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A SYNTHESIS OF 4-ACETAMIDO-4-DEOXY-L-XYLOPYRANOSE*

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A program of synthesis in this laboratory is concerned with 4-amino-4-deoxy sugars[1-3] The 4-amino-4-deoxyhexoses having the D-*manno* and D-*talo* configurations have been prepared[3,4] In an earlier report[5], the synthesis of 4-acetamido-4,5-dideoxy-L-xylose was described, and it was shown that the sugar exists in aqueous solution mainly as the anomeric furanose forms, with nitrogen as the ring hetero-atom Concordant observations have been reported[6] for the D enantiomorph In the case of 4,5-diacetamido-4,5-dideoxy-L-xylose, which has been reported as a syrup[6] and also in crystalline form[7], the more favorable, pyranose ring-form is possible, and this appears to be the ring form adopted in aqueous solution, nitrogen is again the hetero-atom in the ring An acetamido sugar has been prepared by Dick and Jones[8] by treatment of methyl 2,3,4-tri-*O*-(methylsulfonyl)-α-D-xylopyranoside with sodium azide, followed by a series of transformations on the product, and it was deduced on mechanistic grounds and from data of periodate oxidation that the product was 4-acetamido-4-deoxy-L-xylose Infrared spectral data indicated that the favored ring form of the acetamido sugar is pyranoid, with oxygen as the hetero atom in the ring A degradative route to derivatives of this amino sugar, by way of uronic acid intermediates, has been noted[9].

The present report describes the synthesis of 4-acetamido-4-deoxy-L-xylose by a stereochemically definitive route involving C-5 to C-6 cleavage of a 2-amino-2-deoxy-D-glucitol derivative It is shown that the sugar exists in aqueous solution as a mixture of the anomeric pyranose forms

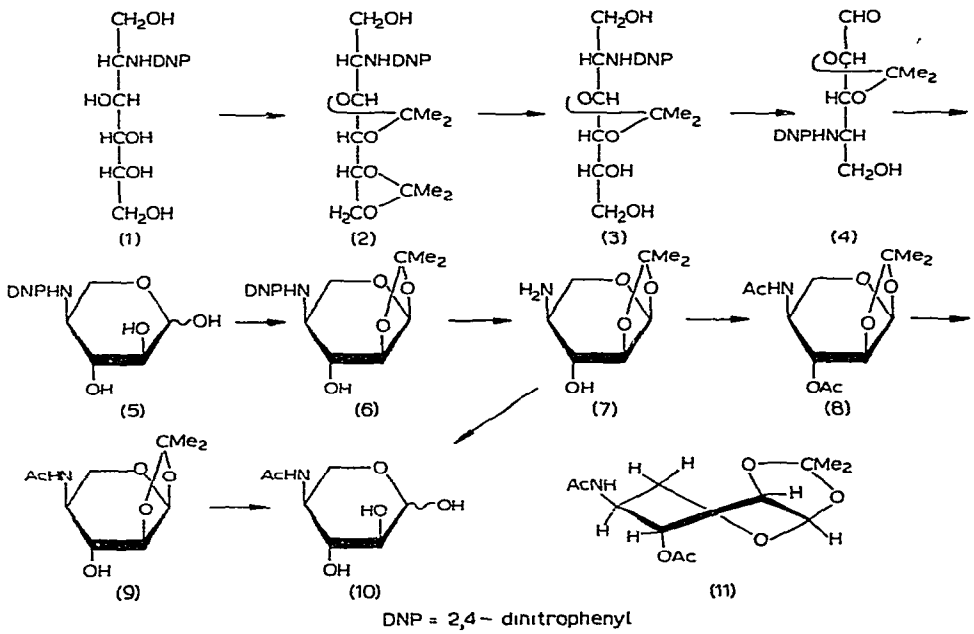
The starting point in the synthesis was 2-deoxy-2-(2,4-dinitroanilino)-D-glucitol (**1**), prepared[10] from 2-amino-2-deoxy-D-glucitol hydrochloride The latter could be obtained by reduction[11] of 2-amino-2-deoxy-D-glucose hydrochloride with hydrogen over Raney nickel Yields were only moderate when this reduction was performed on a 100-g scale *N*-Acetylation[12] of the amino sugar, followed by reduction[11] with hydrogen over Raney nickel, gave 2-acetamido-2-deoxy-D-glucitol, which was hydrolyzed to give 2-amino-2-deoxy-D-glucitol hydrochloride, all products were obtained in crystalline form and in a high yield

Acetonation of **1** gave the crystalline 3,4 5,6-diisopropylidene acetal (**2**), which was further characterized as its 1-*O*-(*p*-tolylsulfonyl) derivative. The positions

*For a preliminary communication, see ref 1

of the *O*-isopropylidene groups in **2** were assigned by analogy with the known 2-acetamido analog[13] of **2**, and also with 2-acetamido-2-deoxy-3,4 5,6-di-*O*-isopropylidene-D-glucose diethyl dithioacetal[5 14 15] Subsequent conversions from **2** verified this assignment

Partial hydrolysis by acid of the disopropylidene acetal (**2**) under mild conditions removed one *O*-isopropylidene group, and the product was shown to be 2-deoxy-2-(2,4-dinitroanilino)-3,4-*O*-isopropylidene-D-glucitol (**3**) by the fact that on periodate oxidation it consumed one mole of oxidant with the formation of a pentose derivative. Substance **3** was encountered as the orange, anhydrous form, m p 128–129°, and also as a stable, yellow, solvated form, m p 95–96° The latter was converted into the former by vigorous drying or by heating to 110°, but it could be recrystallized unchanged



from chloroform Acetylation of either form gave the 1,5,6-triacetate of **3** Removal of the *N*-substituent from **3** by treatment with Dowex-1 (OH^-) ion-exchange resin, with subsequent acetylation, gave crystalline 2-acetamido-1,5,6-tri-*O*-acetyl-2-deoxy-3,4-*O*-isopropylidene-D-glucitol.

Preparative periodate oxidation of **3** (either form) gave 4-deoxy-4-(2,4-dinitroanilino)-2,3-*O*-isopropylidene-*aldehydo*-L-xylose (**4**) as a glass, which in the infrared spectrum showed absorption for the aldehyde group Cyclization of this derivative is presumably prevented by the fact that a *trans*-fused 2,3-*O*-isopropylidene group would result Hydrolysis of the *O*-isopropylidene group with aqueous acetic acid gave crystalline 4-deoxy-4-(2,4-dinitroanilino)-L-xylopyranose (**5**) The ring size of this product was indicated by the absence of carbonyl absorption in the infrared spectrum, and by the fact that acetylation with acetic anhydride–pyridine gave a syrupy triacetate

which showed absorptions for the NH group in the infrared and n m r. spectra A furanose form would have given a tetraacetate having no NH group, and an acyclic form of the free sugar would have exhibited carbonyl absorption.

