The Synthesis of Nitro and Dimeric Nitroso Sugars by Peracid Oxidation of Amino Sugars[1]

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Received January 19, 1973

A number of methyl 3-amino-3-deoxyaldopyranosides were oxidized with *m*-chloroperbenzoic acid. The reaction, which had been previously applied to steroidal amines (6), has provided a new route to nitro sugars and at the same time furnished hitherto unknown nitroso sugar derivatives, namely, dimeric methyl 3-deoxy-3-nitrosoaldopyranosides. Oxidation of a model compound, *trans*-2-aminocyclohexanol, likewise gave the corresponding nitro and dimeric nitroso alcohols. The combined yields of oxidation products ranged from 40 to 95%.

Plusieurs méthyl amino-3 déoxy-3 aldopyranosides ont été oxydés en utilisant l'acide *m*-chloroperbenzoique. Ayant déjà été appliquée aux amines stéroïdales (6), la réaction a ainsi permis une nouvelle approche pour l'obtention de sucres comportant des groupes nitro et ainsi fournir des dérivés de sucres comportant des groupes nitroso jusqu'alors inconnus, à savoir des méthyl deoxy-3 nitroso-3 aldopyranosides dimériques. L'oxydation d'un composé modèle, le *trans*-amino-2 cyclohexanol, a produit tel qu'envisagé les alcools correspondants possèdant un groupe nitro et un groupe nitroso typique du composé dimérique. Les rendements combinés des produits d'oxydation se situent dans l'intervalle de 40 à 95%.
[Traduit par le journal]

Can. J. Chem., 51, 1812 (1973)

In order to complement existing methods for the synthesis of nitro sugars (1), we considered the possibility of oxidizing amino sugar derivatives. Whereas permanganate oxidation is limited to tertiary carbinamines (2) and therefore is not apt to become a general method for the purpose stated, peracid oxidation offered itself as a potential alternative. Aliphatic amines have been oxidized to the corresponding nitro compounds by means of peracetic acid (3, 4), perbenzoic acid (5), and *m*-chloroperbenzoic acid (6). Trifluoroperacetic acid has been stated (3) to be unsuitable for oxidation of amines although it is capable of converting oximes to nitro compounds (7, 8); applications to carbohydrate oximes were reported (9) while the present work was in progress. Of the reagents mentioned, *m*-chloroperbenzoic acid appeared to promise the most convenient and hazard-free use. This stable, commercially available compound is widely employed for various oxidative processes even though use for amine oxidation has been made infrequently.

We now report that certain amino glycosides can indeed be converted into nitro glycosides by treatment with *m*-chloroperbenzoic acid. The reaction proved complicated, however, by the formation of varying proportions of nitroso derivatives along with the desired nitro compounds. Similar observations have been made in previous peracid oxidations (6, 10). The nitroso compounds arise as intermediates and, depending on circumstances, tend to form stable dimers that are oxidized no further. In fact, a dimeric nitroso compound may occasionally be the sole product as was the case in one of our examples and, earlier, in the oxidation of cyclohexylamine with peracetic acid (10). Table I shows the results obtained with five amino glycosides and with *trans*-2-aminocyclohexanol which was included as a model compound. In general, the reactions proceeded quite smoothly in mixtures of chloroform and methanol at reflux temperature, and the combined yields of oxidation products were good.

Even though the original purpose of this enterprise was the search for an alternative route to nitro sugars, the isolation of nitroso carbohydrates was actually of equal interest since very few accounts of such derivatives exist in the literature. Serfontein and coworkers (11) obtained 2-nitrosoglycosyl chlorides by the action of nitrosyl chloride upon glycals. Lemieux and his associates (12) studied the same reaction,

[1]Abstracted from the Ph.D. thesis of S. H. Lee Chiu, University of Ottawa, Ottawa, Canada, 1971, and reported at the 8th International Symposium on the Chemistry of Natural Products (IUPAC), New Delhi, India, February, 1972.

