Commission's Lawrence Livermore Laboratory. A smaller portion was carried out under NSWC Task IR 144.

Registry No.—**1**, 18139-02-1; **2**, 55702-16-4; **3**, 55702-17-5; **4**, 55702-18-6; **5**, 33046-34-3; **6**, 55702-19-7; **7**, 55702-20-0; **10**, 55702-21-1; **11**, 32765-49-4; **12**, 33191-90-1; **14**, 55702-22-2; **15**, 55702-23-3; **16**, 55702-24-4; **17**, 55702-25-5; fluorodinitromethane, 7182-87-8; formaldoxime, 75-17-2; 2,2,2-fluorodinitroethanol, 17003-75-7; ethylenediamine, 107-15-3; *N*-(2,2,2-fluorodinitroethyl)methylamine, 30409-33-7; *N*-bromomethyl-*N*,*N*-bis(2,2,2-fluorodinitroethyl)amine, 55702-26-6.

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Oxidation of Carbohydrates with Chromic Acid. Synthesis of 6-Acetamido-6-deoxy-D-*xylo*-hexos-5-ulose[1]

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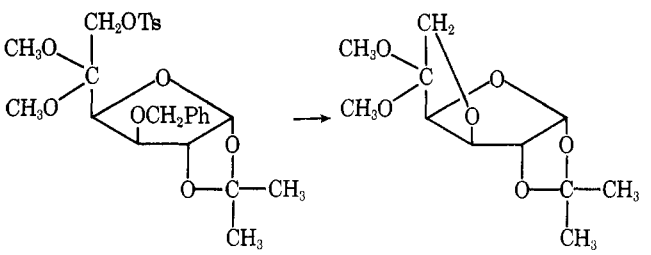
Preparation of the title compound (**8**) was routed through 6-azido-6-deoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**4**). Oxidation of **4** with the Jones reagent[3] gave the ketone **6**, which yielded crystalline 6-acetamido-6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (**7**) upon catalytic hydrogenolysis of the azido and benzyl groups, followed by N-acetylation of the intermediate amine. Alternatively, the hydrogenolyzable groups of **4** were first cleaved to give 6-acetamido-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**5**), which, in turn, was selectively oxidized at the C-5 hydroxyl group with the chromic acid reagent to give **7**. Hydrolysis of the isopropylidene group of **7** afforded the δ-dicarbonyl amino sugar **8** as a mixture of pyranose and furanose ring forms.

Chromic acid in acetone (the Jones reagent[3,4]) is a very convenient and well-known reagent for the oxidation of secondary alcohols to ketones. As far as we are aware, recently published results from this laboratory described the first application of this oxidizing agent in the synthesis of dicarbonyl monosaccharide derivatives.[5] In this paper we describe the synthesis of a new δ-dicarbonyl amino sugar derivative, 6-acetamido-6-deoxy-D-*xylo*-hexos-5-ulose (**8**). As yet, no biological role for **8** or its parent amino sugar has been described, nor have these compounds been isolated from a natural source. However, they are structurally related to the unknown δ-dicarbonyl diamino sugar, 2,6-diamino-2,6-dideoxy-D-*xylo*-hexos-5-ulose, a predicated biogenetic precursor for neosamines B and C.[6] These amino sugars are components of the neomycins and a number of related aminoglycoside antibiotics. In the described synthesis of **8** the key oxidation of a secondary alcohol function was efficiently achieved with chromic acid reagent.