Acetonation of **5** gave a crystalline mono-*O*-isopropylidene derivative in high yield, which was shown to be 4-deoxy-4-(2,4-dinitroanilino)-1,2-*O*-isopropylidene-α-L-xylopyranose (**6**), acetylation gave the crystalline 3-acetate of **6** The structure assigned to **6** was based on the following facts; the substance was nonreducing; it was different from **4**; and removal of the *N*-substituent from **6** gave a nonreducing 4-amino-4-deoxypentose derivative (**7**) which consumed one mole of periodate Further concordant data were provided by the n m r spectra of some of the transformation products No further acetonation of **6** was observed when treatment with acetone was prolonged, even though a 1,2 3,5-di-*O*-isopropylidene derivative of the furanose form might be considered possible

Removal of the *N*-(2,4-dinitrophenyl) group from **6** gave crystalline 4-amino-4-deoxy-1,2-*O*-isopropylidene-α-L-xylopyranose (**7**) in good yield, the product consumed one mole of periodate rapidly (5 min) The oxidant consumption remained constant for several h, and slow overoxidation was subsequently observed

Acetylation of **7** gave crystalline 4-acetamido-3-*O*-acetyl-4-deoxy-1,2-*O*-isopropylidene-α-L-xylopyranose (**8**), and *O*-deacetylation of **8** gave the corresponding syrupy 3-hydroxy derivative (**9**) Removal of the *O*-isopropylidene group from **9** by mild, acid hydrolysis gave 4-acetamido-4-deoxy-L-xylose (**10**) as a chromatographically homogeneous, crystalline product, m p 155–157°, $[\alpha]_D$ −53→−49° (water) The acetamido sugar **10** could also be prepared directly, in one step, from 4-amino-4-deoxy-1,2-*O*-isopropylidene-α-L-xylopyranose (**7**), by treatment of **7** in aqueous solution with acetic anhydride, selective *N*-acetylation took place and the acetic acid formed by hydrolysis of the excess acetic anhydride caused cleavage of the *O*-isopropylidene group

The yields for all steps in the synthesis were at least 50%, and most were considerably higher The overall yield in the conversion of 2-amino-2-deoxy-D-glucose hydrochloride into 4-acetamido-4-deoxy-L-xylose (**10**) was about 10% when purification at some of the intermediate stages was omitted The melting point observed for the final product (**10**) is in good agreement with the value (157–158°) reported by Dick and Jones[8], but the specific rotation (−22→−16° in water) reported[8] for **10** by these authors differs from that found in the present work*

The infrared spectrum of the crystalline acetamido sugar **10** showed absorptions typical of the amide carbonyl and amide NH groups A solution of the sugar in deuterium oxide, at room temperature and at mutarotational equilibrium, showed a narrow doublet in the n m r spectrum, at τ 4 78, $J_{1,2}$ 3 c p s , assigned to the equatorial H-1

*In a personal communication (June 20, 1965) Professor J K N Jones has stated that the i r spectra of our substance **10**, and the product of Dick and Jones[8], are identical. In a repeat preparation, Dick and Jones have observed an equilibrium specific rotation of −43 5° (*c* 0 93, water) for their product A sample provided by Professor Jones had an X-ray powder diffraction pattern identical to that of substance **10**

of the α-L-pyranose anomer of **10**. The signal of the axial H-1 of the β-L anomer was not observable at room temperature because of interference by the HOD signal The latter signal was shifted upfield[16,17] in the spectrum measured at 80° (Fig 1), and the (axial) H-1 signal of the β-L pyranose anomer was clearly observable at τ 5 44 as a wide doublet, $J_{1,2}$ 7 6 c p s , the total integral of both H-1 signals corresponded to one proton The magnitudes of the observed $J_{1,2}$ couplings leave no doubt that the anomeric pyranoses are involved, and the fact that the chemical shifts of the H-1 signals of the anomers correspond closely to those reported[16] for the anomeric D-xylopyranoses provides further confirmation Integration of the spectrum indicated that the α-L and β-L anomers of **10** are present in a 2 3 ratio at equilibrium

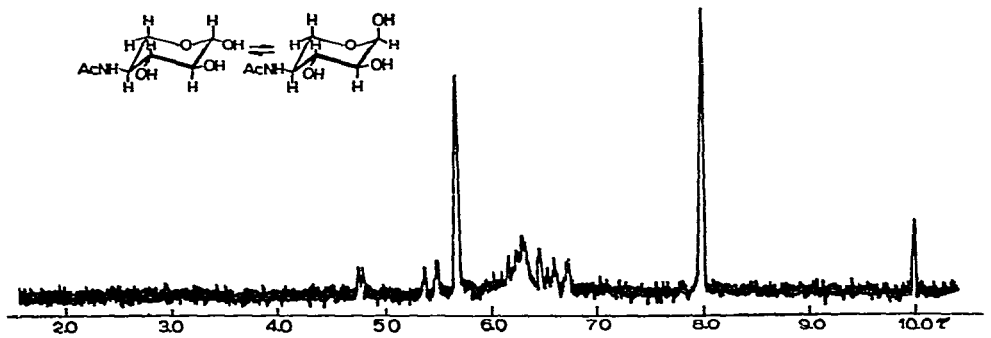


Fig 1 The 60-Mc p s n m r spectrum of 4-acetamido-4-deoxy-L-xylose (**10**) at equilibrium in deuterium oxide, at 80°

The small amount of mutarotation observed with **10**, in relation to the anomeric composition at equilibrium in aqueous solution, suggests that the crystalline product is a co-crystallized mixture of anomers (compare ref. 17). A solution of **10** in methyl sulfoxide-d_6 showed signals for H-1 of both pyranose anomers.