TABLE 1. Yields of oxidation products (%)

Amine	Products	
	Nitro compound	Nitroso dimer
trans-2-Aminocyclohexanol	16	28
Methyl 3-amino-3,6-dideoxy-2,4-di-*O*-methyl-α-L-glucopyranoside	53	0
α-D-glucopyranoside	44*	43*
	51†	33†
	26‡	69‡
	0§	75§
Methyl 3-amino-3-deoxy-β-D-galactopyranoside	28	47
α-D-mannopyranoside	38	32
β-D-xylopyranoside	0	40

*Amine added to oxidant (6.67 mol equiv) over period of 30 min, with final medium being approximately 3:1 chloroform–methanol (v/v); see Experimental.
†Similar to *, with 2:1 chloroform–methanol as final medium.
‡Similar to *, with addition period of 7 min.
§Amine added to oxidant (3 mol equiv) at once, with medium consisting of chloroform only; reaction time, 1 h at reflux temperature.

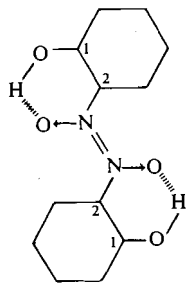
extended it to include the use of dinitrogentetraoxide which afforded 2-nitrosoglycosyl nitrates, established the dimeric structure of these nitroso sugars, and subjected them to some reactions of mechanistic interest and synthetic promise. But apart from these important studies nothing is known about nitroso sugars, and their availability by simple oxidation of amino sugars should stimulate further exploration of their properties and potential usefulness.

Oxidation of *trans*-2-aminocyclohexanol produced known (13) *trans*-2-nitrocyclohexanol together with dimeric *trans*-2-nitrosocyclohexanol (**1**) which apparently has not yet been described. Its structure followed from spectral data. The compound displayed intense u.v. absorption with λ_{max} 296 nm resembling that reported (10) for dimeric nitrosocyclohexane, λ_{max} 290 nm. Broad i.r. absorption in the 3400 cm^{-1} region indicated hydrogen-bonded hydroxyl, and a strong band near 1200 cm^{-1} was due to the N → O stretching vibration of the dimeric nitroso moiety. Complete lack of absorption between 2800 and 1500 cm^{-1} revealed absence of carbonyl, nitro, amino, and (monomeric) nitroso groups. Similar u.v. and i.r. data were found for our dimeric nitroso glycosides, and according to the literature (14) they suggest *trans*-geometry of the azodioxy bridge. Of further interest were the n.m.r. spectra of **1** and 2-nitrocyclohexanol. In the nitro alcohol, the nitromethine and carbinol protons had similar chemical shifts causing overlapping multiplets near δ 4.2. In **1**, only the carbinol proton (H-1) resonated in that region while H-2 was shifted downfield to δ 5.2 (in $CDCl_3$). The strong deshielding effect of the azodioxy group has been noted previously (12, 15).

Independent work in this laboratory (16) had furnished methyl 3,6-dideoxy-2,4-di-*O*-methyl-3-nitro-α-L-glucopyranoside (**2**) and, by catalytic hydrogenation, the corresponding amino glycoside (**3**). The latter has now been reconverted to the former by oxidation. No nitroso derivative was found in this one case.[2]

When methyl 3-amino-3,6-dideoxy-α-D-glucopyranoside (**4**) was oxidized for 1 h with 3 mol equiv of oxidant in refluxing chloroform, the nitroso dimer **5** was isolated in 75% yield as the sole product, although complete absence of nitro compound **6** was not ascertained. An increased amount of oxidant (4.25 mol equiv) gave rise to a mixture of **5** and **6** in which, according to an estimate from the n.m.r. spectrum, the nitroso

[2]It will be noted (Table 1) that **3** was the only amine thus far examined that does not bear a free hydroxyl group vicinal to the nitrogen. Perhaps this feature favors further oxidation of the nitroso intermediate whose dimer, lacking internal hydrogen bond stabilization, would in this case be less stable than in the others. However, in order to validate such an explanation one ought to reexamine the oxidation of cyclohexylamine (10) under our conditions. An alternative explanation might be steric hindrance to dimerization of the nitroso intermediate. Although a strain-free model of the dimer can be constructed, the two methoxyl groups in positions 2 and 4 could nevertheless have a retarding effect upon the rate of dimerization.



