, 83%) proved to be identical with **5** prepared from **2** by i.r. and n.m.r. spectra.

*1,4-Di-*O*-acetyl-3,6-dideoxy-2-*O*-methyl-3-nitro-α-*L*-glucopyranose* (**6**). — A solution of **2** (310 mg) in acetic anhydride (6 ml) was chilled (0°), and 10 drops of boron trifluoride etherate were added. After 1 h the anhydride was removed by azeotropic evaporation with several portions of added toluene (bath temperature, 35°). The resulting yellow syrup was dissolved in ethyl acetate and treated with activated charcoal. Evaporation then gave a solid from which part of **6** (90 mg) crystallized from ethyl acetate–petroleum ether. Chromatography of the mother liquor on a silica gel column with solvent *C* furnished another 196 mg of **6** (total yield, 86%); m.p. 108–109°, $[\alpha]_D$ −123.2° (*c* 1.1, chloroform); ν_{max} 1745 (ester CO) and 1550 cm^{-1} (NO_2). A similar but smaller-scale experiment was processed by pouring the reaction mixture onto ice and extracting the product with chloroform; crystalline **6** was obtained in 91% yield without chromatography. N.m.r. data: τ 3.54 (d, $J_{1,2}$ 3.5 Hz, H-1), 4.76 (t, $J_{3,4}$ and $J_{4,5}$ 10 Hz, H-4), 5.17 (t, $J_{2,3}$ 10 Hz, H-3), 5.98 (q, H-2), 6.03 (m, H-5), 6.61 (s, 3H, OMe), 7.84 ,7.94 (s, 6H, OAc), 8.79 (d, 3H, $J_{5,6}$ 6 Hz, *C*-Me).

Anal. Calc. for $C_{11}H_{17}NO_8$ (291.2): C, 45.39; H, 5.84; N, 4.81. Found: C, 45.20; H, 5.74; N, 4.81.

*Methyl 4-chloro-3,4,6-trideoxy-2-*O*-methyl-3-nitro-α-*L*-galactopyranoside* (**11**). — A briskly stirred mixture of **2** (700 mg), triphenylphosphine (2.1 g), and Drierite (1 g) in carbon tetrachloride (40 ml) was heated for 12 h under reflux. Filtration followed by evaporation of the filtrate gave a yellow syrup that was chromatographed on silica gel (12 g) with solvent *B*. The fractions which, according to t.l.c., contained largely the main reaction product were evaporated to give a white solid. Recrystallization from cold ether–petroleum ether afforded pure **11** (326 mg, 44%), and the colorless mother liquor (dry weight 164 mg) was revealed by n.m.r. spectroscopy to contain **11** and **9** in a ratio of about 1:2. Compound **11** had m.p. 100–101°, $[\alpha]_D$ −180.2 (*c* 1.3, chloroform); ν_{max} 1560 cm^{-1} (NO_2; hydroxyl absorption was absent). The n.m.r. spectrum showed at τ 5.05 two superposed 1-proton signals consisting

of a doublet (H-1, $J_{1,2}$ 3.5 Hz) and a quartet (H-3, $J_{2,3}$ 10 Hz, $J_{3,4}$ 3.5 Hz). Other signals occurred at τ 5.46 (q, H-4, $J_{4,5}$ 1.5 Hz), 5.77 (octet, H-5, $J_{5,6}$ ~6 Hz), 5.86 (q, H-2), 6.52, 6.58 (s, 6H, OMe), 8.68 (d, 3H, *C*-Me). Spin decoupling by double irradiation at τ 5.46 (H-4) changed the H-3 quartet centered at τ 5.05 to a 10-Hz doublet, whereas the H-1 doublet in the same region remained unaffected. Similarly, the H-5 octet collapsed to a quartet while the nearby H-2 quartet was unchanged.

Anal. Calc. for $C_8H_{14}ClNO_5$ (239.7): C, 40.09; H, 5.89; Cl, 14.79. Found: C, 40.23; H, 5.96; Cl, 14.61.

*Methyl 3,4,6-trideoxy-2-O-methyl-3-nitro-α-*L*-erythro-hex-3-enopyranoside* (**9**). — *A. From* **2** *via* **11**. The reaction described in the preceding section was modified as follows. A solution of **2** (22 mg) and triphenylphosphine (22 mg) in carbon tetrachloride (4 ml) refluxed for 20 h, after which time fresh phosphine (22 mg) in carbon tetrachloride (2 ml) was added and refluxing was continued for 26 h. The cooled solution was passed through a small column of silica gel. Elution with benzene removed residual triphenylphosphine, and further elution with solvent *C* then produced **9** (14.5 mg, 72%) as a pale-yellow, crystalline product of sufficient purity for elemental analysis. Recrystallization from ether–petroleum ether gave large, flaky crystals, m.p. 103–105°, $[\alpha]_D$ −206° (*c* 0.9, chloroform); ν_{max} 1670 (C=C), 1515 cm^{-1} (olefinic NO_2); λ_{max} 245 nm (ε, 5300 in chloroform); n.m.r. data: τ 2.94 (d, $J_{4,5}$ 2 Hz, H-4), 5.08 (d, $J_{1,2}$ 3 Hz, H-1), 5.35 (broad q, H-5), 5.59 (q, H-2, with a 2-Hz splitting due to long-range coupling with H-5), 6.43, 6.46 (s, 6H, OMe), 8.62 (d, $J_{5,6}$ 7 Hz, *C*-Me).