Results and Discussion

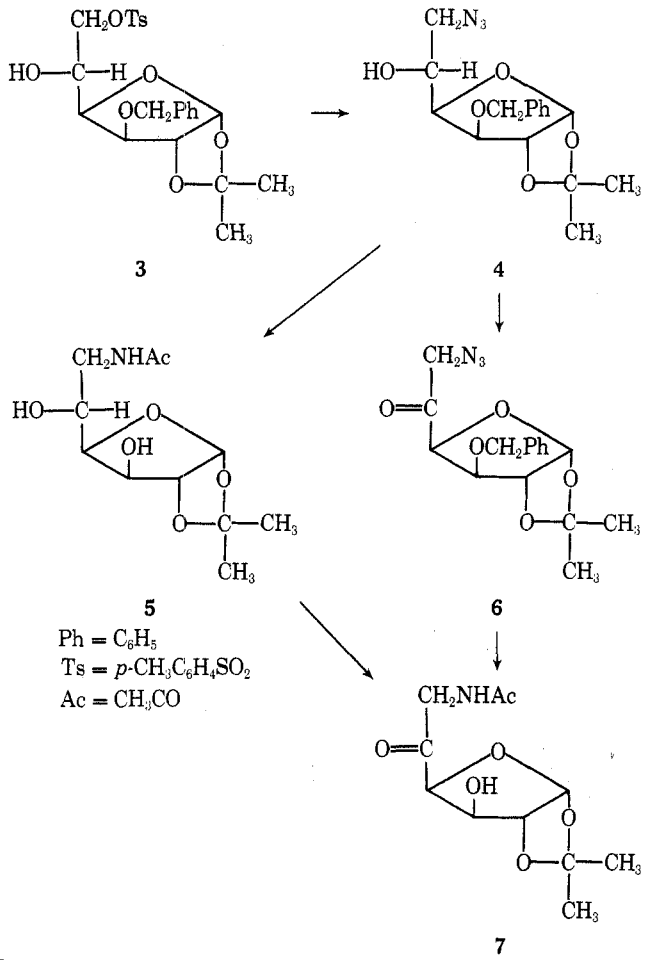
The first approach to the synthesis of the title compound began with the conversion of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose dimethyl acetal[7] to the corresponding 6-*O*-tosyl derivative **1**. However, compound **1** remained completely unchanged when treated with sodium azide in refluxing aqueous acetone. When **1** was treated with sodium azide under more vigorous conditions (in refluxing dimethylformamide) a single syrupy product, identified as the 3,6-anhydro derivative **2**, was isolated. Formation of **2** from **1** can be accounted for on the basis of a simple, direct nucleophilic displacement of the C-6 tosyloxy group by the oxygen of the C-3 benzyloxy group. Alternatively, it may be that a methoxy oxygen provides anchimeric assistance for removal of the proximate tosyloxy group, a step which is then followed by formation of the five-membered ether ring through the C-3 oxygen. Winstein and coworkers[8] concluded from a solvolysis study of 2-methyl-2-methoxy-1-propyl *p*-bromobenzenesulfonate that methoxyl group participation in the rate-determining ionization step is significant and takes place via a three-membered cyclic methyloxonium ion. The same mode of methoxy anchimeric assistance may be operative in the transformation of **1** to **2**.



1 **2**

Ph = C_6H_5
Ts = *p*-$CH_3C_6H_4SO_2$

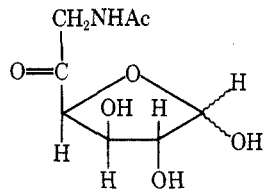
Alternate routes to **8** were then initiated originating from the azide **4**, a compound previously prepared by Saeki and Ohki.[9] Catalytic hydrogenolysis of the azido and benzyl groups of **4**, in acetic acid solution, was then followed by N-acetylation of the resulting amino sugar to give 6-acetamido-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose[10] (**5**). The C-5 hydroxyl group of **5** was then selectively oxidized with the chromic acid reagent, affording **7** in 38%



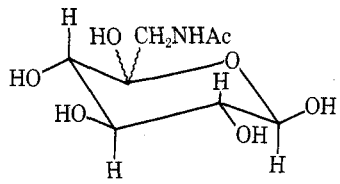
yield. This preference for oxidation at the C-5 hydroxyl has also been observed with other 6-deoxy furanose derivatives.[5,11] In the NMR spectrum of the oxidation product (**7**), the acetamido NH proton, coupled to the two C-6 protons, appeared as a broad triplet at δ 6.72 with a J value of 5.0 Hz. When this exchangeable proton was replaced with deuterium, the signal at δ 6.72 disappeared and the two-proton doublet at δ 4.28 (C-6 protons) collapsed to a broad singlet. The rest of the spectrum was also in agreement with the structure given for **7**.