The n m r. spectrum of 4-acetamido-3-*O*-acetyl-4-deoxy-1,2-*O*-isopropylidene-α-L-xylopyranose (**8**), when measured in chloroform-*d*, showed (Fig 2) a broad, one-proton signal at low field (τ 3 60), which was assigned to the NH proton, since it disappeared on deuteration This observation provided independent evidence that compounds **6**, **7**, **8**, and **9** do not have the nitrogen atom in the ring A two-proton multiplet at τ 4 91 in the spectrum of **8** (in chloroform-*d*) was assigned to H-1 and H-3, the two protons most strongly deshielded of those attached to carbon The overlap of these two signals made analysis difficult, but the signals were well separated when the spectrum was measured in benzene (Fig 2). A sharp doublet at τ 4 96 was assigned to H-1 ($J_{1,2}$ 2 5 c p s), and the narrow signal at τ 4 72 (total width 10 c p s) was assigned to H-3 The fact that the H-3 signal was not observed as a wide (18–20 c p s), symmetrical triplet indicated that H-2, H-3, and H-4 are not *trans*-diaxial [**8** in the *IC* (L) conformation], and that the observed data accord with the formulation of **8** in a skew conformation (**11**) It has been proposed[18,19] that 1,2-*O*-alkylidene acetals

of arabinopyranose, glucopyranose, and related derivatives adopt a skew form as the favored conformation.

The 2,4-dinitroanilino derivatives studied in this work all showed signals at low field for the three aryl protons and the NH proton. None of the signals disappeared when the samples were deuterated in the usual way, even during several days, a fact which indicates that the NH proton could not be exchanged by deuterium oxide alone. However, the signal of the NH proton could be assigned definitively by adding a small amount of tributylamine to the prepared sample in chloroform-*d* containing deuterium

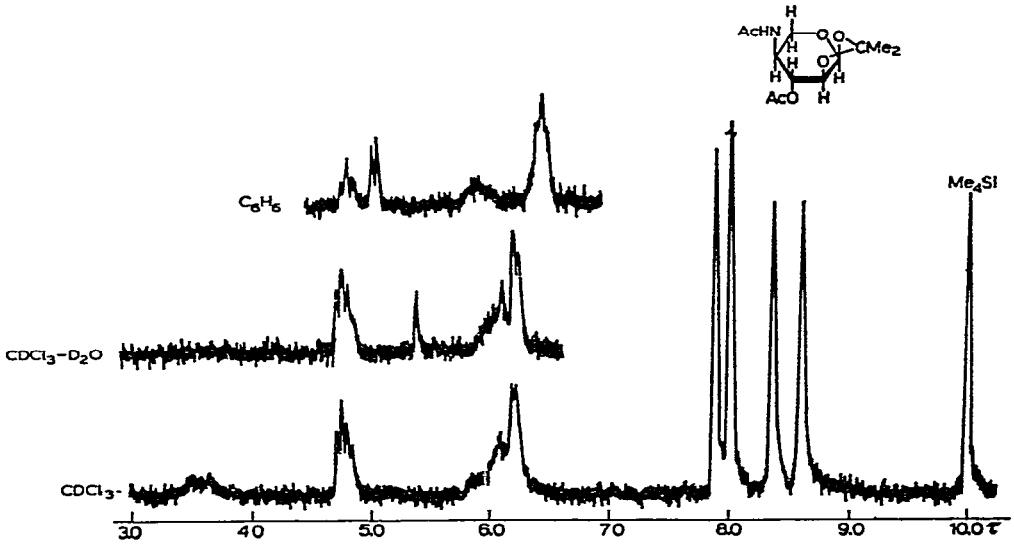


Fig. 2. The 60-Mc p.s. n.m.r. spectrum of 4-acetamido-3-*O*-acetyl-4-deoxy-1,2-*O*-isopropylidene-α-L-xylopyranose (8).

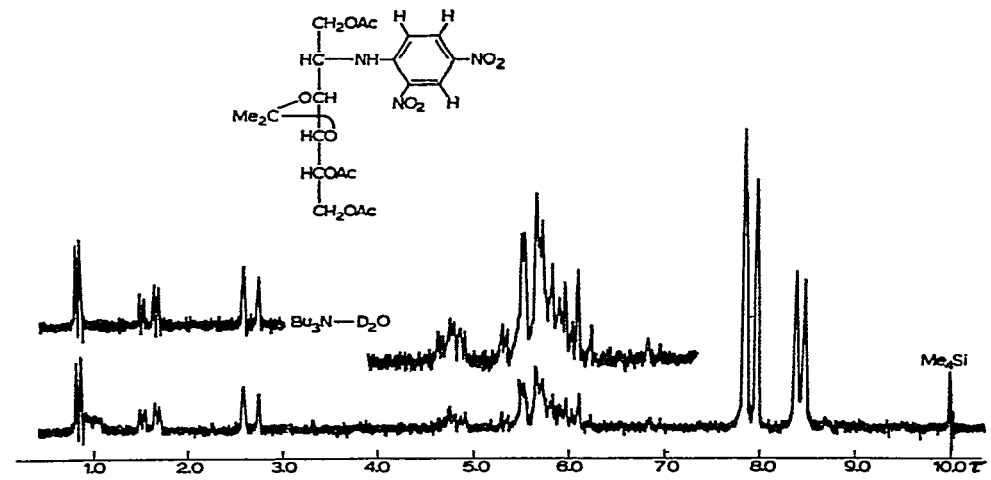


Fig. 3. The 60-Mc p.s. n.m.r. spectrum of 1,5,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-D-glucitol in chloroform-*d*, and in chloroform-*d* containing tributylamine in deuterium oxide.

oxide; this caused immediate exchange of the NH proton A typical example is provided by the spectrum of 1,5,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-3,4-*O*-isopropylidene-D-glucitol, which is shown (Fig. 3) before and after addition of tributylamine in deuterium oxide The broadened doublet at τ 1 01, which disappears on treatment with base, may clearly be assigned to the NH proton The narrow doublet at lowest field (τ 0 85), the doublet of doublets (τ 1.60), and the wide doublet (τ 2 68) can thus be assigned unambiguously to H-3, H-5, and H-6, respectively, of the 2,4-dinitrophenyl group. In a number of 2,4-dinitroanilino derivatives of sugars[20,21], the signal of the NH group appears as a wide doublet, and unambiguous differentiation of this signal from the signal of H-6 of the aryl residue cannot be made without exchange of the NH proton Exchange experiments have now shown that the tentative assignments made for the aryl H-6 and the NH proton, of the anomeric 2-deoxy-2-(2,4-dinitroanilino)-D-glucopyranose tetraacetates[20] and the derived 1-bromide[21], must be reversed. N m r data on *N*-methyl-2,4-dinitroaniline[22] and *N*-(2,4-dinitrophenyl)serine derivatives[23] are in agreement with the present work

