REACTIONS OF NITRO SUGARS

I. SOME BENZYLIDENE AND ACYL DERIVATIVES OF METHYL 3-DEOXY-3-NITRO-D-HEXOPYRANOSIDES

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ABSTRACT

The 4,6-*O*-benzylidene derivatives VII, VIII, and XVII of methyl 3-deoxy-3-nitro-β-D-mannopyranoside, -β-D-galactopyranoside, and -α-D-glucopyranoside, respectively, were prepared. Acetylation of the β-D-*manno* derivative (VII) led, depending upon the reaction conditions, to its 2-*O*-acetate (IX) and, by way of an unexpected epimerization, to the 2-*O*-acetate (V) of the corresponding β-D-*gluco* isomer. There is evidence that this epimerization proceeds through methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-*erythro*-hexopyranos-2-enide (VI). This nitroolefin was obtained by a Schmidt–Rutz reaction from IX (as earlier from V) and was shown to add acetic acid readily giving V. It also added ethanol producing a 2-*O*-ethyl glycoside (XII). Acetylation of the *galacto* derivative (VIII) did not afford an acetate but proceeded with dehydration yielding methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-*threo*-hexopyranos-2-enide (X).

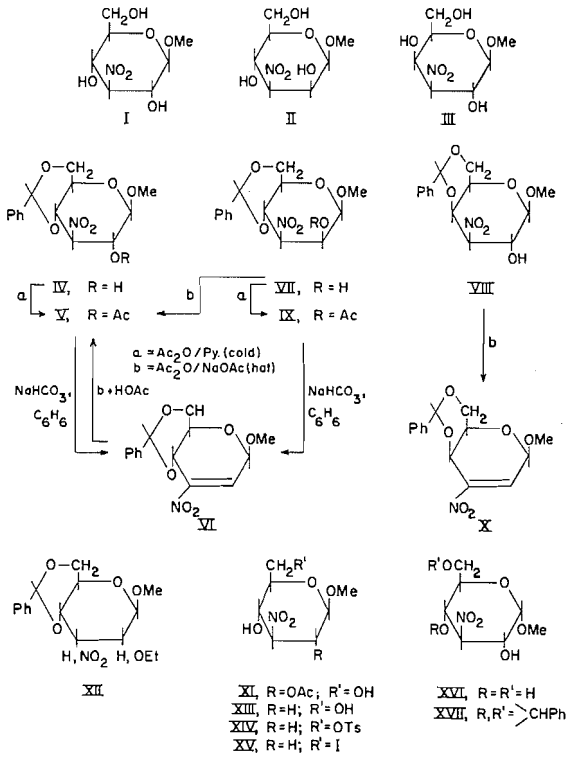
A number of further derivatives of methyl 3-deoxy-3-nitro-β-D-glucopyranoside were prepared, viz., the 2-*O*-acetyl (XI), 2-deoxy-6-*O*-tosyl (XIV), and 2,6-dideoxy-6-iodo (XV) derivatives.

A recent article (1) has described the synthesis of 3-amino-2,3-dideoxy-D-*arabino*-hexose via the corresponding methyl 2,3-dideoxy-3-nitro-β-glycoside (XIII). In view of the potential usefulness of nitro sugar intermediates for similar syntheses which may lead to rare amino sugars, a number of additional 3-deoxy-3-nitro-hexose derivatives have been prepared and some of their reactions have been studied.

Nitromethane cyclization of L′-methoxy-D-hydroxymethyldiglycolic aldehyde (periodate-oxidized methyl β-D-hexopyranosides) had afforded (2, 3, 4) crystalline methyl 3-deoxy-3-nitro-β-D-glucopyranoside (I), -D-mannopyranoside (II), and -D-galactopyranoside (III). The 4,6-*O*-benzylidene derivative (IV) of I had been acetylated (1) to methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-3-nitro-β-D-glucopyranoside (V) which was subsequently converted into a nitroolefin, methyl 2,3-dideoxy-3-nitro-β-D-*erythro*-hexopyranos-2-enide (VI) by treatment with sodium bicarbonate in refluxing benzene (Schmidt–Rutz reaction). We have now prepared the 4,6-*O*-benzylidene derivatives VII and VIII from II and III, respectively, and have studied their behavior in similar reaction sequences.

