Reactions of nitro sugars. V. Some reactions with methyl 3-deoxy-3-nitro-α-D-hexopyranosides[1]

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The acetylations and catalytic hydrogenations of derivatives of methyl 3-deoxy-3-nitro-α-D-hexopyranosides were compared with the analogous reactions previously performed in the β-anomeric series. The acetylation of methyl 4,6-*O*-benzylidene-3-deoxy-3-nitro-α-D-glucopyranoside (II) gave its 2-*O*-acetyl derivative III, which, upon base-catalyzed elimination of acetic acid, yielded the nitroolefin, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-α-D-*erythro*-hexopyranos-2-enide (IV), whereas acetylation of the corresponding α-D-talopyranoside XI proceeded with dehydration, giving directly the α-D-*threo* nitroolefin XIII. These courses of reaction had their counterparts in the β-series and are believed to depend on the configurations at C-4. On the other hand, palladium-catalyzed hydrogenations of the nitroolefins IV and XIII gave results that were similar to each other but different from those obtained in the β-series. Besides the expected saturated nitro glycosides with α-D-*arabino* (V) and α-D-*lyxo* (XV) configurations, two oximes (VI and XIV) were produced in yields of 49 and 30%, respectively. This may be attributed to a measure of steric interference by the glycosidic methoxyl group during the hydrogenation of the olefinic double bonds in IV and XIII. Amino glycosides were obtained from V and XV by debenzylidenation and platinum-catalyzed hydrogenation.

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Previous work in this laboratory on the chemistry of 3-deoxy-3-nitrohexoses has dealt with the preparation of derivatives such as acetals, esters, ethers, and olefinic and deoxy compounds, and in particular has been directed toward the synthesis of aminodideoxy and diaminodideoxy sugars (1–4). The work had concentrated on the use of methyl 3-deoxy-3-nitro-β-D-glycosides for the simple reason that these were available in pure, crystalline form, whereas their α-D-anomers have been known as epimeric mixtures only. Analogous investigations in the α-series, however, seemed desirable not only for the obvious reason of systematic comparison but also because such studies should serve as a groundwork for certain synthetic projects to be carried out later in the enantiomeric α-L-series. Some results are reported in the present article.

From an amorphous mixture of methyl 3-deoxy-3-nitro-α-D-glucopyranoside (I) and -mannopyranoside (5, 6), crystalline I and its 4,6-*O*-benzylidene derivative II have recently been prepared (2). Since the operations were unsatisfactory from a preparative viewpoint, we have resorted now to acetylating the crude benzylidenated mixture in pyridine at 0°, thus obtaining without much difficulty methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-3-nitro-α-D-glucopyranoside (III). The yield of crystalline III was 12% based upon the original starting material, methyl α-D-glucopyranoside, from which the nitro sugar was made by successive periodate oxidation, nitromethane cyclization, benzylidenation, and acetylation. Since only common reactants and easy operations were involved in all the steps, this yield was deemed acceptable.[2]

The acetate III was converted by elimination of acetic acid into the nitroolefin, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-α-D-*erythro*-hexopyranos-2-enide (IV). The progress of this reaction was followed by infrared spectroscopy, which indicated a gradual decrease in the intensities of the acetyl and nitroalkane frequencies at 1 745 and 1 560 cm^{-1}, respectively, and the concomitant appearance of a nitroolefin peak at 1 535 cm^{-1}. Complete conversion was attained only after 9 days of refluxing in dry benzene over sodium bicarbonate,

[1]For part IV in this series, see ref. 13.

[2]It should be remembered that a large part of the nitro sugar mixture possesses the D-*manno* configuration (6); the D-*manno* isomer of III may therefore be presumed to be present in the crude product, but thus far it has not crystallized.

whereas 1 to 2 days was usually enough for the β-anomer (1). It appears plausible that the axial methoxyl group in III may interfere in the approach of the bicarbonate crystal surface to the lower side of the sugar molecule, from where the hydrogen at C-3 must be abstracted. Another pronounced effect that must be ascribed to the (now quasi-axial) disposition of the glycosidic methoxyl was observed in the subsequent palladium-catalyzed hydrogenation of nitroolefin IV. Under the conditions employed it was expected that the olefinic double bond would be hydrogenated smoothly and that the nitro group would be retained. Only 43.5% of the expected saturated nitro compound, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-α-D-*arabino*-hexopyranoside (V), was obtained, whereas in the β-series the yield of the isolated analogue had been over 87% (1). In addition to V, however, there was isolated, in a 49% yield, a new product for which no counterpart had been found in the β-series. It was methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-oximino-α-D-*erythro*-hexopyranoside (VI); proof of its structure will be given in a subsequent paragraph. The formation of this product appears to be a consequence of hydrogenation of the nitro group to the hydroxylamino stage; this process presumably becomes competitive when hydrogenation of the carbon–carbon double bond is retarded because of the steric requirement of the nearby axial methoxyl.