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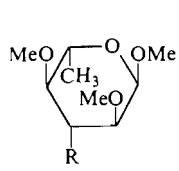
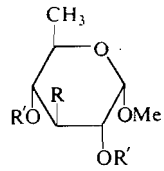
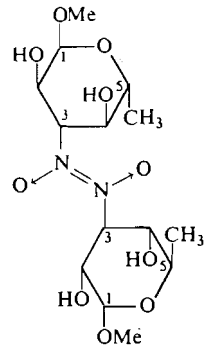


2 R = NO_2
3 R = NH_3Cl



4 R = NH_2; R′ = H
6 R = NO_2; R′ = H
7 R = NO_2; R′ = Ac



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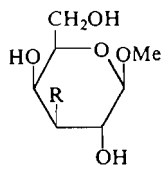
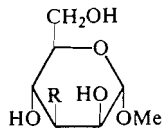
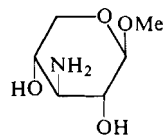


8 R = NH_2
9 R = NO_2



11 R = NH_2
12 R = NO_2



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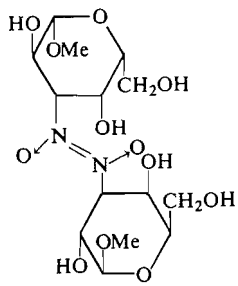

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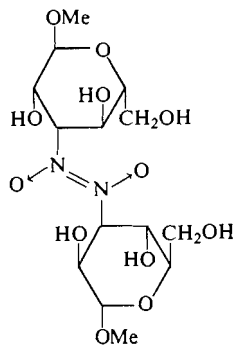

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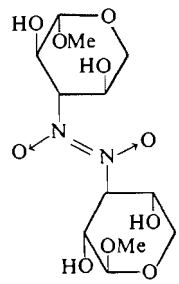

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compound still preponderated about 1.5-fold. Best results in terms of oxidation to the nitro stage were achieved when the amine was added gradually to a larger excess (6–7 equiv) of oxidant in refluxing chloroform–methanol mixtures. While relatively rapid addition gave predominantly **5**, slow addition changed the product ratio in favor of **6**. An increase in methanol concentration in the reaction medium likewise operated in this direction (Table 1). One may probably conclude from these observations that rapid oxidation of the amine to monomeric nitroso intermediate is followed by slow oxidation of the latter to the nitro compound in competition with dimerization. Thus, if the concentration of the monomeric nitroso derivative is allowed to build up due to a high initial amine concentration and the presence of only a moderate excess of oxidant, dimerization and hence protection from further oxidation is favored. But when the nitroso monomer concentration is kept low by slow introduction of the amine into the reaction medium, and when a larger excess of oxidant is available, then complete oxidation

wins over dimerization. The effect of added methanol may consist of opposing dimerization by increasing solvation of the monomer and (or) interfering with internal hydrogen bond stabilization in the dimer.

The nitro glycoside **6**, whose 2,4-diacetate **7** was also prepared for further characterization, was identified by comparison with its known L-enantiomer (17, 18). The nitroso dimer **5** showed spectral characteristics similar to **1**, namely, a high-intensity u.v. band with λ_{max} 298 nm and a strong i.r. band at 1190 cm^{-1}. The n.m.r. spectra of **5** and **6** were similar to each other in most respects (see Experimental) but differed significantly by a downfield shift experienced by the H-3 signal of **5**. Its chemical shift of *ca.* δ 6.0 compared well with data recorded (12) for protons at carbon bearing the azodioxy bridge in dimeric nitroso sugars (δ 5.38–5.53).

Oxidation of methyl 3-amino-3-deoxy-β-D-galactopyranoside (**8**) and its α-D-*manno* isomer (**11**) afforded the corresponding nitro glycosides **9** and **12** as well as the dimeric nitroso glycosides **10** and **13**. Like the preceding products the nitro sugars were identified by comparison with authentic samples, and the new nitroso derivatives were structurally elucidated through their spectral properties. Limited attempts to change the product ratios from those listed in Table 1 were to no avail.