Further details of n.m r measurements and assignments, for a number of compounds in this work, are given in the experimental section

EXPERIMENTAL

General

Melting points were determined with a Thomas–Hoover "Unimelt" apparatus (Arthur H Thomas Co , Philadelphia, Pennsylvania) Specific rotations were determined in a 2-dm polarimeter tube Infrared spectra were measured with a Perkin–Elmer "Infracord" infrared spectrometer N m r spectra were measured with a Varian A-60 spectrometer equipped with a Varian V-6040 variable-temperature probe Tetramethylsilane (τ 10 00) was used as the internal standard, except for spectra measured in deuterium oxide, for which the internal standard was sodium 4,4-dimethyl-4-silapentane-1-sulfonate (τ 10 00) The first-order coupling constants recorded are the measured peak spacings and are considered accurate to $\pm$ 0 5 c p s Unless otherwise stated, the spectra were measured at about 40° Deuteration was performed by adding one drop of deuterium oxide to the prepared sample Microanalytical determinations were made by W. N. Rond X-ray powder diffraction data give interplanar spacings, Å, for CuKα radiation The camera diameter was 114 59 mm Relative intensities were estimated visually s, strong, m, moderate; w, weak, v, very. The strongest lines are numbered (1, strongest), double numbers indicate approximately equal intensities Thin-layer chromatography was performed on Silica Gel G (E Merck, Darmstadt, Germany) activated at 110°, with sulfuric acid as the indicator Unless otherwise stated, ethyl acetate was used as the developer

Preparation of 2-acetamido-2-deoxy-D-glucitol[11]

2-Amino-2-deoxy-D-glucose hydrochloride (100 g) was *N*-acetylated[12] and the resultant, crystalline 2-acetamido-2-deoxy-α-D-glucose (95–100 g), dissolved in 20%

aqueous ethanol (1 l), was shaken in a 2-l autoclave with Raney nickel* (40 g) for 36 h at 100° under an atmosphere of hydrogen at 1000 lb in^{-2} pressure The catalyst was filtered from the cooled suspension, the filtrate was concentrated, and the product, which crystallized on standing, was filtered off and washed with a little ethanol, yield 92 g (91%), m p 150–151°, $[\alpha]_D^{21}$ −9±1° (*c* 1.3, water) [lit [11] m p 153°, $[\alpha]_D^{21}$ −11° (water), λ_{max}^{KBr} 3 00 (OH, NH), 6 05, 6 30 μ (NHAc), no absorption in the range 11 7–12 1 μ, X-ray powder diffraction data 16 06 m, 10 16 m, 8 93 vw, 6 70 vs (1,1), 4 92 vs (1,1), 4 69 m, 4 41 m, 4 27 m, 4 06 s (2,2), 3 91 s (2,2), 3 46 s (3).

*Preparation of 2-deoxy-2-(2,4-dinitroanilino)-*D*-glucitol*[10] (**1**)

2-Acetamido-2-deoxy-D-glucitol (30 g) was heated with 6N hydrochloric acid (400 ml) for 1 h at 100°, the solution was evaporated (codistillation with propyl alcohol), and the crystalline residue was recrystallized from methanol–ether to give 2-amino-2-deoxy-D-glucitol hydrochloride, yield 25 g (85%), m p 160–162° (lit [11] 160–161°), $[\alpha]_D^{23}$ −2 7±0 6° (*c* 1 8, water), ninhydrin-positive, λ_{max}^{KBr} 3 0 (OH), 3 30, 4 90, 6 18 μ (NH_3^+); X-ray powder diffraction data 7 47 m, 5 64 m, 5 29 m, 4 53 w, 4.33 vs (1,1), 4 15 vs (1,1), 3 74 vs (1,1), 3 63 vs (1,1), 3 44 w, 3 35 m, 3 26 s (2), 3 13 m, 3 00 m

To a solution of the foregoing product (20 g) in 50% aqueous ethanol (240 ml) was added sodium hydrogen carbonate (15 4 g) and 1-fluoro-2,4-dinitrobenzene (17 0 g) and the mixture was stirred for 18 h at room temperature. The yellow solid which separated was filtered off, washed with small amounts of water and ethanol, and then washed thoroughly with ether, yield 22 g (69%) Recrystallization from methanol gave **1** as fine yellow needles, m p 162–163° (lit [10] 163–164°), $[\alpha]_D^{24}$ +95° (*c* 1, methanol), R_F 0 12, λ_{max}^{KBr} 3 0 (NH, OH), 6 14, 6 30, 6 70 (aryl C=C), 7 44 (NO_2), 13 45 μ (substituted benzene), X-ray powder diffraction data 9 11 w, 8 19 m, 7 19 m, 6 23 w, 5 40 vw, 4 74 s (2,2), 4 62 m, 4 21 s (2,2), 3 98 m, 3 83 s (2,2), 3 61 vw, 3 38 vs (1)

*2-Deoxy-2-(2,4-dinitroanilino)-3,4 5,6-di-*O*-isopropylidene-*D*-glucitol* (**2**)

A solution of **1** (11 g) in dry acetone (200 ml) was shaken with concentrated sulfuric acid (2 ml) and anhydrous cupric sulfate (15 g) for 21 h at room temperature The mixture was filtered, the filtrate was poured into an excess of aqueous sodium hydrogen carbonate, the acetone was evaporated, and the resultant solution was extracted with 3 100-ml portions of chloroform The combined extracts were washed with water, dried (sodium sulfate), and evaporated, and the crystalline residue was recrystallized from ether; yield 8 5 g (63%), m p 164–165°, $[\alpha]_D^{20}$ +103±1° (*c* 0 7, chloroform); R_F 0.9, λ_{max}^{KBr} 2 91 (OH), 3 08 (NH), 6 20, 6 32, 6 70 (aryl C=C), 7 30 (CMe_2), 7 55 (NO_2), 13 48, 13.80 μ (substituted benzene), n m r data (chloroform-*d*), τ 0 85 (1-proton doublet, $J_{3',5'}$ 2 8 c p s , H-3'), τ 0 90 (1-proton broadened doublet, unchanged on deuteration, disappears after addition of 0 01 ml of tributylamine, NH),

* Raney nickel catalyst, no 28, Raney Catalyst Division of the W R Grace Co , Chattanooga, Tennessee

τ 1 72 (1-proton quartet, $J_{5',6'}$ 9 5 c p s, H-5'), τ 2 79 (1-proton doublet, H-6'), τ 5 48–6.52 (8-proton multiplet, H-1,2,3,4,5,6), τ 7 39 (1-proton triplet, J 6 c p s, disappears on deuteration, OH), τ 8 48, 8.57, 8.65, 8 68 (3-proton singlets, CMe_2), X-ray powder diffraction data· 8.84 m, 7 86 w, 6 88 vs (1), 6 60 vw, 6 02 m, 5 60 s (2), 5 14 w, 4 72 m, 4 15 m, 3 97 m, 3 86 m, 3 76 m, 3 59 w.