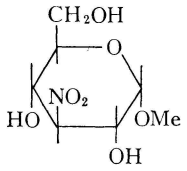
The reduction of saturated aliphatic nitro compounds to amines is known to pass through the hydroxylamino stage (7). With nitroolefins, the hydroxylamino intermediate, which is an enamine, may tautomerize to an oxime that is much more resistant towards further hydrogenation and thus escapes conversion into the amine. The generation of oximes from nitroolefins under certain reaction conditions is, of course, quite common (8). The present case is of particular interest because of the directive influence of the methoxyl group and, furthermore, because of the peculiar stability of the oxime VI against further reduction. Not only was VI stable under the conditions of its formation, but also the isolated compound failed to be reduced by hydrogen with either a palladium or a platinum catalyst, or by zinc and acetic acid. Lithium aluminium hydride also seemed to be of little effect. Although this behavior contrasts with that of the oxime of methyl 3-*keto*-β-D-glucopyranoside, which Lindberg and Theander were able to reduce to the amine stage (9), it reminds one of the difficulties recently encountered by Lemieux and his co-workers (10) in the attempted reductions of some oximino α-glycosides.

Hydrolytic removal of the benzylidene blocking group from the nitro glycoside V produced methyl 2,3-dideoxy-3-nitro-α-D-*arabino*-hexopyranoside (VII), and catalytic hydrogenation over platinum converted VII into methyl 3-amino-2,3-dideoxy-α-D-*arabino*-hexopyranoside (VIII). Acetylation of VIII gave the triacetate IX.

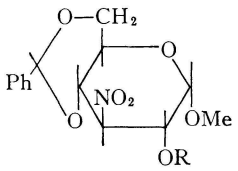
Since the formation of compound V involved the generation of an asymmetric center at C-3, it was necessary to provide proof of configuration. The nuclear magnetic resonance (n.m.r.) spectrum[3] of the triacetate IX in deuteriochloroform showed three signals, each corresponding to three protons, at 7.94, 7.96, and 8.11 τ. The first two were due to the equatorial acetoxy and acetoxymethyl groups at C-4 and C-5, in accord with the known stereochemistry at those carbons. The resonance at 8.11 τ clearly indicated an equatorial acetamido group, thereby confirming the D-*arabino* configuration (1, 3, 11). The signal for the glycosidic methoxyl group (corresponding to three protons) occurred at 6.67 τ, in line with its axial arrangement (1, 3, 11, 12). Additional evidence for the configuration of compound V and its derivatives VII–IX was obtained from acid hydrolysis of VIII, giving a reducing sugar that was chromatographically identical with the 3-amino-2,3-dideoxy-D-*arabino*-hexose obtained analogously in the β-series (1).

It had been demonstrated earlier (6) that the sodium nitronates of the methyl 3-deoxy-3-nitro-α-D-gluco- and -manno-

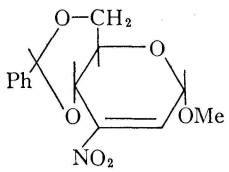
[3]Taken on a Varian HA-60 instrument.



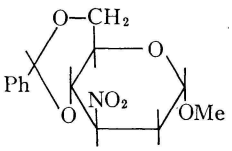
I



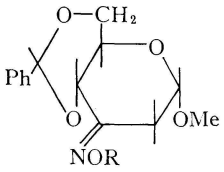
II R = H
III R = Ac



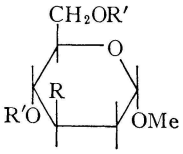
IV



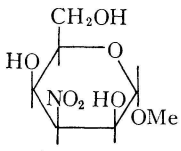
V



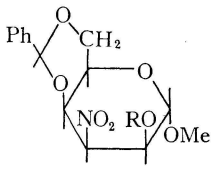
VI R = H
VI*a* R = Ac



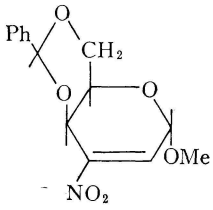
VII R = NO_2, R′ = H
VIII R = NH_2, R′ = H
IX R = NHAc, R′ = Ac



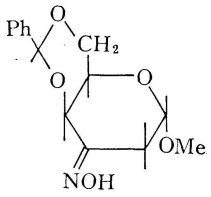
X



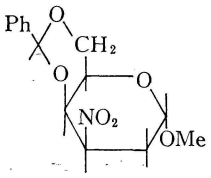
XI R = H
XII R = Ac



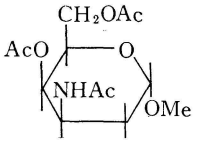
XIII



XIV



XV



XVI

pyranosides epimerize in aqueous solution to a mixture which, upon deionization, contains mainly the taloside X and a smaller amount of the *galacto* isomer.[4] This had been established by the isolation of crystalline hydrogenation products, but attempts to crystallize the glycosides at the nitro stage had not been successful. It has now been possible to isolate, upon benzylidenation of the epimerized mixture, the 4,6-*O*-benzylidene derivative (XI) of X in a crystalline form. Although its yield was poor (5%), sufficient material was obtained to compare some of its reactions with those of the isomer II.