The course of oxidation of methyl 3-amino-3-deoxy-β-D-xylopyranoside (**14**) differed from the aforedescribed experiments insofar as a crystalline product separated directly from the reaction medium during the reflux period. It was sparingly soluble in all solvents tried, including water and dimethyl sulfoxide. For this reason no n.m.r. spectrum could be obtained. The product was different from known (19) methyl 3-deoxy-3-nitro-β-D-xylopyranoside, and its u.v. and i.r. data suggested that it was the nitroso dimer **15**. It seems that the high degree of insolubility of the dimer caused the monomer to be removed from solution so rapidly that it failed to be oxidized to the nitro stage.

Experimental

All reactions were monitored by t.l.c. on 7.5-cm silica gel G plates. The spots were made visible by use of 1% ceric sulfate in 10% sulfuric acid as a spray reagent, and heating. Column chromatography was performed with silica gel 7734 (0.05–0.20 mm) of E. Merck AG, Darmstadt, Germany. I.r. spectra were taken on a Beckman IR-20 spectrometer and refer to Nujol mulls unless otherwise stated; only the most prominent bands are listed for characterization of compounds. Optical rotations were measured with a Perkin–Elmer Model 141 automatic polarimeter at room temperature. Chemical shifts in n.m.r. spectra taken in $CDCl_3$ refer to the tetramethylsilane signal, and in those taken in D_2O, to the DOH signal. U.v. spectra were recorded on a Perkin–Elmer Model 202 spectrophotometer.

Materials

trans-2-Aminocyclohexanol

The amino alcohol was prepared according to Brunnel (20) by reaction of cyclohexene oxide (5.3 ml) in methanol (50 ml) with liquid ammonia (40 ml) in a sealed tube for 2 h at 80° and 12 h at room temperature. The product was purified by sublimation at 45° and 2 Torr. It was obtained as colorless needles, m.p. 67–69°, in 63% yield; lit. (20), m.p. 67–68°. I.r. and n.m.r. spectra were in agreement with the structure. Treatment with ethanolic hydrochloric acid furnished the *hydrochloride* which upon recrystallization from 95% ethanol melted at 178.5–180°; lit. (20), m.p. 175°, 176–177°.

Amino Glycosides 3, 4, 8, and 14

The known compounds **8** (21, 22) and **14** (23, 24) were on hand from earlier work in this laboratory. Compound **3** (dec. 263–265°, $[\alpha]_D$ −133° in chloroform) was kindly provided by Dr. Chung-Wai Chiu who had synthesized it from known, crystalline methyl 3,6-dideoxy-3-nitro-α-L-glucopyranoside (25, 17) by an unpublished procedure (16). The known compound **4** (26) was obtained by a new synthesis to be described elsewhere (27).

Methyl 3-Amino-3-deoxy-α-D-mannopyranoside (11)

The free amino glycoside **11**, which has not been described previously, was made from its known hydrochloride (28). A solution of the latter (0.33 g) in 95% ethanol (25 ml) was passed through a column containing 10 g of dry Dowex 1X2 (OH^-) anion exchange resin. The effluent was evaporated to give **11** which was recrystallized from ethanol; m.p. 160–162°, $[\alpha]_D$ +70 (*c*, 1 in H_2O) and +91° (*c*, 1 in methanol). The yield was 0.24 g (86%).

Anal. Calcd. for $C_7H_{15}NO_5$ (mol. wt. 193.2): C, 43.51; H, 7.83; N, 7.25. Found: C, 43.48; H, 7.80; N, 7.21.

Oxidations with m-Chloroperbenzoic Acid. General Procedure

m-Chloroperbenzoic acid (MCPA) was supplied by Aldrich Chemical Co. According to specifications its degree of purity was 85%; the amounts given in the following have been calculated to represent pure MCPA. A solution of the reagent in chloroform (unless otherwise indicated) was heated to reflux, with efficient magnetic stirring, in a vessel equipped with condenser and dropping funnel. A solution (or partial suspension) of the amine to be oxidized, in chloroform or chloroform–methanol mixture as indicated, was admitted slowly over the period of time stated in parentheses. Refluxing was then continued for another period of time, and the reaction mixture was subsequently cooled and worked-up as described.