Anal. Calc. for $C_8H_{13}NO_5$ (203.2): C, 47.29; H, 6.45; N, 6.89. Found: C, 47.43; H, 6.60; N, 7.02.

Alternatively, crystalline **11** (30 mg) was placed on a 10-g silica gel column, which was eluted slowly with solvent *C*. The eluate was evaporated to dryness, furnishing 21 mg (83%) of **9**, m.p. 102–104°. I.r. and n.m.r. spectra were identical to those of the previous sample.

B. By methylation of **7**. The unsaturated glycoside[18] **7** (20 mg) in anhydrous ether was cooled (0°), and 1 drop of boron trifluoride etherate was added. Ice-cold, ethereal diazomethane generated from 2 g of *N*-nitrosomethylurea was then cautiously added, with swirling, at approximately the rate at which it was visibly consumed. No excess of the reagent was allowed to accumulate. Methylation was complete within 10 min, as indicated by t.l.c. (solvent *D*). Polymethylene was filtered off and the solution was evaporated to give crystalline **9** (20 mg, 93%), m.p. 102–103°, $[\alpha]_D$ −204.5° (*c* 1, chloroform). The i.r. spectrum was identical with that of the previous sample.

*Methyl 3,4,6-trideoxy-2-O-methyl-3-nitro-α-*L*-threo-hex-3-enopyranoside* (**10**). — A sample (30 mg) of methyl 3,4,6-trideoxy-3-nitro-α-L-*threo*-hex-3-enopyranoside[18] (**8**, $[\alpha]_D$ −198° in chloroform) was methylated in ether solution as described for its isomer **7**. Diazomethane from 4 g of *N*-nitrosomethylurea was used, and a larger amount of boron trifluoride etherate (0.5 ml) was added as the reaction appeared to proceed less readily than that of **7**. Isolation after 1.5 h gave an oily product that

contained starting material **8** and faster-migrating **10** (t.l.c. with solvent *B*). By column chromatography on silica gel with solvent *B*, 17 mg of **10** and 12 mg of **8** were isolated, both as syrups. The methyl ether **10** was shown to be identical with a product of different origin[18] by comparison of i.r. and n.m.r. spectra.

*Methyl 3,4,6-trideoxy-2-*O*-methyl-3-nitro-α-*L*-xylo-hexopyranoside* (**12**). — A solution of the nitroolefin **9** (60 mg) in ethanol (8 ml) was treated with sodium borohydride (60 mg) at 0°. Methanol (5 ml) was added after 15 min, and the solution was deionized with Amberlite IR-120 (H^+). Evaporation gave an oil from which several portions of added methanol were successively evaporated until boric acid was absent. The saturated nitro glycoside **12** (ν_{max} 1555 cm^{-1}) was obtained as a chromatographically homogeneous, colorless syrup; $[\alpha]_D$ −195° (*c* 0.6, chloroform); n.m.r. data (60 MHz): τ 5.0 region (d, $J_{1,2}$ 3.5 Hz, H-1, superposed on octet of H-3, $J_{2,3}$ 10, $J_{3,4a}$ 12, $J_{3,4e}$ 5.5 Hz), 6.1 (q, *J* 3.5 and 10 Hz, H-2, superimposed on broad H-5 multiplet), 6.54 (s, 3H, OMe), 7.7 (octet, $J_{4a,4a}$ 12, $J_{3,4a}$ 5.5, $J_{4e,5}$ 3 Hz, H-4e), 8.1 (q, $J_{4a,5}$, $J_{3,4e}$, $J_{4a,4e}$ 12 Hz, H-4a), 8.75 (d, 3H, $J_{5,6}$ 6 Hz, *C*-Me).