Anal Calc for $C_{18}H_{25}N_3O_9$. C, 50 58, H, 5 85, N, 9 83 Found: C, 50 88, H, 5 73; N, 9 89

*2-Deoxy-2-(2,4-dinitroanilino)-3,4 5,6-di-*O*-isopropylidene-1-*O*-(p-tolylsulfonyl)-*D*-glucitol*

A solution of **2** (0 6 g) in pyridine (5 ml) was treated at 0° with *p*-toluenesulfonyl chloride (0 38 g), and, after 24 h at 25°, the mixture was poured into water to yield a solid Recrystallization from ethanol gave very fine, yellow crystals, yield 0 6 g (75%), m p. 161–162°, $[\alpha]_D^{25}$ + 60±1° (*c* 1 2, chloroform), R_F 0 88 (9 1 benzene–methanol); λ_{max}^{KBr} 3 03 (NH), 6 18, 6 28, 6 67 (aryl C=C), 8 50 (sulfonate), 13 43, 13 70 μ (substituted benzene).

Anal Calc for $C_{25}H_{31}N_3O_{11}S$ C, 51 63; H, 5 33; N, 7 23, S, 5 50 Found: C, 51 56, H, 5 45, N, 7.55, S, 5 45

*2-Deoxy-2-(2,4-dinitroanilino)-3,4-*O*-isopropylidene-*D*-glucitol* (**3**)

To a solution of **2** (2 0 g) in methanol (95 ml) was added N aqueous hydrochloric acid (25 ml), and the mixture was kept for 5 h at 25° An excess of lead carbonate was added and the mixture was filtered The filtrate was concentrated until most of the methanol had been removed, water was added to a total volume of 75 ml, and the small amount of solid starting-material which separated was removed by filtration The filtrate was extracted with 3 75-ml portions of chloroform, and the aqueous phase, which contained a small amount of **1**, was discarded The dried (magnesium sulfate) chloroform extract was concentrated to 30 ml, and the yellow solid (solvate of **3**) which separated on standing was filtered off, yield 0.1 g. The remaining chloroform solution was evaporated and the residual syrup was crystallized from ether to give solvent-free **3** as orange granules, yield 0 85 g (47%, total yield of both forms 53%), m p. 128–129°, $[\alpha]_D^{25}$ +78±2° (*c* 1, acetone), R_F 0 22, λ_{max}^{KBr} 3 00 (OH, NH), 6 18, 6.30, 6 60 (aryl C=C), 7 20 (CMe_2), 7 50 (NO_2), 13 48 μ (substituted benzene); n m r data (acetone-d_6) τ 0 98 (1-proton doublet, $J_{3',5'}$ 2 7 c p s, H-3'), τ 1 00 (1-proton broad doublet, NH), τ 1 82 (1-proton quartet, H-5'), τ 2.71 (1-proton doublet, $J_{5',6'}$ 9 5 c p s, H-6'), τ 8 51, 8 60 (3-proton singlets, CMe_2), X-ray powder diffraction data. 11 26 m, 9 99 w, 8 42 vw, 6 86 vs (2), 6 15 vw, 5 86 vw, 5 54 vs (1), 4 79 m, 4 48 m, 4 07 m, 3 78 m, 3 53 vw, 3 37 s (3), 3 27 s

Anal. Calc for $C_{15}H_{21}N_3O_9$ C, 46 51, H, 5 42, N, 10 85 Found C, 46.30, H, 5 49, N, 11 06

Periodate oxidation of **3**, at 25° with a 5-molar excess of oxidant, showed a consumption of oxidant (Fleury–Lange method[24]) of 1 00 mole/mole after 5 min, 1.05 moles/mole after 24 h

The preparation was repeated 20 times, and although the total yield of both forms was approximately the same each time, the proportion of the solvated form was frequently much higher than that described, and the ratio of the two forms appeared to depend on minor variations in experimental procedure Recrystallization of the solvate from chloroform gave fine, yellow needles, m p 95–96° (with effervescence, solidifying at higher temperature and remelting at 126–127°); R_F 0 22; X-ray powder diffraction data 12 27 m, 9 40 w, 8 11 w, 6 81 m, 6 32 w, 5 90 w, 5 57 s (2), 5.12 vs (1).

Anal Calc for $(C_{15}H_{21}N_3O_9)_3 \cdot CHCl_3$· C, 43.12, H, 5 03, N, 9 84 Found C, 42 72; H, 4 92; N, 10 34

A sample of the solvate, kept for 2 h at 110° over phosphoric oxide, lost 10% of its weight (calc 9 4%) and gave the solvent-free form, m p and mixed m p 126–127°

Anal Calc for $C_{15}H_{21}N_3O_9$· C, 46 51, H, 5 42; N, 10 85 Found C, 46.33, H, 5 27, N, 11.11

The solvate showed the same molar uptake of periodate as the non-solvated form, and the n m r spectra of the two forms were identical except for the fact that the solvate showed an additional signal at τ 2 80 (singlet, 1/3 proton, $CHCl_3$) The i r. spectra (KBr disc) of the two forms were very similar, but were not completely superposable.