First, it was established that the benzylidene derivative isolated was in fact the *talo* isomer XI (debenzylidenation followed by catalytic hydrogenation gave the known (6) methyl 3-amino-3-deoxy-α-D-talopyranoside hydrochloride).

The crude benzylidene taloside XI had been recrystallized from 80% ethanol. From the mother liquor was isolated a crystalline by-product (m.p. 232°), whose infrared spectrum lacked hydroxyl absorption although it revealed the presence of benzylidene and nitroalkane groupings. Elemental analysis and mass spectrum established the formula $C_{16}H_{21}NO_7$, which corresponded to an ethyl ether of XI. In the light of previous experience (2, 4), it is likely that this by-product arose during recrystallization of crude XI through ethanol addition across the double bond of some nitroolefin XIII that may have been present as an impurity, engendered by dehydration of XI. The by-product would therefore be a methyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-ethyl-3-nitro-α-D-hexopyranoside. Its stereochemistry, however, has not been investigated.

Acetylation of the benzylidene taloside

[4]Prolonged exposure to alkaline conditions leads to the formation of unsaturated products with an allylnitronate structure. This has been investigated in detail for β-glycosides and is mentioned briefly for I, too (13).

XI to produce its 2-*O*-acetyl derivative XII was attempted with acetic anhydride and pyridine, but failed. This result has its parallel in the failure (2) of methyl 4,6-*O*-benzylidene-3-deoxy-3-nitro-β-D-galactopyranoside to be acetylated under the same conditions, and it provides an interesting contrast to the ease with which the α-D-glucoside II as well as the corresponding β-D-glucoside and β-D-mannoside underwent acetylation. Apparently an axial substituent at C-4 tends to hinder reaction at the 2-hydroxyl group.[5]

When the benzylidene taloside XI was heated briefly with acetic anhydride and sodium acetate, dehydration took place and crystalline methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-α-D-*threo*-hexopyranos-2-enide (XIII) was obtained in 54–69% yield. Again, this result is in agreement with the pattern encountered in the β-series, where the same treatment unexpectedly had caused dehydration of the *galacto* isomer (axial 4-substituent) to the olefin (i.e. the anomer of XIII) (2).

Hydrogenation of olefin XIII in the presence of palladium catalyst gave 60% of the saturated nitro glycoside, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-α-D-*lyxo*-hexopyranoside (XV), and 30% of the oxime, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-oximino-α-D-*threo*-hexopyranoside (XIV). The nitro glycoside XV was assigned its configuration on the basis of the n.m.r. spectrum of the amine triacetate XVI, which was obtained upon debenzylidenation, catalytic hydrogenation, and acetylation of XV. The spectrum of a deuteriochloroform solution of XVI showed substituent resonances, of intensities corresponding to three protons each, at 7.86, 7.96, and 8.09 τ. The first two signals were due to the axial acetoxy group at C-4 and the equatorial acetoxymethyl group at C-5, in accord with the known stereochemistry at these centers; the third signal indicated an equatorial acetamido group at C-3, thus confirming the D-*lyxo* configuration. The methoxy resonance (three-proton intensity) was at 6.66 τ (11, 12).

In summary, the studies reported in this paper have shown that the syntheses of 3-amino-2,3-dideoxy-D-*erythro*- and -D-*lyxo*-hexoses can be accomplished via the series of α-glycosides beginning, ultimately, with methyl α-D-glucopyranoside. Although the previously reported routes (1, 3) via the β-glycosides are superior because of better crystallization and higher yields at certain stages, the present work is of interest for potential applications in the enantiomeric series of L-sugars which are related structurally and configurationally to the antibiotic components daunosamine and rhodosamine. Methyl β-L-hexopyranosides are not practical starting materials for the nitro sugars required in the L-series, but entry into that series can be gained from the reasonably accessible methyl L-pentofuranosides. This has been verified with methyl β-L-arabinofuranoside (3). It appears, however, that methyl α-L-arabinofuranoside can be obtained more easily than its β-anomer, and hence the α-L-glycoside approach may become attractive.