The benzylidene mannoside (VII) furnished its 2-*O*-acetate (IX) on treatment with acetic anhydride in cold pyridine. Acetylation with hot acetic anhydride and anhydrous sodium acetate, however, did not lead to the same acetate but gave, surprisingly, the 2-*O*-acetyl glucoside (V). This glucoside acetate was also obtained when the nitroolefin (VI) was heated with a mixture of acetic anhydride, acetic acid, and sodium acetate. It appears, therefore, that under the more vigorous acetylation conditions the mannoside (VII) undergoes dehydration followed by addition, to intermediate VI, of a molecule of acetic acid in such a way as to favor equatorial orientation of the nitro and acetoxy substituents (i.e., *gluco* configuration).

The 2-*O*-acetyl-mannoside (IX) furnished *isolable* nitroolefin (VI) by Schmidt–Rutz elimination of acetic acid, as did the glucoside (V). It was noted that the reaction rates were of similar magnitude for V and IX; however, this observation should not be stressed



too much since slightly varying conditions may have prevailed in the heterogeneous reaction media.

When acetylation of the benzylidene galactoside (VIII) was attempted with acetic anhydride and pyridine, decomposition occurred; and acetylation with cold acetic anhydride and sodium acetate led to recovery of starting material. When, however, VIII was *heated* for a few minutes in an acetic anhydride – sodium acetate mixture, a new crystalline product was formed in 96% yield. It was not the expected nor any other *O*-acetate, but proved to be the nitroolefin, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-*threo*-hexopyranos-2-enide (X). Further refluxing of (isolated) X in a glacial acetic acid – acetic anhydride mixture for 2.5 h yielded only starting material. A comparison of these results with those in the *manno* and *gluco* series described above shows that the C-4 configuration influences remarkably the stability of the 2,3-olefinic bond.

Further, it was of interest to study the feasibility of preparing nitroolefins by the Schmidt–Rutz reaction in the absence of a benzylidene blocking group at C-4 – C-6. Compound V was therefore debenzylidenated with a cation exchange resin in aqueous methanol, and crystalline methyl 2-*O*-acetyl-3-deoxy-3-nitro-β-D-glucopyranoside (XI) was obtained. Treatment of XI with sodium bicarbonate in refluxing benzene gave only an intractable mixture, possibly owing to intermolecular addition and (or) polymerization reactions of the nitroalkenediol presumably produced. It is of interest in this connection that the benzylidene nitroolefin (VI) readily added ethanol when refluxed in this solvent.[1]

[1]*This was discovered during an attempt to recrystallize VI from hot ethanol. The addition was probably promoted by the presence of a trace of alkali. Alkali-catalyzed additions of alkoxyl to nitroolefins are well known: cf. (5, 6, 7) and earlier literature cited there.*

The crystalline product obtained had the composition of a methyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-ethyl-3-nitro-β-D-hexopyranoside (XII), but no attempt was made to elucidate its stereochemistry. This type of addition reaction should lend itself to the synthesis also of other 2-*O*-alkylated 3-nitro (and thence amino) sugars and possibly of 2-linked disaccharides.

One of the possible ways to synthesize 3-amino-2,3,6-trideoxy sugars (such as occur in certain antibiotics) was seen in a conversion of a 2,3-dideoxy-3-nitro hexoside into its 6-*O*-*p*-toluenesulfonyl and thence its 6-deoxy-6-iodo derivative, followed by reduction. To explore this route, methyl 2,3-dideoxy-3-nitro-β-D-*arabino*-hexopyranoside (XIII) (1) was monotosylated to XIV. That the tosyloxy group in XIV was indeed a primary one (i.e., located at C-6) was shown by its facile displacement by iodine on refluxing with sodium iodide in acetone. Unfortunately, reduction of the 6-iodo derivative (XV) has as yet been unsuccessful.[2]