2-Acetamido-1,5,6-tri-O-acetyl-2-deoxy-3,4-O-isopropylidene-D-glucitol

A solution of **3** (8 g) in acetone (280 ml) and water (120 ml) was passed slowly through a column (35 × 3 5 cm) of Dowex-1 (OH^-) ion-exchange resin which had been pre-washed with 7 3 (v/v) acetone–water. The column was washed with 7.3 (v/v) acetone–water until the effluent gave a negative ninhydrin reaction, and the combined effluent was evaporated The dried residual syrup (4 2 g) was dissolved in pyridine (25 ml), acetic anhydride (45 ml) was added, and the solution was kept for 18 h at room temperature The solution was poured into ice and water (200 ml), and the mixture was extracted with 3 75-ml portions of chloroform The extract was washed successively at 0° with dilute sulfuric acid, aqueous sodium hydrogen carbonate, and water, the dried (sodium sulfate) solution was evaporated, and the residue was crystallized from ether, yield 2 21 g, m p 93–94°, $[\alpha]_D^{25}$ +31±1° (*c* 1 7, chloroform), R_F 0 42, λ_{max}^{KBr} 3 08 (NH), 5 73 (OAc), 6 08, 6 53 (NHAc), 7 28 μ (CMe_2); n m r. data (chloroform-*d*) τ 3 89 (1-proton doublet, *J* 8 5 c p s , NH), τ 4 80 (1-proton octet, width 16 c p s , H-5), τ 5 30–6 30 (7-proton multiplet, H-1,2,3,4,6), τ 7 89, 7.95 (singlets, 3 and 9 protons, acetyls), τ 8 59, 8 61 (3-proton singlets, CMe_2), X-ray powder diffraction data 7 69 s (1), 6 97 w, 5 71 m, 5 43 m, 4 64 m, 4 25 s (2), 3 81 m

Anal Calc for $C_{17}H_{27}NO_9$· C, 52 44, H, 6 94, N, 3 60 Found C, 52 52; H, 6 89; N, 3 84

1,5,6-Tri-O-acetyl-2-deoxy-2-(2,4-dinitroanilino)-3,4-O-isopropylidene-D-glucitol

A solution of **3** (430 mg) in pyridine (4 ml) was treated with acetic anhydride (2 5 ml) at room temperature, and after 24 h, the solution was poured into water.

The product was extracted with dichloromethane and processed in the usual way, to give the triacetate of **3** as a yellow glass, yield 435 mg (76%); R_F 0 54 (1 3 ethyl acetate–benzene), λ_{max}^{film} 3 02 (NH), 5 77 (OAc), 6 20, 6 30, 6 60 (aryl C=C), 7.34 (CMe_2), 13.25 μ (substituted benzene); n m r data in chloroform-*d* (See Fig 3): τ 0 85 (1-proton doublet, $J_{3',5'}$ 2 7 c p s , H-3'), τ 1 01 (1 proton, broad, NH), τ 1 60 (1-proton quartet, H-5'), τ 2 68 (1-proton doublet, $J_{5',6'}$ 9 5 c p s , H-6'), τ 4 78 (1-proton octet, width 16.5 c p s., H-5), τ 5 26-6 30 (7-proton multiplet, H-1,2,3,4,6), τ 7.85, 7 87, 7 98 (3-proton singlets, acetyls), τ 8 40, 8 50 (3-proton singlets, CMe_2)

Anal Calc for $C_{21}H_{27}N_3O_{12}$ C, 49 12, H, 5 62, N, 8 19 Found C, 48 66; H, 5 89, N, 8.16.

The signal at τ 1 01 was not affected by deuteration, even after 57 h at room temperature, but the signal disappeared (Fig 3) rapidly when 0 01 ml of tributylamine was added to the prepared sample, and a 1-proton singlet appeared at τ 5 31 (HOD)

Acetylation of the yellow solvate of **3** gave a product whose n m r spectrum was identical to that recorded above

4-Deoxy-4-(2,4-dinitroanilino)-2,3-O-isopropylidene-aldehydo-L-*xylose* (**4**)

A solution of sodium metaperiodate (1.81 g, 1 1 molar equiv) in water (30 ml) was added to a solution of **3** (3 0 g) in 1 4 ethanol–water (75 ml) The mixture was kept for 25 min in the dark at room temperature, and was then evaporated at 30° Anhydrous sodium sulfate (~3 g) was added to the residue, and the solid mixture was extracted repeatedly with ether Evaporation of the extract gave **4** as a yellow glass, yield 2 4 g (87%), R_F 0 40, λ_{max}^{film} 2 95 (OH), 3 05 (NH), 3 50, 5 80 (CHO), 6 20, 6 30, 6 65 (aryl C=C), 7 33 (CMe_2), 7 55 (NO_2), 12 25, 13 20 μ (substituted benzene)

Anal Calc for $C_{14}H_{17}N_3O_8$ C, 47 32, H, 4 79, N, 11 83 Found C, 47 18; H, 5 46, N, 11 77.

4-Deoxy-4-(2,4-dinitroanilino)-L-*xylopyranose* (**5**)

A solution of **4** (3 29 g) in 50% aqueous acetic acid (16 ml) was heated for 2 5 h at 95°, and then evaporated Addition of ethanol to the residual syrup gave the crystalline product, yield 2 54 g (84%), m p 194–195° (dec), $[\alpha]_D^{23}$ +37±1° (*c* 1, acetone), R_F 0 15, R_F 0 69 (papergram, 40 11 19 butyl alcohol–ethanol–water); λ_{max}^{KBr} 2 9 (OH), 3 05 (NH), 6 20, 6 30, 6 60 (aryl C=C), 7 52 (NO_2), 13 50, 14 0 μ (substituted benzene); X-ray powder diffraction data 10 46 m, 6 02 m, 5 08 vs (1), 4 44 m, 4 06 m, 3 44 s (3), 3 20 s (2), 3 06 vw, 2 91 vw

Anal Calc for $C_{11}H_{13}N_3O_8$ C, 41 90, H, 4 21, N, 13 33 Found C, 41 42, H, 4 38, N, 13 59

1,2,3-Tri-O-*acetyl-4-deoxy-(2,4-dinitroanilino)*-L-*xylopyranose*

To a solution of **5** (0 5 g) in pyridine (6 ml) was added acetic anhydride (3 ml) The mixture was kept for 24 h at room temperature, and then processed in the usual way to give the product as a yellow, distillable glass, yield 0 35 g (50%), R_F 0 60 and 0 70 (1 1 ethyl acetate–benzene), λ_{max}^{film} 3 05 (NH), 5 70 (OAc), 6 15, 6 30, 6 60 (aryl

C=C), 13 40 μ (substituted benzene), n m r data (chloroform-*d*) $\tau\sim$0 88, 1 0-1 2, 1 68, 2 78 (multiplets, 4 protons, H-3′,5′,6′, and NH, of anomers), τ 7 77, 7 81, 7 91, 7 95 (singlets, 9 protons, acetyls)

Anal Calc for $C_{17}H_{19}N_3O_{11}$ N, 9 52 Found N, 9 74

4-Deoxy-4-(2,4-dinitroanilino)-1,2-O-isopropylidene-α-L-xylopyranose (**6**)