Characterization of the Oximes VI and XIV

The structure of the oxime VI was based on elemental analysis and the following observations. The infrared spectrum showed broad absorption centered at 3 350 cm^{-1} (hydroxyl) and a weak band at 1 660 cm^{-1} (C=N), but there were no peaks attributable to aliphatic nitro or amino groups. Acetylation gave a crystalline monoacetate VI*a*, which showed carbonyl absorption at 1 770 cm^{-1} and no hydroxyl absorption. Compound VI gave a positive test with α-naphthylamine, indicative of an oxime (14).[6] Brief hydrolysis of VI with *N* hydrochloric acid released a substance that reduced cold Fehling solution (hydroxylamine). The n.m.r. spectrum[3] of VI (Fig. 1) shows at highest field (7.8 τ) a quartet of integrated intensity 1. It is assigned to one

[5]Acetylation, however is not altogether impossible. We have in the meantime successfully acetylated the β-*galacto* isomer of XI by using boron trifluoride etherate as catalyst (unpublished results). Preliminary experiments indicated that XI, too, can be acetylated by this technique.

[6]Hydroxamic acids, which also give this test, cannot arise from secondary nitro compounds by hydrogenation.

of the hydrogens at C-2 and shows splitting caused by geminal ($J_{2,2'}$ = 15 c.p.s.) and vicinal ($J_{2,1}$ = 5 c.p.s.) coupling. The other hydrogen at C-2 produced a quartet at 6.5 τ with $J_{2,2'}$ = 15 c.p.s. and $J_{2',1}$ = 1 c.p.s. The signal of the anomeric proton at C-1 is a quartet at 5.1 τ ($J_{1,2}$ = 5 c.p.s., $J_{1,2'}$ = 1 c.p.s.). The signal of the benzylidene hydrogen is found as a singlet at 4.40 τ, and a singlet of intensity 3 at 6.69 τ represents the axial methoxyl group. No definite assignments could be made for the remaining peaks. In a separate spectrum a signal at 0.82 τ was observed. This can be attributed to the hydrogen of the oximino group, for which a range of 0.3–0.8 τ has been reported in similar cases (10). The isomeric oxime XIV also was characterized by analysis, the α-naphthylamine test, and its infrared spectrum. Unfortunately, no n.m.r. spectrum could be obtained because of insufficient solubility in suitable solvents.

EXPERIMENTAL

Melting points were determined in capillaries in an electrically heated aluminium block apparatus equipped with a calibrated thermometer. Petroleum ether refers to the fraction boiling at 30–60°.

Methyl 2-O-Acetyl-4,6-O-benzylidene-3-deoxy-3-nitro-α-D-glucopyranoside (III)

From 15.56 g (0.08 mole) of methyl α-D-glucopyranoside, a mixture of methyl 3-deoxy-3-nitro-α-D-hexopyranosides containing mainly the *manno* and *gluco* isomers was prepared according to the published (6) directions. Specifically, the procedure involving nitromethane condensation in methanolic solution was employed. The dry, amorphous product ($[\alpha]_D^{23}$ ca. +100° (in water)) and benzaldehyde (80 ml) were stirred together with anhydrous zinc chloride (20 g) for 18 h at room temperature. The brownish mixture was then poured into 200 ml of water; after 5 min of vigorous mechanical stirring, petroleum ether (200 ml) was added and the stirring was continued for another 10 min. The heterogeneous mixture was allowed to settle in three layers. The oily middle layer, which contained the desired product II, was washed twice with 50 ml of water and twice with 100 ml of petroleum ether, and then dried for 2 h at 40° in a high vacuum. The material was acetylated by treatment with acetic anhydride (40 ml) and pyridine (20 ml) at 0° overnight. Ethanol (40 ml) was added to destroy the excess anhydride, and after 30 min the reaction mixture was poured into 500 ml of ice water. Stirring for 10 min failed to produce a solid product; the emulsion that formed was allowed to settle, and the bottom layer was separated and dissolved in 50 ml of hot