*Methyl 3-amino-3,6-dideoxy-2,4-di-*O*-methyl-α-*L*-glucopyranoside hydrochloride* (**13**). — Compound **3** (150 mg) in ethanol (1 ml) was introduced into a suspension of prereduced platinum dioxide (100 mg) in 0.1M hydrochloric acid (6.4 ml). The mixture was hydrogenated at ambient temperature and pressure. Hydrogen consumption was extremely slow. Evaporation of the solution after 2 weeks gave a white solid that was washed by trituration with ethyl acetate. The dried product (95 mg, 62%) decomposed at 263–265°, $[\alpha]_D$ −133° (*c* 1, chloroform); ν_{max} 3200–3000 w, bd (NH), 2800–2500 m (several bands), 1600 and 1500 cm^{-1} (NH_3^+); n.m.r. data (60 MHz in D_2O with acetone as internal reference): 0.87 p.p.m. upfield (d, $J_{5,6}$ 6 Hz, *C*-Me), 1.20–1.30 p.p.m. downfield (3 singlets, OMe).

Anal. Calc. for $C_9H_{20}ClNO_4$ (241.7): C, 44.72; H, 8.34; Cl, 14.67. Found: C, 44.87; H, 8.11; Cl, 14.88.

*Methyl 3-acetamido-3,6-dideoxy-2,4-di-*O*-methyl-α-*L*-glucopyranoside* (**14**). — To an ice-cooled mixture of **13** (30 mg), water (3 ml), methanol (1 ml) and Dowex-1 X8 (carbonate form, 1 ml) was added acetic anhydride (0.5 ml). The mixture was stirred for 90 min, filtered, and passed through a column containing 10 ml of Amberlite IR-120 (H^+) resin, which was washed with water. The effluent was heated for 15 min on a steam bath and then evaporated to dryness at 45°. Crystallization of the residue from ethyl acetate gave long needles of **14** (26 mg, 85%), m.p. 210–211°, $[\alpha]_D$ −128.4° (*c* 0.7, methanol); ν_{max} 3290, 3100 (NH), 1650 (amide I), 1560 cm^{-1} (amide II); n.m.r. data: τ 5.22 (d, $J_{1,2}$ 4 Hz, H-1), 6.08 (m, H-3), 6.22–6.92 (m, 3H, H-2, -4, and -5), 6.54, 6.60 (s, 9H, OMe); 8.01 (s, 3H, *N*-Ac); 8.74 (d, 3H, $J_{5,6}$ 6 Hz, *C*-Me).

Anal. Calc. for $C_{11}H_{21}NO_5$ (247.3): C, 53.42; H, 8.56; N, 5.66. Found: C, 53.28; H, 8.49; N, 5.75.

*Methyl 3-amino-3,4,6-trideoxy-2-*O*-methyl-α-*L*-xylo-hexopyranoside hydrochloride* (**15**). — The nitro glycoside **12** (60 mg) was hydrogenated for 4 h at ambient temperature and pressure over platinum catalyst (60 mg) in 30 ml of 0.01M hydro-

chloric acid. Compound **15** (57 mg, 92%) was obtained as white crystals that melted with decomposition at 206–208°; $[\alpha]_D$ −145° (*c* 0.7, methanol).

Anal. Calc. for $C_8H_{18}ClNO_3$ (211.7): C, 45.39; H, 8.57; Cl, 16.75. Found: C, 45.27; H, 8.52; Cl, 16.92.

*Methyl 3-acetamido-3,4,6-trideoxy-2-*O*-methyl-α-*L*-xylo-hexopyranoside* (**16**). — The hydrochloride **15** (22 mg) was *N*-acetylated for 2 h at 0° in a mixture of water (10 ml), methanol (1 ml), Dowex-1 X8 (carbonate form, 3 ml) and acetic anhydride. Conventional isolation gave **16** (19 mg, 84%), m.p. 178–179°, $[\alpha]_D$ −160.5° (*c* 0.9, chloroform); n.m.r. data: τ 5.12 (d, $J_{1,2}$ 3 Hz, H-1), 5.82–6.14 (m, 2H, H-3 and 5), 6.59 (s, 6H, OMe), 6.76 (q, $J_{2,3}$ 10 Hz, H-2), 7.71 (octet, H-4e), 7.95 (m, H-4a), 8.04 (s, 3H, *N*-Ac), 8.83 (d, 3H, $J_{5,6}$ 6Hz, *C*-Me).

Anal. Calc. for $C_{10}H_{19}NO_4$ (217.3): C, 55.28; H, 8.82; N, 6.45. Found: C, 55.45; H, 8.74; N, 6.44.

*Methyl 4-amino-3,4,6-trideoxy-2-*O*-methyl-3-nitro-α-*L*-glucopyranoside hydrochloride* (**17**). — Acetyl derivative **5** (200 mg) in anhydrous ether (30 ml) was added dropwise to liquid ammonia (10 ml) that was stirred in a Dry Ice bath. After 6 h, a precipitate of ammonium acetate was removed and the ammonia was allowed to evaporate. Several portions of ether were evaporated from the colorless, syrupy residue, which was finally titrated to neutrality with ethereal hydrogen chloride. The crystalline hydrochloride that separated was recrystallized, with use of some activated carbon, from a mixture of methanol, ethyl acetate, and petroleum ether to give 188 mg (96%) of **17**, m.p. 156–157° (dec.), raised to 161–163° (dec.) by another recrystallization; $[\alpha]_D$ −130.6° (*c* 0.8, methanol); ν_{max} 3120 (bd), 2800–2400 (bd), 1590 and 1505 (NH_3^+), 1550 cm^{-1} (NO_2).