A more efficient conversion of **4** to **7** was effected by reversing the order of the hydrogenolysis and oxidation steps. Oxidation of **4** with chromic acid in acetone at 0–5° for 6 hr gave, after purification of the reaction mixture by column chromatography, syrupy 6-azido-6-deoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (**6**) in 67% yield. Subsequent hydrogenolysis of the azido and the benzyl groups of **6**, in acetic acid solution, followed by N-acetylation of the product, gave the crystalline acetamido derivative **7**. The yield from the conversion of **4** to **7** by this route was 33%, whereas when the hydrogenolysis was the first step in the sequence, the overall yield was only 15%. This difference is partly attributed to the efficient recovery of the water-insoluble ketone **6** during the oxidation work-up procedure. In contrast, the somewhat water-soluble crude acetamido derivative **7** was obtained in lower yields when isolated as the direct oxidation product of **5**.

In order to obtain the final desired product, 6-acetamido-6-deoxy-D-*xylo*-hexos-5-ulose (**8**), the isopropylidene group of **7** was removed by acid-catalyzed hydrolysis. The hydrolysate was concentrated by freeze drying and the residual gum was found to be chromatographically homogeneous by microcrystalline cellulose TLC. The ir spectrum of this material included a medium strength ketone carbonyl (5.75 μ) as well as a strong amide carbonyl absorption (6.05 μ), suggesting that **8**, as a mixture of ring isomers, contained a significant amount of the furanose forms **8a** and **8b**. A first-order analysis of the anomeric proton region (δ 4.7–5.7) of the NMR spectrum of **8** (Figure 1) provided further evidence that this was the case. However, after carrying out some proton decoupling experiments and measuring the coupling constants for coupled ring protons, we concluded that the pyranose anomer **8c** with H-1 and H-2 anti-diaxial is the major component in the tautomeric equilibrium mixture of **8**.



8a, α-furanose
8b, β-furanose



8c

The equilibrium between the pyranose and furanose forms of aldoses in deuterium oxide has been thoroughly investigated through the use of ^{1}H NMR spectroscopy.[12–15] The furanose anomeric protons have been generally observed at lower field strength than those of the corresponding pyranoses. Furthermore, the signal from the C-1 proton of the furanose 1,2-cis anomer ($J_{1,2} \simeq$ 3–5 Hz) is usually downfield to that of the furanose 1,2-trans anomer ($J_{1,2} \simeq$ 0–2 Hz). As regards the pyranose forms of the aldoses, a coupling constant of 7 Hz or more for the C-1 proton doublet indicates a 1,2-diaxial relationship between H-1 and H-2, whereas a smaller coupling constant signifies a gauche relationship between the two protons.

Three signals attributed to the anomeric protons of **8** were clearly observed in its spectrum, δ 5.60 (d, J = 4.0 Hz), 5.36 (s), and 4.93 (d, J = 8.0 Hz). The δ 5.60 and 5.36 signals have been assigned to the furanose 1,2-cis and 1,2-trans anomers (**8a** and **8b**) on the basis of the generalizations observed for the field positions and coupling constants of aldose anomeric protons.