All the experiments described above and those done previously (1) relate to the β-D-hexopyranoside series. Their performance was facilitated by the fact that I, II, and III were fairly readily available in pure, crystalline condition. It should be interesting to investigate the course of these reactions in the α-anomeric series as well. However, such undertaking remains unattractive so long as the corresponding α-glycosides, known only as amorphous mixtures of isomers (8, 9), cannot be separated into stereochemically homogeneous compounds. A first step in this direction has now been accomplished by the isolation, through column chromatography, of crystalline methyl 3-deoxy-3-nitro-α-D-glucopyranoside (XVI) and by its conversion into a crystalline 4,6-*O*-benzylidene derivative (XVII). Proof of the identity of XVI was furnished by hydrogenation and acetylation giving the known methyl 3-acetamido-3-deoxy-2,4,6-tri-*O*-acetyl-α-D-glucopyranoside.

EXPERIMENTAL

Unless otherwise indicated, evaporations were carried out *in vacuo* at 35–40° (bath temperature), petroleum ether refers to the fraction boiling at 30–60°, melting points were taken with an aluminium block apparatus and calibrated thermometer, and infrared spectra were measured using the Nujol mull technique and a Parkin-Elmer Infracord instrument.

Methyl 4,6-O-Benzylidene-3-deoxy-3-nitro-β-D-mannopyranoside (VII)

Methyl 3-deoxy-3-nitro-β-D-mannopyranoside (II; 150 mg) (4) was magnetically stirred for 15 h with 2 ml of benzaldehyde and 400 mg of anhydrous zinc chloride. The partly solidified reaction mixture was taken up with 150 ml of water and 50 ml of petroleum ether, and the heterogeneous mixture was vigorously stirred for 30 min. A solid material which separated was filtered off, washed with water and petroleum ether, and dried in a desiccator. The weight was 130 mg (62%). Recrystallization from ethanol containing a few drops of water afforded 70 mg of colorless leaflets melting at 194–196° and showing $[\alpha]_D^{23}$ −107.5° (*c*, 1 in ethanol).

Anal. Calcd. for $C_{14}H_{17}NO_7$ (311.3): C, 54.01; H, 5.51; N, 4.50. Found: C, 54.02; H, 5.62; N, 4.45.

It was not necessary to use pure II for this preparation. Rather, the material that was left in the mother liquor when methyl 3-deoxy-3-nitro-β-D-galactopyranoside (III) was prepared (4) and that consisted largely of II together with remnant III, could be utilized. Scaled-up runs could conveniently be performed. The crude benzylidenated product was then subjected to fractional crystallization from absolute ethanol, in which the *galacto* derivative VIII is less soluble than VII. Thus, in one experiment using about 25 g of a sirup of II and III there was obtained, after several recrystallizations, about 2.5 g of pure VIII from the forefractions and about 9.5 g of pure VII with m.p. 198–199° and $[\alpha]_D^{23}$ −105° (*c*, 1 in dimethylformamide). For characteristic infrared absorption bands see the second paragraph of the next section.

Methyl 4,6-O-Benzylidene-3-deoxy-3-nitro-β-D-galactopyranoside (VIII)

Pure methyl 3-deoxy-3-nitro-β-D-galactopyranoside (4) (III; 200 mg) was benzylidenated as described above for II. After recrystallization of the crude product from absolute ethanol, 140 mg (50%) of VIII

[2]*Hydrogenations using platinum catalyst or Raney nickel were tried. The choice of reducing agents was limited since alkaline conditions had to be avoided because of danger of epimerization in the nitroalcohol part of the molecule.*

was obtained as colorless, long needles having m.p. 230–231° (decomp.) and $[\alpha]_D^{23}$ +24.8° (*c*, 1 in dimethylformamide). A large run using 7.7 g of crystalline but unpurified III afforded 6.0 g (56%) of pure VIII after recrystallization.

Anal. Calcd. for $C_{14}H_{17}NO_7$ (311.3): C, 54.01; H, 5.51; N, 4.50. Found: C, 54.16; H, 5.50; N, 4.70.