Oxidation of trans-2-Aminocyclohexanol

trans-2-Nitrocyclohexanol

The amino alcohol (100 mg, 0.865 mmol) in chloroform (8 ml) was added (5 min) to MCPA (450 mg, 2.6

mmol) in chloroform (5 ml). The reaction was stopped after 1 h, at which time t.l.c. (10% ethyl acetate in benzene) showed two new spots, R_f 0.6 and 0.3. The solution was cooled in a refrigerator, filtered, washed with ice cold sodium bicarbonate solution, dried (Na_2SO_4), and evaporated. The semi-solid material so obtained was chromatographed on a column of silica gel (5 g). Elution was performed with benzene containing, respectively, 5% ethyl acetate (20 ml), 10 and 25% of the same (20 ml each), and 20% ethyl acetate plus 10% ethanol (40 ml). The faster-moving product, isolated from early fractions that showed a single spot on t.l.c., was a yellow oil which crystallized on trituration with benzene–pentane and cooling. The needles (20 mg, 16%) melted at 46–47°. Recorded (13) for *trans*-2-nitrocyclohexanol, m.p. 46–48°. I.r. absorption was at 3340 (broad; OH), 2930, 2860, 1545, 1450, 1370, 1065, 970, 860, and 735 cm^{-1} (from liquid film). N.m.r. (100 MHz, $CDCl_3$): 2-proton multiplet centered near δ 4.2 (H-1 and -2); 2.74 (s, 1H, exchangeable with D_2O; hydroxy proton); 2.50–0.9 (unresolved, intensity 8H; methylene protons).

*trans-2-Nitrosocyclohexanol Dimer (**1**)*

The fractions containing the slow-moving product from the column mentioned above were evaporated to give a white solid, m.p. 118–122°. Recrystallization from ethyl acetate – petroleum ether (b.p. 60–80°) afforded **1** (31 mg, 28%) as fine needles, m.p. 130–132°. U.v. absorption in methanol: λ_{max} 296 nm (ε 7500). I.r. bands: 3400 (broad), 1195, 1175, 1065, 690 cm^{-1}. N.m.r. (60 MHz, $CDCl_3$): δ 5.2 (m, 1H, H-2); 4.1 (m, 1H, H-1); 3.43 (hydroxyl proton); 2.5–1.0 (unresolved, intensity 8H; methylene protons).

Anal. Calcd. for $C_{12}H_{22}N_2O_4$ (mol. wt. 258.3): C, 55.79; H, 8.59; O, 24.78. Found: C, 55.54; H, 8.38; O, 24.95.

Oxidation of *trans*-2-aminocyclohexanol hydrochloride gave similar results.

*Methyl 3,6-Dideoxy-2,4-di-O-methyl-3-nitro-α-L-glucopyranoside (**2**)*

The amino glycoside hydrochloride **3** (50 mg, 0.21 mmol) in methanol (3 ml) and chloroform (8 ml) was added (20 min) to MCPA (312 mg, 1.81 mmol) in chloroform (10 ml). Although only a trace of **3** remained 5 min later, boiling was continued for another 20 min. One major product spot (R_f 0.70) and a faint shadow just above the baseline were then seen on t.l.c. (15% ethyl acetate in benzene). The reaction mixture was evaporated to dryness and the residue was carefully triturated with chloroform (10 ml) to give a suspension which was strongly cooled (−19°) for some time and then filtered. The filtrate on evaporation gave a material which was chromatographed on silica gel (17 g) using 15% ethyl acetate in benzene (150 ml) as the eluant. The fractions containing the major reaction product yielded a semi-solid mixture of **2** and aromatic acid. Passage of this mixture through a small column (1.5 × 2.0 cm) of aluminum oxide (Woelm, neutral), with benzene as eluant, gave pure **2** as a syrup (26 mg, 53%) from early fractions. The product showed $[\alpha]_D$ −144.3° (*c*, 0.6 in $CHCl_3$), and its spectral data were in agreement with those of an independently synthesized sample (16) which showed $[\alpha]_D$ −141.3° (*c*, 1.6 in $CHCl_3$). Liquid film i.r. absorptions were at 2930, 2840, 1560, 1100, 1050, and 995 cm^{-1}. N.m.r. (60 MHz in $CDCl_3$): δ 4.9–4.8 (2H, d and t overlapping; H-1 and -3 with $J_{1,2} = 3.5$ and $J_{2,3} = J_{3,4} = 10.5$ Hz); 3.82 (1H, q, H-2, with $J_{1,2} = 3.5$ and $J_{2,3} = 10.5$ Hz); 3.65–3.25 (overlapping signals of H-4 and -5, and prominent singlets at 3.47 and 3.42 due to three OCH_3 groups; total intensity 11 H); 1.31 (3H, d, $J_{5,6} = 6$ Hz; C—CH_3).