Anal. Calc. for $C_8H_{17}ClN_2O_5$ (256.7): C, 37.43; H, 6.68; Cl, 13.81. Found: C, 37.31; H, 6.59; Cl, 13.73.

*Methyl 4-acetamido-3,4,6-trideoxy-2-*O*-methyl-3-nitro-α-*L*-glucopyranoside* (**18**). — *A. From* **5**. Dry ammonia gas was passed for 5 h through a solution of **5** (35 mg) in anhydrous ether (20 ml) in a Dry Ice bath. The solution was then kept overnight at room temperature, ammonium acetate was filtered off, and the solvent was removed. Several 2-ml portions of acetic anhydride were then evaporated from the amorphous residue, at 40° (bath temperature). Crystallization from ethyl acetate–petroleum ether thereafter gave fine needles of **18** (28 mg, 80%), m.p. 206–208°, $[\alpha]_D$ −134.6° (*c* 1.6, chloroform); ν_{max} 3310 (NH), 1660 (amide I), 1560–1540 cm^{-1} (NO_2 and amide II); n.m.r. data: τ 4.03 (d, broad, NH), 5.09 (d, $J_{1,2}$ 3.5–4 Hz, H-1), 5.18 (t, $J_{2,3}$ and $J_{3,4}$ 10 Hz, H-3), 5.75 (q, $J_{3,4}$, $J_{4,5}$ and $J_{4,NH}$ 10 Hz, H-4), 6.10 (q, H-2), 6.20 (m, H-5), 6.50, 6.61 (s, 6H, OMe), 8.05 (s, 3H, *N*-Ac), 8.77 (d, 3H, $J_{5,6}$ 6 Hz, *C*-Me).

Anal. Calc. for $C_{10}H_{18}N_2O_6$ (262.3): C, 45.79; H, 6.92; N, 10.68. Found: C, 45.69; H, 6.73; N, 10.56.

B. From **17**. The hydrochloride **17** (100 mg) was *N*-acetylated (2 h at 0°) in a mixture of water (10 ml) and methanol (2 ml) in the presence of acetic anhydride (2 ml) and Dowex-1 X8 (carbonate form, 2 ml). Isolation in the usual manner and

crystallization from abs. ethanol–petroleum ether yielded beautiful needles (97 mg, 95%) that were in all respects identical with **18** of section *A*.

Methyl 3,4-diamino-3,4,6-trideoxy-2-O-methyl-α-L-glucopyranoside dihydrochloride (**19**). — The aminonitro compound **17** (100 mg) in water (10 ml) and 0.1M hydrochloric acid (3.9 ml) was hydrogenated over platinum catalyst for 4 h at ambient temperature and pressure. Evaporation gave a white solid (**19**) that was recrystallized from ethanol–ethyl acetate; yield 95 mg (93%), m.p. 188–190° (dec., with gradual browning from 150°), $[\alpha]_D$ −111° (*c* 0.7, methanol); ν_{max} 3400 (NH), 2800–2400, 1595, 1505 cm^{-1} (NH_3^+).

Anal. Calc. for $C_8H_{20}Cl_2N_2O_3$ (263.2): C, 36.51; H, 7.66; Cl, 26.95. Found: C, 36.77; H, 7.84; Cl, 26.90.

Methyl 3,4-diacetamido-3,4,6-trideoxy-2-O-methyl-α-L-glucopyranoside (**20**). — Compound **19** (60 mg) was *N*-acetylated as described for **13**, **15**, and **17**. The derivative **20** crystallized from ethanol–ethyl acetate in a yield of 55 mg (88%). It sublimed at 298–300° and had $[\alpha]_D$ −201° (*c* 0.6, methanol); ν_{max} 3300, 3100 (NH), 1640 (amide I), 1560, 1540 cm^{-1} (amide II); n.m.r. data (in $CDCl_3$ with a small amount of methanol added for solubilization): τ 2.9 (broad 2H signal, NH), 5.17 (d, $J_{1,2}$ 3.7 Hz, H-1), 5.8 (broad quartet, H-3 or 4), 6.58, 6.60 (s, OMe, superposed on unresolved multiplets of the remaining ring protons), 8.08 (s, 6H, *N*-Ac), 8.85 (d, $J_{5,6}$ 5.5. Hz, *C*-Me).

Anal. Calc. for $C_{12}H_{22}N_2O_5$ (274.3): C, 52.54; H, 8.08; N, 10.21. Found: C, 52.35; H, 7.97; N, 10.21.

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