Infrared data:[3] The three stereoisomeric benzylidene derivatives IV, VII, and VIII show sharp hydroxyl bands at 3 450 and nitro bands at 1 560 cm^{-1}. Characteristic differences are seen in the 900–700 cm^{-1} region. IV: 880(w), 857(w), 762–755(s), 730(w), 697(s). VII: 877(s), 850(w), 815(w), 775(ms), 750(s), 725(ms), 697(s). VIII: 872(w), 827(w), 790(w), 755(w), 744(s), 697(s).

*Methyl 2-O-Acetyl-4,6-O-benzylidene-3-deoxy-3-nitro-β-*D*-mannopyranoside (IX)*

Benzylidene mannoside (VII) (200 mg) in pyridine (2 ml) was acetylated at room temperature with acetic anhydride (0.6 ml). The reaction mixture was allowed to stand overnight and was then poured into 50 ml of ice water, and the precipitate which formed was thoroughly washed with water. Recrystallization from aqueous ethanol gave 130 mg (57%) of colorless acetate IX melting at 136–137°.

Anal. Calcd. for $C_{16}H_{19}NO_8$ (353.2): C, 54.40; H, 5.42; N, 3.97. Found: C, 54.52; H, 5.55; N, 3.93.

The infrared spectrum[3] lacked hydroxyl absorption and showed a strong carbonyl peak at 1 740 and a nitro peak at 1 560 cm^{-1}. The spectrum differed from that of V in the 900–700 cm^{-1} region. IX: 917(m), 905(w), 872(m), 760–750–745(m), 722(m), 697(s), 690(w). V: 917(s), 890(m), 875(w), 763(s), 733(w), 703–697(s).

Acetylation of VII with Acetic Anhydride – Sodium Acetate

A sample of VII (300 mg) was refluxed with sodium acetate (1.2 g) in acetic anhydride (5 ml) for 6 min. Decomposition of the reaction mixture with ice water (50 ml) led to the formation of a white solid within 10 min. The solid was collected, washed thoroughly with cold water, and dried in a desiccator. The m.p. of the crude product (290 mg) was 151–154°; it was raised to 191–193° by two recrystallizations from ethyl acetate – petroleum ether. The yield of pure V was 160 mg; its infrared spectrum was identical with that of a sample prepared from IV (1) and differed from that of IX (see preceding section). The m.p. recorded (1) for V is 193–194°.

Acetoxylation of Nitroolefin (VI)

An 80 mg sample of nitroolefin (VI) from previous work (1) was refluxed for 6 min in 1 ml of acetic anhydride containing 240 mg of anhydrous sodium acetate and 40 mg of glacial acetic acid. Decomposition of the reaction mixture with 10 ml of ice water furnished 72 mg of crystals showing an unsharp m.p. of 142–148°. Since recrystallization (ethyl acetate – petroleum ether) failed to give a pure product, the whole material—crystals and evaporated mother liquor of recrystallization—was subjected once more to an identical treatment of acetoxylation, but for 2 min only. Work-up as described then afforded 60 mg of crystals melting at 152–154°. After two recrystallizations from aqueous ethanol the m.p. was 192–193° and the yield was 22 mg. The product was identified as V by its infrared spectrum.

Nitroolefin (VI) from IX

The Schmidt–Rutz elimination of acetic acid from the nitromannoside (IX) was done[4] essentially as described (1) for V. Nitromannoside (IX) (2 g) in dry benzene (50 ml) was refluxed with 10 g of finely ground, dry sodium bicarbonate. Small amounts of the solution were withdrawn from time to time, allowed to evaporate, and inspected by infrared spectroscopy. Progress of the reaction was revealed by diminution of the acetate carbonyl peak at 1 740 cm^{-1} and the nitroalkane peak at 1 560 cm^{-1} with concurrent appearance and increase of a peak at 1 533 cm^{-1} which was due to the olefinic nitro group produced. Progress was slight after 30 min, considerable after 3 and 4.5 h, and very large though incomplete after 27 h. Only VI and no more starting material was detected after 48 h when the reaction mixture was worked up by filtration, evaporation, and recrystallization of the residue from the minimum amount of ethyl acetate – petroleum ether (b.p. 60–80°). There was obtained 1.1 g of VI melting at 140–141° (yield, 70%). The infrared spectrum was identical with that of material prepared (1) from V.