A solution of **5** (1 84 g) in acetone (400 ml) was shaken with anhydrous cupric sulfate (5 g) and conc sulfuric acid (0 5 ml) for 1 day at room temperature The mixture was filtered, the filtrate was neutralized with aqueous sodium hydrogen carbonate, the acetone was evaporated, and the product was extracted with 3 75-ml portions of ethyl acetate The extract was washed with water, dried (sodium sulfate), and evaporated, and the crystalline residue was recrystallized from ethyl acetate, yield 1 64 g (79%), m p 220–222° (dec), $[\alpha]_D^{25}$ +175±2° (*c* 1 1, acetone), R_F 0 70, λ_{max}^{KBr} 3 00 (OH, NH), 6 20, 6 32, 6 62 (aryl (C=C), 7 22, 7 30 (CMe_2), 7 56 (NO_2), 13 42, 14 10 μ (substituted benzene), n m r data (pyridine) τ 4 39 (1-proton doublet, $J_{1\,2}$ 2 c p s , H-1), τ 5 24-6 13 (5-proton multiplet, H-2,3,4,5), τ 8 23, 8 60 (3-proton singlets, CMe_2), X-ray powder diffraction data 13 29 w, 8 97 w, 7 86 w, 6 70 m, 5 57 vs (1), 5 15 s (2), 4 79 s (3,3), 4 53 s (3,3), 4 27 s (3,3), 4 09 s (3,3), 3 77 s (3,3), 3 63 s (3,3)

Anal. Calc for $C_{14}H_{17}N_3O_8$ C, 47 32, H, 4 82, N, 11 83 Found C, 47 55, H, 5 09, N, 12 23

Only one product could be detected by t l c in the above preparation, and no difference in the yield of **6** was observed when the time of reaction was extended to 4 days

3-O-Acetyl-4-deoxy-4-(2,4-dinitroanilino)-1,2-O-isopropylidene-α-L-xylopyranose

A solution of **6** (175 mg) in pyridine (2 ml) and acetic anhydride (3 ml) was kept for 1 day at room temperature, and then poured into ice and water The precipitated solid was filtered off, washed with water, dried, and recrystallized from methanol, yield 130 mg (66%), m p 171–172°, $[\alpha]_D^{21}$ +190±2° (*c* 1, chloroform), R_F 0 84; λ_{max}^{KBr} 3 02 (NH), 5 77 (OAc), 6 18, 6 30, 6 60 (aryl C=C), 7 30 (CMe_2), 13 45, 14.10 μ (substituted benzene), n m r data (chloroform-*d*) τ 0 84 (1-proton doublet, $J_{3',5'}$ 2 7 c p s , H-3′), τ 0 88 (1-proton, broad, disappears on addition of tributylamine in deuterium oxide, NH), τ 1 66 (1-proton quartet, H-5′), τ 2 68 (1-proton doublet, $J_{5',6'}$ 9 5 c p s , H-6′), τ 4 69 (2-proton multiplet, width 10 c p s , H-1, H-3), τ 5 92-6 38 (4-proton multiplet, H-2,4,5), τ 7 78 (3-proton singlet, OAc), τ 8 33, 8 62 (3-proton singlets, CMe_2)

Anal Calc for $C_{16}H_{19}N_3O_9$ N, 10 58 Found N, 10 72

4-Amino-4-deoxy-1,2-O-isopropylidene-α-L-xylopyranose (**7**)

A solution of **6** (0 72 g) in acetone (60 ml) and water (20 ml) was stirred with Dowex-1 (OH^-) ion-exchange resin, added in small portions at 45–50° until the solution became colorless. The mixture was filtered, and the resin was washed with hot methanol (500 ml) The filtrate and washings were evaporated to a colorless syrup

which crystallized from ether, yield 0.247 g (65%), m.p. 131–132°, $[\alpha]_D^{24}$ +32.5±1° (*c* 1, methanol); λ_{max}^{KBr} 3.4, 6.3 (NH), 7.25 μ (CMe_2), X-ray powder diffraction data: 7.97 vs (2), 6.23 w, 5.79 vw, 5.27 vs (1), 5.01 m, 4.77 m, 4.39 s (3), 4.00 m, 3.64 m, 3.14 vw, 3.01 vw, 2.85 m.

Anal. Calc. for $C_8H_{15}NO_4$: C, 50.80; H, 7.93; N, 7.40. Found: C, 50.62; H, 7.73; N, 7.67.

Periodate oxidation of **7** (40 mg) at 25° in water (20 ml) containing a 5-molar excess of oxidant showed consumption of oxidant (Fleury–Lange method[24]) as follows (time and moles per mole of oxidant consumed given): 5 min, 1.03; 1 h, 1.05; 2 h, 1.07; 4 h, 1.14; 8 h, 1.28; 22 h, 1.51; 46 h, 1.75; 70 h, 1.82.

4-Acetamido-3-O-acetyl-4-deoxy-1,2-O-isopropylidene-α-L-xylopyranose (**8**)

A solution of **7** (590 mg) in pyridine (5 ml) and acetic anhydride (5 ml) was kept for 1 day at room temperature, and then poured into ice and water. The product was extracted with 3 60-ml portions of dichloromethane, the extract was washed with aqueous sodium hydrogen carbonate, dried (sodium sulfate), and evaporated (codistillation with toluene). The resulting syrup crystallized on storage, and recrystallization from chloroform gave **8** as fine needles, yield 596 mg (70%), m.p. 109–110°, $[\alpha]_D^{22}$ +68±1° (*c* 1, chloroform), R_F 0.40, λ_{max}^{KBr} 3.04 (NH), 5.73 (OAc), 6.08, 6.52 (NHAc), 7.22 μ (CMe_2), n.m.r. data in chloroform-*d* (see Fig. 2): τ 3.60 (1-proton broad doublet, J 8 c.p.s., disappears on deuteration, NH), τ 4.91 (2-proton multiplet, H-1,3), τ 5.85–6.50 (4-proton multiplet, H-2,4,5), τ 7.90, 8.03 (3-proton singlets, acetyls), τ 8.38, 8.63 (3-proton singlets, CMe_2), in benzene (see Fig. 2): τ 4.72 (1-proton multiplet, width 10 c.p.s., H-3), τ 4.96 (1-proton doublet, $J_{1,2}$ 2.5 c.p.s., H-1), τ 5.70–5.95 (1-proton multiplet) and τ 6.20–6.50 (3-proton multiplet) (H-2,4,5), τ 8.33, 8.37 (3-proton singlets, acetyls), τ 8.51, 8.82 (3-proton singlets, CMe_2); X-ray powder diffraction data: 8.88 m, 7.47 vs (3), 6.23 m, 5.54 vs (2), 5.15 s, 4.72 m, 4.37 vs (1), 4.08 m, 3.92 m, 3.58 m, 3.43 w, 3.18 m, 2.98 m.