*Oxidation of Methyl 3-Amino-3,6-dideoxy-α-D-glucopyranoside (**4**)*

The typical procedure described yielded approximately equal amounts of **5** and **6**. Reactions performed in the same general fashion but with variations as specified in Table 1 led to the different yields there recorded.

*Methyl 3,6-Dideoxy-3-nitroso-α-D-glucopyranoside Dimer (**5**)*

Compound **4** (169 mg, 0.95 mmol) in a mixture of methanol (7 ml) and chloroform (10 ml) was added (30 min) to MCPA (1.35 g, 6.67 mmol) in chloroform (12 ml). Ten minutes after the addition, **4** had completely disappeared and two products (R_f 0.23 and 0.1) were formed according to t.l.c. with 5% ethanol in benzene. Another 45 min of refluxing was allowed before the solvent was evaporated. The residue was extracted with water (4 × 5 ml). The material that remained undissolved was mainly aromatic acid and was discarded. Evaporation of the aqueous extract gave a solid (212 mg after drying) which by means of chloroform containing 5% of methanol was passed through a column of 5 g of aluminum oxide (Woelm, neutral, activity grade III). The effluent furnished the nitrogenous sugars still contaminated with aromatic acid. Good separation was then achieved by chromatography on silica gel (9 g) by use of 8 and 10% ethanol in benzene (120 and 50 ml, respectively). The product eluted first (R_f 0.23) was the nitro sugar **6** (see the next section). The fractions that contained the more slowly moving product only were evaporated to give colorless crystals of **5** (78 mg, 43%), m.p. 148–152°. Recrystallization from a small amount of ethyl acetate containing a few drops of absolute ethanol was achieved by adding a few drops of petroleum ether and cooling overnight. The fine prisms then melted at 154–156°, with the melt turning red and decomposing at 165°; $[\alpha]_D$ +152° (*c*, 0.4 in water). U.v. absorption in water, λ_{max} 298 nm (ε 7600). I.r. bands: 3440–3360 (broad), 1295, 1193, 1130, 1095, 1053, 1035, and 960 cm^{-1}. N.m.r. (60 MHz, D_2O): downfield from DOH, 1.25 (t, 1H, $J_{2,3} = J_{3,4} = 10$ Hz; H-3) and 0.20 p.p.m. (d, 1H, $J_{1,2} = 3.7$ Hz; H-1); upfield from DOH, 0.55 p.p.m. (q, 1H, $J_{1,2} = 3.7$, $J_{2,3} = 10$ Hz; H-2); 0.8–1.1 (m, 2H; H-4 and -5); 1.18 (s, 3H; OCH_3); 3.36 (d, 3H, $J_{5,6} = 6$ Hz; C—CH_3).

Anal. Calcd. for $C_{14}H_{26}N_2O_{10}$ (mol. wt. 382.4): C, 43.97; H, 6.85; O, 41.85. Found: C, 43.85; H, 6.70; O, 41.87.

*Methyl 3,6-Dideoxy-3-nitro-α-D-glucopyranoside (**6**)*

The chromatographic fractions containing the faster-moving product (see the preceding section) were evaporated to give a syrup which crystallized on drying *in vacuo* (87 mg, 44%). Recrystallization from chloroform – petroleum ether (b.p. 60–80°) afforded **6** as long needles, m.p. 140–141° and $[\alpha]_D$ +160° (*c*, 1 in water). Data reported (17) for the L-enantiomer: m.p. 136–139°, 141–143°, 142–145°; $[\alpha]_D$ −164.5°, −162°. Compound **6** gave an i.r. spectrum superimposable on that of the enantiomer, and its n.m.r. data agreed completely with those published (25) for the enantiomer.