Acetylation of Benzylidene Galactoside (VIII)

(a) Attempted O-Acetylation

Samples of VIII (about 50 mg each) were treated with acetic anhydride in pyridine in the manner described above for VII. The reaction mixtures turned dark brown and black on standing overnight at 0° and 23°, respectively. No crystalline acetate could be isolated, and benzaldehyde was detected during work-up. When acetylation was attempted with sodium acetate and acetic anhydride at 4° (24 h), only starting material was recovered. Under similar conditions but at room temperature a crystalline material was obtained that, according to its infrared spectrum, consisted of starting material and nitroolefin (X) (see under (*b*)).

*(b) Methyl 4,6-O-Benzylidene-2,3-dideoxy-3-nitro-β-*D*-threo-hexopyranos-2-enide (X)*

Pure benzylidene galactoside (VIII) (3 g) was refluxed for 6 min with 12 g of anhydrous sodium acetate

[3]*Frequencies ν_{max} in cm^{-1}. Relative intensities are given in parentheses: s = strong, m = medium, w = weak.*

[4]*We are obliged to Dr. M. C. Cook of this laboratory for performing some confirmatory experiments.*

in 30 ml of acetic anhydride. The slightly yellowish reaction mixture was allowed to cool under tap water and then poured into 200 ml of ice water. Stirring for 10 min resulted in the separation of a crystalline solid that was collected and washed well with water. The yield was 2.7 g (96%) of desiccator-dried, crude X which melted at 152–155° and was suitable for further experiments. An analytical sample was obtained by recrystallization from ethyl acetate – petroleum ether giving beautiful needles of m.p. 162° and $[\alpha]_D^{23}$ −47.8° (*c*, 1 in dimethylformamide).

Anal. Calcd. for $C_{14}H_{16}NO_6$ (293.3): C, 57.33; H, 5.16; N, 4.78. Found: C, 57.56; H, 5.32; N, 4.99.

When a sample of X was refluxed for 2.5 h in glacial acetic acid containing acetic anhydride, starting material was recovered and no evidence for the formation of an *O*-acetate was obtained.

Characteristic infrared bands[3]: No hydroxyl absorption; olefinic nitro group, 1 525 cm^{-1}. Comparison of X and VI in the 900–700 cm^{-1} region: X, 895(w), 877(w), 855(w), 820(m), 795(m), 752(s), 738(s), 692(s); VI, 890(w), 865(w), 802(m), 751(s), 738(w), 695(s), 675(w).

Methyl 2-O-Acetyl-3-deoxy-3-nitro-β-D-glucopyranoside (XI)

Benzylidene acetate (V) (500 mg) was refluxed for 4 h with 1.5 g of Dowex 50W-X8 (H^+) in 40 ml of methanol and 10 ml of water. The resin was removed and the filtrate was taken to dryness. Crystallization of the colorless residue (370 mg) from ethyl acetate – petroleum ether gave needles or platelets (200 mg, 54%) melting at 190–191°.

Anal. Calcd. for $C_9H_{15}NO_8$ (265.2): C, 40.76; H, 5.70; N, 5.28. Found: C, 40.31; H, 5.80; N, 5.51.

Refluxing of XI in benzene (25 parts) in the presence of solid sodium bicarbonate (5 parts) produced a dark intractable sirup.

Addition of Ethanol to Nitroolefin (VI)

Crude nitroolefin (VI) that had been obtained from 200 mg of benzylidene acetate (V) by a Schmidt–Rutz reaction as previously described (1), was refluxed for 2 h in 25 ml of ethanol. Upon addition of water and cooling there separated 120 mg (63% based on V) of needles with m.p. 122–123° and $[\alpha]_D^{23}$ −88.0° (*c*, 1.16 in ethanol). Analysis and infrared spectrum were in agreement with structure XII of a methyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-ethyl-3-nitro-β-D-hexopyranoside.

Anal. Calcd. for $C_{16}H_{21}NO_7$ (339.3): C, 56.63; H, 6.24; N, 4.13. Found: C, 56.70; H, 6.22; N, 4.31.