Anal. Calc. for $C_{12}H_{19}NO_6$: C, 52.74; H, 6.96; N, 5.12. Found: C, 52.79; H, 6.86; N, 5.05.

4-Acetamido-4-deoxy-1,2-O-isopropylidene-α-L-xylopyranose (**9**)

A solution of **8** (0.5 g) in anhydrous methanol (10 ml) was treated with a very small piece of metallic sodium, and after 2 h at room temperature, the solution was neutralized with Amberlite IR-120 (H^+) ion-exchange resin. Evaporation of the solution gave **9** as a colorless syrup, yield 0.36 g (85%), R_F 0.15; λ_{max}^{film} 2.85–3.10 (OH, NH), 6.10, 6.50 (NHAc), 7.30 (CMe_2).

4-Acetamido-4-deoxy-L-xylopyranose (**10**)

(*a*) *From 4-acetamido-4-deoxy-1,2-O-isopropylidene-α-L-xylopyranose* (**9**). A solution of **9** (350 mg) in water (10 ml) was stirred with Amberlite IR-120 (H^+) ion-exchange resin (1.5 g) for 2.5 h at 60°. The resin was filtered, and washed with methanol, and the filtrate was evaporated to a chromatographically homogeneous

syrup which crystallized after trituration with ethanol and ethyl acetate, yield 152 mg (53%) After recrystallization from methanol–ether, the product had m p 155–157°, $[\alpha]_D^{24}$ −53→ −49° (*c* 3 3, water), $R_{Rhamnose}$ 0 85 (papergram, 3.1·1 butyl alcohol–ethanol–water); λ_{max}^{KBr} 3 00 broad (NH, OH), 6 18, 6 44 μ (NHAc), X-ray powder diffraction data 9 30 m, 7 86 vw, 6 02 s (3,3), 5 71 vs (2), 5 09 w, 4 67 vs (1), 4 33 s (3,3), 4 03 s (3,3), 3 80 m, 3 64 m, 3 37 vw, 3 18 m, 3 05 m, 2 93 s

Anal Calc. for $C_7H_{13}NO_5$. C, 43 97, H, 6 85, N, 7 32 Found C, 43 67, H, 6 91; N, 7.69

For this compound, prepared by a different route, Dick and Jones reported[8] m p. 157–158°, $[\alpha]_D$ −22→−16° (*c* 1, water) and $R_{Rhamnose}$ 0.81 (papergram, 3 1:1 butyl alcohol–ethanol–water); a revised value of $[\alpha]_D$ − 43 5° (equil , *c* 0 93, water) was subsequently reported (see footnote p 193)

(*b*) *From 4-amino-4-deoxy-1,2-O-isopropylidene-α-L-xylopyranose* (7) To a solution of 7 (200 mg) in methanol (1 ml) and water (4 ml) was added acetic anhydride (1 ml), and the mixture was kept for 2 h at room temperature Examination by t l c (1 2 isopropyl alcohol–benzene) revealed that the starting material **7** (R_F 0 17) was completely converted into **9** (R_F 0 72) Water (2 ml) was added and the solution was heated for 3 h at 90°, by which time conversion of **9** into **10** (R_F 0 07) was complete Evaporation of the solution (codistillation with toluene), and crystallization of the residue from ethanol–ether gave **10**, yield 120 mg (60%), m p 155–157°, identical by mixed m p and i r spectrum with the product prepared by procedure (*a*)

N m r spectrum of 4-acetamido-4-deoxy-L-xylose

The n m r. spectrum of **10** (Fig 1), measured at 80° in deuterium oxide with an equilibrated solution gave the following data τ 4 78 (doublet, $J_{1,2}$ 3 0 c p s, H-1 of α-L anomer) and τ 5 44 (doublet, $J_{1,2}$ 7 6 c p s., H-1 of β-L anomer) (total integral, 1 proton, relative intensities 2 3), τ 5 89-6 28 (5-proton multiplet, H-2,3,4,5), τ 7 99 (3-proton singlet, NAc) The signal at τ 5 44 was partially obscured by the HOD signal when the spectrum was measured at 40°.

A spectrum of **10**, measured 2 min after dissolution in deuterium oxide, showed the signal at τ 4 78 The relative intensity of the latter was not appreciably different from its intensity in the spectrum of the equilibrated solution The spectrum of **10**, measured 30 min after dissolution in methyl sulfoxide-d_6, showed signals at τ 4 79 (H-1 of α-L pyranose anomer) and τ 5 46 (H-1 of β-L pyranose anomer), a singlet at τ 8 00 (NAc), and a broad signal, $\tau \sim 4$ 7 which disappeared on deuteration (NH) The spectrum of the deuterated sample, measured at 80°, showed the H-1 signals as sharp doublets at τ 4 79 ($J_{1,2}$ 2 8 c p s) and τ 5 46 ($J_{1,2}$ 7 2 c p s), total integral 1 proton, in approximately 2 3 ratio. The H-2,3,4,5 signals were observed as a 5-proton multiplet, τ 5 95-6 86

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SUMMARY

Acetonation of 2-deoxy-2-(2,4-dinitroanilino)-D-glucitol (**1**) gave the 3,4 5,6-diisopropylidene acetal (**2**), which was converted by mild, acid hydrolysis into the 3,4-monoisopropylidene acetal (**3**) Periodate oxidation of **3**, followed by mild hydrolysis of the oxidation product (**4**) gave 4-deoxy-4-(2,4-dinitroanilino)-L-xylopyranose (**5**), which underwent condensation with acetone to give the 1,2-*O*-isopropylidene derivative (**6**) Removal of the *N*-substituent from **6** gave 4-amino-4-deoxy-1,2-*O*-isopropylidene-α-L-xylopyranose (**7**), which was acetylated to give 4-acetamido-3-*O*-acetyl-4-deoxy-1,2-*O*-isopropylidene-α-L-xylopyranose (**8**) *O*-Deacetylation of **8**, followed by mild hydrolysis of the product (**9**), gave 4-acetamido-4-deoxy-L-xylose (**10**), substance **10** was also prepared from **7** in one step In aqueous solution, the acetamido sugar (**10**) underwent equilibration to give a mixture of the α-L and β-L pyranose anomers in 2 3 ratio Structural assignments were supported by n m r. and other physical data

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