Methyl 2,4-Di-O-acetyl-3,6-dideoxy-3-nitro-α-D-glucopyranoside (7)

A sample of **6** (35 mg) was acetylated (0°, 30 min) with acetic anhydride (1 ml) and ethereal boron trifluoride (2 drops). Excess anhydride was decomposed with ice-water and the product extracted with chloroform from which, on evaporation with added toluene, a dry syrup was obtained. The syrup crystallized on trituration with petroleum ether, and recrystallization from ethyl acetate – petroleum ether gave colorless needles (40 mg, 81%) showing m.p. 108–110° and $[\alpha]_D$ +154° (*c*, 0.3 in $CHCl_3$). Reported for the L-enantiomer: m.p. 109–110° and $[\alpha]_D$ −154° (18); m.p. 113–113.5° and $[\alpha]_D$ −155.3° (16). I.r. spectra of **7** and its enantiomer were identical.

Oxidation of Methyl 3-Amino-3-deoxy-β-D-galactopyranoside (8)

Methyl 3-Deoxy-3-nitro-β-D-galactopyranoside (9)

The amino glycoside **8** (193 mg, 1.0 mmol) in a 1:1 methanol–chloroform mixture (8 ml) was added (20 min) to MCPA (1.28 g, 6.32 mmol) in the same solvent (19 ml). Refluxing was continued for another 20 min. Complete consumption of **8** and formation of two products, R_f 0.5 and 0.25, was revealed by t.l.c. (20% methanol in chloroform). The white residue obtained upon evaporation of the reaction mixture was extracted with ether (2 × 10 ml). The part that remained undissolved was dealt with as described later on. The ether extract, which contained part of **9** and aromatic acid, was washed with water (3 × 5 ml) which upon evaporation gave a semi-solid material (89 mg). Passage of this material by means of chloroform containing 5% of methanol through a small silica gel column (5 g) yielded syrupy **9** that crystallized from acetone–chloroform. The colorless product (36 mg) exhibited $[\alpha]_D$ +32.5° (*c*, 0.5 in water) and melted at 80–82° (air dried) and at 125–128° (dried for 12 h *in vacuo* at 56°); lit. (21): $[\alpha]_D$ +32.6°; m.p. 87–89 and 131–132°, respectively. Identity of the product with previously prepared **9** (21) was confirmed by i.r. spectra. The n.m.r. spectrum (100 MHz in D_2O) was in accord with the β-D-*galacto* configuration: downfield from DOH, 0.22 p.p.m. (q, 1H, $J_{2,3}$ = 10, $J_{3,4}$ = 3.5 Hz; H-3); upfield from DOH, 0.21 (d, 1H, $J_{1,2}$ = 8 Hz; H-1), 0.55 (q, 1H, $J_{1,2}$ = 8, $J_{2,3}$ = 10 Hz; H-2), 1.07 p.p.m. (s, 3H; OCH_3).

The ether-insoluble residue mentioned above was suspended in methanol (5 ml) whereby it partly dissolved, leaving behind 80 mg of chromatographically pure nitroso dimer **10** (see the next section). The methanolic solution contained both **9** and **10** (t.l.c.). Evaporation followed by chromatography on silica gel (8 g) with chloroform containing increasing amounts of methanol furnished 26 mg of **9** and 17 mg of **10**, thus raising the total yields to 62 (28%) and 97 mg (47%), respectively.

Methyl 3-Deoxy-3-nitroso-β-D-galactopyranoside Dimer (10)

Compound **10** isolated as just described was recrystallized from methanol–water to form colorless needles; m.p. 141–143°, $[\alpha]_D$ +165° (*c*, 0.6 in water); λ_{max} 295 nm (ε 7500, in water). I.r. bands were at 3300 (broad), 1190, 1160, 1130, 1055, 1020, and 980 cm^{-1}. Most of the n.m.r. signals (60 MHz, D_2O) were poorly resolved, but the signal at lowest field (0.69 p.p.m. downfield from DOH) was a clear quartet assignable to H-3 ($J_{2,3}$ = 10, $J_{3,4}$ = 3 Hz). The OCH_3 singlet occurred 1.08 p.p.m. upfield from DOH.

Anal. Calcd. for $C_{14}H_{26}N_2O_{10}$ (mol. wt. 414.4): C, 40.58; H, 6.42; O, 46.34. Found: C, 40.64; H, 6.42; O, 46.26; mol. wt., 423 (osmometrically in water).