Infrared bands (cm^{-1}): no hydroxyl; 1550, 1375 (nitroalkane); 1087, 1075, 990, 970 (ether C—O—C); 763, 700 (benzylidene).

Methyl 2,3-Dideoxy-3-nitro-6-O-p-toluenesulfonyl-β-D-arabino-hexopyranoside (XIV)

To a solution of 840 mg of methyl 2,3-dideoxy-3-nitro-β-D-*arabino*-hexopyranoside (XIII) (1) in 1 ml of pyridine was added a solution of tosyl chloride (810 mg, 1.05 molar equiv) in dichloromethane (25 ml). The mixture was left overnight at room temperature and then extracted thrice with 25 ml of 0.2 *N* hydrochloric acid, washed thrice with 25 ml of water, dried over anhydrous magnesium sulfate and finally evaporated. The colorless residue was crystallized from ethyl acetate – petroleum ether and furnished 955 mg (65%) of XIV as needles with m.p. 115°.

Anal. Calcd. for $C_{14}H_{19}NO_8S$ (361.2): C, 46.51; H, 5.31; N, 3.88; S, 8.87. Found: C, 46.75; H, 5.45; N, 4.01; S, 8.74.

Methyl 6-Iodo-3-nitro-2,3,6-trideoxy-β-D-arabino-hexopyranoside (XV)

Monotosylate (XIV) (380 mg) and sodium iodide (1.6 g) were refluxed in acetone (25 ml) for 24 h. After cooling, sodium tosylate (200 mg, 98%) was filtered off and the filtrate was evaporated. Water (25 ml) was added to the residue, and the mixture was extracted four times with 25 ml of chloroform. The combined chloroform extracts were washed once with a dilute sodium thiosulfate solution in order to remove a small amount of free iodine formed in a side reaction. Washing with water (3 × 25 ml), drying over anhydrous magnesium sulfate, and evaporation of the chloroform gave a crystalline residue which was recrystallized from ethyl acetate – petroleum ether. There was obtained 200 mg of colorless crystals, m.p. 147–148°, and a second crop (150 mg) of crystals of lesser purity. The crops were jointly recrystallized from the same solvents giving 305 mg (91%) of XV melting at 147–148°.

Anal. Calcd. for $C_7H_{12}INO_5$ (317.1): C, 26.51; H, 3.81; I, 40.03; N, 4.42. Found: C, 26.73; H, 3.92; I, 40.28; N, 4.53.

Methyl 3-Deoxy-3-nitro-α-D-glucopyranoside (XVI)

An amorphous mixture of methyl 3-deoxy-3-nitro-α-D-hexopyranosides was prepared, starting from 3.88 g (0.02 mole) of methyl α-D-glucopyranoside, in the fashion described on p. 86 of ref. 9 and relating to the nitromethane condensation in methanolic solution. The product ($[\alpha]_D^{23}$ ca. +100°, in water) was liquefied with a small amount of a chromatographic solvent mixture which consisted of the upper layer formed on mixing 1-butanol – acetic acid – water (4:1:5, v/v), and placed on a column (4.2 × 100 cm) of powdered cellulose. Elution was performed with 1.5 l of the solvent mixture, and 13-ml fractions were collected and checked polarimetrically in a 2-dm tube. Fraction No. 65 was the first to show optical activity (α_D +0.08°); maximum rotation (α_D +2.52°) was observed in fraction No. 77; then followed a gradual decrease with fraction No. 112 showing α_D +0.04° and the subsequent fractions having zero rotation. Paper chromatography using the same solvent system revealed that separation on the column had been rather unsatisfactory,

as all the fractions gave two or three spots. Some accumulation of product and, probably, removal of impurities was nevertheless achieved resulting in the crystallization of XVI from certain fractions. Fractions 69–73 were combined and evaporated. The residue was taken up in a small amount of tetrahydrofuran, excess ethyl ether was added, and the solution was placed in a refrigerator for crystallization. The same procedure was followed for fractions 77–80. There crystallized in the course of 2 and 4 d 51 and 98 mg of products, melting at 127–133° (decomp.) and 129–133° (decomp.), respectively. Jointly recrystallized from tetrahydrofuran–ether (with an activated charcoal treatment included) the material (59 mg) melted at 136–137° (decomp.). All the other fractions were combined and, together with the mother liquors from fractions 69–73 and 77–80, were worked up in similar fashion. Seeding with the above crystals gave another crop, which upon recrystallization weighed 104 mg and also melted at 136–137° (decomp.).