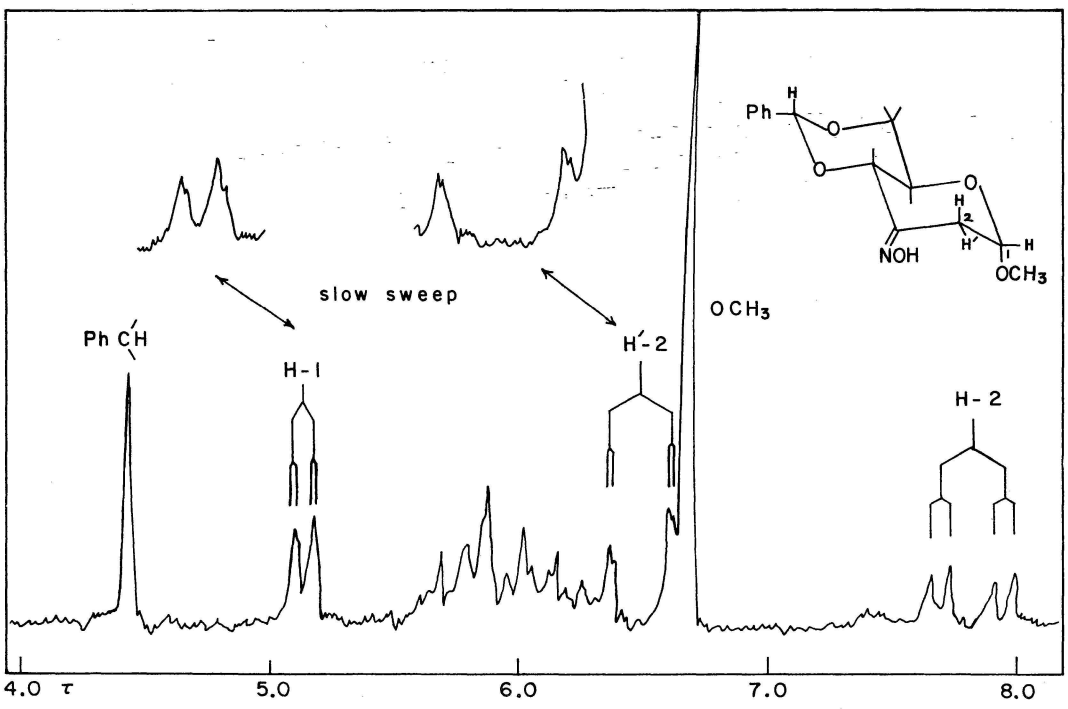


FIG. 1. The n.m.r. spectrum (60 Mc.p.s.) of oxime VI in deuteriochloroform.

ethanol. With continued heating, water was slowly added to incipient cloudiness. After the solution was slowly cooled and left at room temperature for 24 h, it yielded 3.37 g (11.9%) of acetate III, m.p. 198°, $[\alpha]_D^{23}$ +82.9° (*c*, 1.1 in chloroform). A brownish discoloration, if any, was removed with a little cold ether. The infrared spectrum was identical with that of III obtained from pure II as described subsequently.

Crystalline methyl 4,6-*O*-benzylidene-3-deoxy-3-nitro-α-D-glucopyranoside (110 mg) (2) was dissolved in tetrahydrofuran (10 ml) and pyridine (1 ml), and acetic anhydride (0.5 ml) was added. The solution, which remained colorless, was kept at room temperature for 15 h and was then poured into 30 ml of ice water. Stirring for 10 min gave a white precipitate, which was filtered off, washed with cold water, and dried in a desiccator to yield 120 mg of III melting at 193–194°. Recrystallization from aqueous ethanol gave 70 mg of stout needles with m.p. 198° and $[\alpha]_D^{23}$ +83° (*c*, 0.9 in chloroform).

Anal. Calcd. for $C_{16}H_{19}NO_8$ (353.3): C, 54.40; H, 5.42; N, 3.97. Found: C, 54.61; H, 5.60; N, 3.97.

Methyl 4,6-O-Benzylidene-2,3-dideoxy-3-nitro-α-D-erythro-hexopyranos-2-enide (IV)

Acetate III (1 g) and dry sodium bicarbonate (2 g) were refluxed, with magnetic stirring and exclusion of moisture, in 50 ml of reagent-grade benzene that had been dried over and distilled from sodium wire. Small samples of the solution were withdrawn from time to time and their residues of evaporation were inspected in the infrared. Completion of the reaction, which took at least 9 days, was indicated by the absence of the acetyl and nitroalkane frequencies at 1 745 and 1 560 cm^{-1}, respectively, and by the constancy in the strength of the nitroolefin frequency at 1 535 cm^{-1}. The mixture was then allowed to cool, filtered, and evaporated to give a white solid residue of IV. The crude product (800 mg, 96.5%) of m.p. 176–179° was recrystallized from ethyl acetate – petroleum ether to yield prisms with m.p. 183° and $[\alpha]_D^{23}$ −93° (*c*, 0.9 in ethyl acetate).

Anal. Calcd. for $C_{14}H_{15}NO_6$ (293.3): C, 57.33; H, 5.16; N, 4.78. Found: C, 57.35; H, 5.25; N, 5.02.

Methyl 4,6-O-Benzylidene-2,3-dideoxy-3-oximino-α-D-erythro-hexopyranoside (VI)

Nitroolefin IV (2 g) in ethyl acetate (100 ml) was shaken under hydrogen for 10 min in the presence of 300 mg of 10% palladium on charcoal. The gas uptake was rapid, but the rate sharply decreased after 242 ml (standard temperature and pressure) had been consumed. The consumption of hydrogen corresponded to 1.56 moles. The filtrate from the catalyst was evaporated, leaving a crystalline residue, which was immediately recrystallized from ethyl acetate – petroleum ether to give 0.93 g (48.7%) of VI melting at 202° with decomposition. Recrystallization from the same solvents gave long needles with m.p. 203° (decomp.) and $[\alpha]_D^{23}$ +172° (*c*, 0.9 in chloroform).