Oxidation of Methyl 3-Amino-3-deoxy-α-D-mannopyranoside (11)

Methyl 3-Deoxy-3-nitro-α-D-mannopyranoside (12)

The amino glycoside **11** (110 mg, 0.57 mmol) in a mixture of methanol (9 ml) and chloroform (4 ml) was added (20 min) to MCPA (800 mg, 3.94 mmol) in chloroform (8 ml). After continued refluxing for another 20 min all **11** had been consumed and two products (R_f 0.6 and 0.23, with 3:1 benzene–ethanol) were seen. The residue obtained on solvent evaporation was extracted with ether (4 × 10 ml) and set aside for further use (see below). The ethereal extract was shaken four times with 5 ml of 50% aqueous tetrahydrofuran. The water phase that separated contained part of **12** along with some aromatic acid. The latter could be removed by chromatography of the solute on silica gel (5 g) using chloroform with increasing proportions of methanol (0, 5, 10, 15%) as eluant. The colorless syrup of **12** obtained from the eluate crystallized from ethyl acetate and petroleum ether after prolonged cooling, forming rosettes of large crystals (23 mg), m.p. 120–120.5° $[\alpha]_D$ +37.2° (*c*, 0.6 in water). The i.r. spectrum was identical with that of authentic **12**; lit. (29): m.p. 113–115° (from tetrahydrofuran–ether); $[\alpha]_D$ + 44.5°.

The crude reaction residue that had been extracted with ether (see above) was fractionated on a silica gel column (8 g) with chloroform–methanol as described. An additional 26 mg of the faster-moving nitro sugar **12** was thereby obtained in crystalline form, raising its yield to 49 mg (38.5%). Later fractions contained the nitroso dimer **13**.

Methyl 3-Deoxy-3-nitroso-α-D-mannopyranoside Dimer (13)

Evaporations of the fractions just mentioned gave **13** as a foam which was dried *in vacuo* to a white, hygroscopic powder (40 mg, 34%) melting at 93–96° and exhibiting $[\alpha]_D$ −14° (*c*, 0.2, in water). All attempts at recrystallization failed. The product showed λ_{max} 293 nm (ε 4000, in water) and i.r. bands at 3300 (broad), 1195, 1140, 1060 (broad), and 975 cm^{-1}. Most of the n.m.r. signals (100 MHz in D_2O) were poorly resolved, but the signal at lowest-field (0.69 p.p.m. downfield from DOH) was a well-separated quartet assignable to H-3 ($J_{2,3}$ = 3, $J_{3,4}$ = 10.5 Hz). The OCH_3 singlet occurred at 1.29 p.p.m. upfield from DOH.

Oxidation of Methyl 3-Amino-3-deoxy-β-D-xylopyranoside (14)

A solution of amino glycoside **14** (26.5 mg, 0.16 mmol) in methanol (2 ml) and chloroform (4 ml) was added (10 min) to MCPA (200 mg, 1.16 mmol) in chloroform (6 ml). The initially clear reaction mixture became turbid during this period due to the separation of crystals, and this condition persisted even when more methanol was added. It was seen on t.l.c. that all the starting glycoside had reacted shortly after its introduction, and only one new spot was detected (R_f 0.27). The crystals (11 mg) were collected after cooling of the solution and recrystallized from hot methanol–water. The fine colorless needles melted at 168–170°, turning dark red in the process. The product was assumed to be methyl 3-deoxy-3-nitroso-β-D-

xylopyranoside dimer (**15**) on grounds of its spectral data, low R_f-value, and poor solubility even in water and DMSO. It displayed λ_{max} 300 nm (ε 7000 in water) and i.r. bands at 3400 (broad), 1295, 1215, 1195, 1150, 1120, 1090, 1060, 1020, 985, and 875 cm^{-1}. No NO_2 vibration was present in the 1550 cm^{-1} region. The product was clearly different in all these characteristics from known methyl 3-deoxy-3-nitro-β-D-xylopyranoside (19) which melts at 186–187°, shows greater solubility, and gives a nitro band in the i.r. but no high-intensity u.v. absorption in the 300 nm region.

Support of this work by the Defence Research Board of Canada is gratefully acknowledged.

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