Pure XVI formed colorless, elongated prisms which were chromatographically uniform; R_f 0.67; $[\alpha]_D^{23}$ +166° (*c*, 1 in water).

Anal. Calcd. for $C_7H_{13}NO_7$ (223.2): C, 37.67; H, 5.87. Found: C, 38.19; H, 5.93.

The anomeric glycosides XVI and I exhibit characteristic differences in their infrared spectra,[3] particularly in the region 950–700 cm^{-1}: XVI, 927(w), 903(m), 860(m), 800(m), 750–700(m, broad, with maximum at 725); I, 935(w), 918(m), 890(m), 790–700(m, broad, with maximum at 740).

To establish the configuration of crystalline XVI it was converted into known methyl 3-acetamido-3-deoxy-2,4,6-tri-*O*-acetyl-α-D-glucopyranoside. An aqueous solution containing 30 mg of XVI and an equivalent amount of (dilute) hydrochloric acid was hydrogenated catalytically over prehydrogenated platinum dioxide. A sirupy but chromatographically uniform amine hydrochloride was obtained; it traveled more slowly than a comparison sample of the corresponding mannoside (8, 9). Acetylation of the amine hydrochloride using 2 ml of acetic anhydride and 500 mg of sodium acetate (5 min at reflux temperature) gave after work-up in the usual manner rectangular prisms (18 mg, from ethanol) with m.p. 180–181° and $[\alpha]_D^{23}$ +108.5° (*c*, 1 in chloroform), in excellent agreement with the literature (9, 10). A mixture melting point with an authentic sample was undepressed and the infrared spectra were identical.

Methyl 4,6-O-Benzylidene-3-deoxy-3-nitro-α-D-glucopyranoside (XVII)

An amorphous mixture of methyl 3-deoxy-3-nitro-α-D-hexopyranosides (0.02 mole) was obtained according to the directions cited in the preceding section. Instead of chromatography the material was subjected to benzylidenation. The material was stirred overnight at room temperature with 4 g of anhydrous zinc chloride in 25 ml of benzaldehyde. To the reaction mixture was then added 150 ml of water and 50 ml of petroleum ether (b.p. 80–100°). When no solid had separated after 30 min of vigorous magnetic stirring, the emulsion was allowed to settle into three layers. The oily middle layer was presumed to contain the desired product. This layer was isolated, washed several times with fresh petroleum ether, then taken up in 10 ml of ethanol, and water was added to incipient turbidity. On standing at 23° for 2 d and at 4° for another day there crystallized 100 mg of XVII melting at 163–164°. Several additional crops totalling 196 mg and having slightly lower melting points were deposited by the mother liquor on prolonged standing. Recrystallization from aqueous ethanol afforded platelets of m.p. 167° and $[\alpha]_D^{23}$ +87.2° (*c*, 1 in ethanol).

Anal. Calcd. for $C_{14}H_{17}NO_7$ (311.3): C, 54.01; H, 5.51. Found: C, 54.03; H, 5.45.

The infrared spectrum shows hydroxyl (3 330 cm^{-1}) and nitro (1 550 cm^{-1}) bands and in the region 900–700 cm^{-1} the following characteristic peaks: 893(w), 865(w), 850(w), 790(m), 757(s), 697(s).

A sample of 50 mg of XVII was hydrogenated at room temperature with a platinum catalyst in 10 ml of *N*/10 hydrochloric acid. The benzylidene group was thereby removed and the nitro group reduced. The resulting amine hydrochloride failed to crystallize but gave on acetylation (as described in the preceding section) crystalline methyl 3-acetamido-3-deoxy-2,4,6-tri-*O*-acetyl-α-D-glucopyranoside, m.p. 179°, which was identified by an undepressed mixture melting point and by its infrared spectrum.

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