Anal. Calcd. for $C_{14}H_{17}NO_5$ (279.3): C, 60.21; H, 6.14; N, 5.02; O, 28.64. Found: C, 60.10; H, 6.14; N, 5.22; O, 28.82.

A small sample of VI was boiled for 5 min in *N* hydrochloric acid. The cooled solution was neutralized with *N* sodium hydroxide solution and then found to reduce Fehling solution without warming.

Another sample (10 mg) was subjected to a spot test for oximes with α-naphthylamine (14). A red to purple color developed.

Methyl 3-Acetoximino-4,6-O-benzylidene-2,3-dideoxy-α-D-erythro-hexopyranoside (VIa)

Oxime VI (100 mg) was acetylated with 0.75 ml of acetic anhydride and 1.5 ml of pyridine at room temperature during 18 h. Work-up with ice water gave 98 mg of crystalline acetate VI*a* with m.p. 202°, raised to 205° by recrystallization from ethanol. A mixture melting point with VI was depressed to 170–179°.

Anal. Calcd. for $C_{16}H_{19}NO_6$ (321.3): C, 59.80; H, 5.92; N, 4.36. Found: C, 59.63; H, 6.12; N, 4.36.

Methyl 4,6-O-Benzylidene-2,3-dideoxy-3-nitro-α-D-arabino-hexopyranoside (V)

The mother liquors from the recrystallizations of crude oxime VI, above, were combined, concentrated to a small volume, and placed in a refrigerator. After 18 h, 880 mg (43.5%) of nitro glycoside V was deposited, m.p. 101°. Recrystallization from 50% aqueous ethanol gave crystals of m.p. 112° and $[\alpha]_D^{23}$ +67° (*c*, 0.7 in chloroform).

Anal. Calcd. for $C_{14}H_{17}NO_6$ (295.3): C, 56.94; H, 5.83; N, 4.74. Found: C, 57.13; H, 5.85; N, 4.82.

Methyl 2,3-Dideoxy-3-nitro-α-D-arabino-hexopyranoside (VII)

A solution of benzylidene derivative V (500 mg) in 70% acetic acid (10 ml) was heated on a steam bath for 30 min and then evaporated to a syrup. The residue was twice evaporated with water, dissolved in water, decolorized with activated charcoal, and evaporated to a syrup again. Crystallization of VII began when the syrup was left at room temperature overnight, and was completed by trituration with a mixture of ether and petroleum ether (1:1). The yield was 230 mg, m.p. 88°, unchanged on recrystallization from the same solvents; $[\alpha]_D^{23}$ +132° (*c*, 1 in water).

Anal. Calcd. for $C_7H_{13}NO_6$ (207.2): C, 40.58; H, 6.33; N, 6.77. Found: C, 40.50; H, 6.27; N, 6.67.

Methyl 3-Amino-2,3-dideoxy-α-D-arabino-hexopyranoside (VIII)

An aqueous solution of nitro glycoside VII (180 mg), to which 9 ml of 0.1 *N* hydrochloric acid and 40 mg of prehydrogenated platinum dioxide catalyst were added, was hydrogenated at ordinary temperature and pressure. The uptake of 3 moles of hydrogen (70 ml) was complete within 1 h. Evaporation gave the hydrochloride of VIII as a syrup that failed to crystallize. Paper chromatography with the Fischer–Dörfel system (15) gave a single spot ($R_{glucosamine-HCl}$ 1.56) of brown-violet color (ninhydrin spray). The product was dissolved in water, deionized with Dowex 1-X2 (CO_3^{2-}), and evaporated, with several additions of ethanol, to a syrup. From a small amount of ethanol – ethyl acetate (1:1), crystals of

VIII were deposited at 0°, but they were difficult to isolate and wash. The yield was 22 mg, m.p. 144–146°, $[\alpha]_D^{23}$ +105° (*c*, 0.5 in water).

Anal. Calcd. for $C_7H_{15}NO_4$ (177.2): C, 47.44; H, 8.54; N, 7.91. Found: C, 47.25; H, 8.47; N, 8.37.

A 5 mg sample of VIII was hydrolyzed in 1 ml of *N* hydrochloric acid in a sealed tube for 1 h at 100°. Subsequent paper chromatography (15) showed a single spot of $R_{glucosamine-HCl}$ 1.28. An authentic sample of 3-amino-2,3-dideoxy-D-*arabino*-hexose (1) traveled at the same speed.

Methyl 3-Acetamido-4,6-di-O-acetyl-2,3-dideoxy-α-D-arabino-hexopyranoside (IX)

The mother liquor from the crystallization of the amine VIII, above, was evaporated and the partly crystalline residue was acetylated (24 h at 25°) with acetic anhydride (0.5 ml) in pyridine (1 ml). Work-up by the usual chloroform extraction procedure gave 93 mg of crystalline IX, m.p. 171° after crystallization from chloroform–ether, $[\alpha]_D^{23}$ +153° (*c*, 0.9 in ethanol).

Anal. Calcd. for $C_{13}H_{21}NO_7$ (303.3): C, 51.47; H, 6.98; N, 4.62. Found: C, 51.75; H, 7.02; N, 4.80.

Methyl 4,6-O-Benzylidene-3-deoxy-3-nitro-α-D-talopyranoside (XI)

From 7.76 g (0.04 mole) of methyl α-D-glucopyranoside, a mixture of methyl 3-deoxy-3-nitro-α-D-hexopyranosides containing mainly the *talo* and *galacto* isomers was prepared by nitromethane cyclization, epimerization of the nitronates, and deionization as previously described (6). The dry product was benzylidenated by agitation for 18 h with 50 g of benzaldehyde and 30 g of zinc chloride. The dark-brown mixture was poured into 200 ml of ice water and 200 ml of petroleum ether; after 10 min of vigorous stirring and separation of the phases, the oily product was dissolved in methanol (40 ml) and dropped into 200 ml of water. A dark, crystalline material separated when the mixture was stirred for 15 min. It was recrystallized from 80% ethanol to yield 700 mg (5.6%) of XI, m.p. 175°. Another recrystallization did not change the melting point; $[\alpha]_D^{23}$ +68° (*c*, 1 in chloroform).

Anal. Calcd. for $C_{14}H_{17}NO_7$ (311.3): C, 54.01; H, 5.51; N, 4.50. Found: C, 54.24; H, 5.62; N, 4.67.

Debenzylidenation and Hydrogenation

A sample of XI (160 mg) was heated in 70% acetic acid (15 ml) for 20 min on a steam bath. Removal of the solvent by evaporation, eventually with several additions of ethanol, gave a syrup that failed to crystallize. Subsequent hydrogenation in water (10 ml) and 0.1 *N* hydrochloric acid (6 ml) in the presence of platinum catalyst (50 mg, prehydrogenated) produced a syrup which gave crystals (35 mg) after crystallization from ethanol – ethyl acetate, m.p. 188° (decomp.), $[\alpha]_D^{23}$ +88° (*c*, 0.9 in water) (reported (6) for methyl 3-amino-3-deoxy-α-D-talopyranoside hydrochloride, m.p. 187–188° (decomp.), $[\alpha]_D^{20}$ +90° (*c*, 2 in water)). Its identity was confirmed by comparison of the infrared spectra of an authentic and the present sample.

Methyl 4,6-O-Benzylidene-3-deoxy-2-O-ethyl-3-nitro-α-D-hexopyranoside of m.p. 232°

The aqueous ethanolic mother liquor from the recrystallization of crude benzylidene taloside XI, above, was concentrated, thereby depositing a crystalline solid of m.p. 223°. Its infrared spectrum showed nitroalkane absorption but no hydroxyl absorption. The material was twice recrystallized from chloroform–methanol (1:1 v/v) to give plates (250 mg) of m.p. 232° and $[\alpha]_D^{23}$ +90° (*c*, 1 in dimethylformamide).

Anal. Calcd. for $C_{16}H_{21}NO_7$ (339.3): C, 56.63; H, 6.24; N, 4.13. Found: C, 56.83; H, 6.45; N, 4.23; mol. wt. (by mass spectrometry) 339.

Methyl 4,6-O-Benzylidene-2,3-dideoxy-3-nitro-α-D-threo-hexopyranos-2-enide (XIII)

A mixture of nitro glycoside XI (100 mg), anhydrous sodium acetate (200 mg), and acetic anhydride (2 ml) in a 10 ml Erlenmeyer flask was heated on a hot plate to gentle boiling for 3 min. The slightly yellowish mixture was cooled and then stirred for 10 min with ice water (10 ml). A white precipitate was collected, washed with water, dried in a desiccator, and recrystallized from ethyl acetate – petroleum ether to yield 51 mg (54.3%) of XIII as fine needles of m.p. 185–186°.

Anal. Calcd. for $C_{14}H_{15}NO_6$ (293.3): C, 57.33; H, 5.16. Found: C, 57.52; H, 5.22.

A similarly performed experiment with 1.7 g of XI, 3.4 g of sodium acetate, and 15 ml of acetic anhydride gave 1.1 g (69%) of recrystallized XIII.

In attempts to obtain the 2-*O*-acetate XII, the nitro glycoside XI was treated with acetic anhydride and pyridine at 0–20°; the reaction mixtures turned dark, and no identifiable compound could be isolated.

Methyl 4,6-O-Benzylidene-2,3-dideoxy-3-oximino-α-D-threo-hexopyranoside (XIV)

Nitroolefin XIII (1.0 g, 3.4 mmoles) in ethyl acetate (50 ml) was hydrogenated in the presence of 200 mg of 10% palladium on charcoal. Rapid hydrogen uptake (90 ml, ca. 1.25 *M* equivalents) ceased after 10 min. Evaporation gave a syrup that was dissolved in a small volume of aqueous ethanol, from which crude oxime XIV crystallized slowly in two batches (206 + 80 mg, m.p. 190–200°). Recrystallized twice from absolute ethanol, the fine needles melted at 219–220° (decomp.). The compound gave a red to purple color in the α-naphthylamine test for oximes (14).

Anal. Calcd. for $C_{14}H_{17}NO_5$ (279.3): C, 60.21; H, 6.14; N, 5.02. Found: C, 59.92; H, 6.24; N, 5.12.

Methyl 4,6-O-Benzylidene-2,3-dideoxy-3-nitro-α-D-lyxo-hexopyranoside (XV)

The mother liquor from which the oxime XIV had been collected was evaporated and the residue was dissolved in a small amount of ethanol. Crystallization of XV occurred at 0° during 24 h. The yield was ca. 0.6 g (60%), m.p. 95–98°. Recrystallization from ethanol–water raised the melting point to 108°.

Anal. Calcd. for $C_{14}H_{17}NO_6$ (295.3): C, 56.94; H, 5.83; N, 4.74. Found: C, 57.12; H, 5.89; N, 4.96.

Methyl 3-Acetamido-4,6-di-O-acetyl-2,3-dideoxy-α-D-lyxo-hexopyranoside (XVI)

A sample of nitro glycoside XV (200 mg) was debenzylidenated by heating it for 20 min on a steam bath in 70% acetic acid (20 ml). The product was evaporated to dryness and, since it could not be induced to crystallize, was hydrogenated in water (20 ml) containing 0.1 *N* hydrochloric acid (8 ml) and prehydrogenated platinum dioxide (80 mg). When hydrogen consumption had ceased, the ninhydrin-positive solution was treated with 10 ml of Dowex 1-X2 (CO_3^{2-}) to remove chloride ion; then it was evaporated to a syrup that was dehydrated with ethanol. Treatment with acetic anhydride (1 ml) and pyridine (2 ml) during 18 h at 23° followed by a work-up by the common chloroform extraction procedure gave the acetate XVI as a syrup. It showed a single spot on a silica gel G thin-layer plate irrigated with ethyl acetate–petroleum ether (1:1 v/v). The infrared and n.m.r. spectra were in agreement with formula XVI.

Most Characteristic Infrared Frequencies (ν_{max} in cm^{-1})[7]

III: 1 748 (acetate CO), 1 560 and 1 375 (NO_2), 1 223 (acetate C—O—C), and 765 and 700 (phenyl).

IV: 1 535 and 1 370 (NO_2), 1 085 and 1 010 (C—O—C), and 760 and 700 (phenyl).

V: 1 555 and 1 375 (NO_2), 1 090 (C—O—C), and 760 and 705 (phenyl).

VI: 3 400 – 3 300 (OH), 1 660 (C=N), 1 050 and 990 (C—O—C), and 750 and 695 (phenyl).

VI*a*: 1 770 (acetate CO), 1 655 (C=N), 1 045 and 990 (C—O—C), and 750 and 695 (phenyl).

VII: 3 430 – 3 300 (OH), 1 550 and 1 375 (NO_2), and 1 040 and 980 (C—O—C).

VIII: 3 400 and 3 300 (OH and NH), 1 600 (NH_2), and 1 055 (C—O—C).

IX: 3 300 (NH), 1 735 (acetate CO), 1 650 (amide I), 1 550 (amide II), 1 230 – 1 225 (acetate C—O—C), and 1 040 – 1 030 (C—O—C).

XI: 3 520 (OH), 1 550 and 1 375 (NO_2), 1 065 and 1 000 (C—O—C), and 760 and 700 (phenyl).

XIII: 1 535 and 1 370 (NO_2), 1 135 and 1 050 (C—O—C), and 760 and 700 (phenyl).

XIV: 3 400 – 3 300 (OH), 1 670 (C=N), 1 040 and 1 000 (C—O—C), and 755 and 695 (phenyl).

XV: 1 550 and 1 375 (NO_2), 1 060 (C—O—C), and 750 and 695 (phenyl).

XVI: 3 330 (NH), 1 740 (acetate CO), 1 655 (amide I), 1 550 (amide II), 1 250 – 1 220 (acetate C—O—C), and 1 060 – 1 040 (C—O—C).

[7]Obtained from Nujol mulls with a Perkin–Elmer Infracord instrument.

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