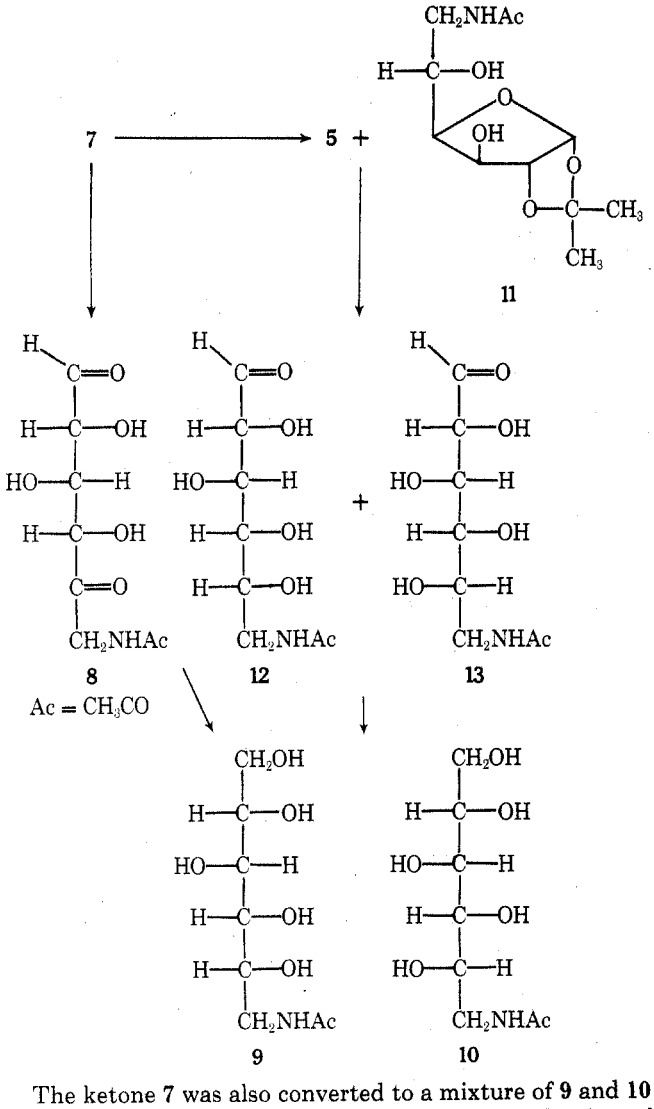
In the first decoupling experiment irradiation of the large δ 4.93 signal converted the δ 3.27 multiplet to a doublet with J = 9.2 Hz. Irradiation at the δ 3.27 signal simplified the quartet centered at δ 4.28, although the change was somewhat masked owing to overlapping signals from, in part, the methylene protons of the furanose rings **8a** and **8b**. These experiments established the anti-diaxial relationship for the H-1 (δ 4.93, $J_{1,2}$ = 8.0 Hz) and H-2 (δ 3.27) as well as the H-2 and H-3 (δ 4.28, $J_{2,3}$ = 9.2 Hz) protons of the pyranose ring **8c**. The large doublet at δ 3.65 (J = 9.2 Hz) is assigned to the H-4 proton of **8c**, it also being in a trans-diaxial relationship to the vicinal proton at C-3. An attempt to decouple H-3 from H-4 was unsuccessful because spectrometer beats obscured the resulting transitions at δ 3.68 when the signal at δ 4.28 was irradiated. The spectrum for the ring protons of **8c** was consistent with a theoretical spectrum generated by a full matrix computer program[16] for the spin system ABCD.

The singlet at δ 3.40 is attributed to the methylene protons of the predominant C-5 epimer of **8c**. Although we favor the predicted more stable epimer, i.e., with a C-5 equatorial acetamidomethyl substituent, direct evidence to support this particular stereochemical assignment is still lacking.

The mixture obtained from the acid hydrolysis of **7** is clearly a complex one. That it contains components in equilibrium with others than those already described is

borne out by the presence of additional overlapping, but yet unassigned, signals in the anomeric region of the spectrum.

Indirect evidence also helped to establish that the hydrolysis product of 7 was 6-acetamido-6-deoxy-D-*xylo*-hexos-5-ulose. When the hydrolysate was reduced with sodium borohydride, and the reduction products analyzed by GLC as their trimethylsilyl derivatives, a chromatogram with two predominant peaks (ratio of their areas 9:1) was obtained. The larger of the two peaks was unsymmetrical, suggesting that it resulted from two structurally related components in the reduction mixture. When an authentic sample of 6-acetamido-6-deoxy-D-glucitol (**9**), one of the two predicted reduction products from **8**, was cochromatographed with the mixture, the larger peak was enhanced. It is quite reasonable that the other predicted reduction product, 6-acetamido-6-deoxy-L-iditol (**10**), is also responsible in part for the principal peak in the gas chromatogram of the mixture. However, an authentic sample of **10** was not available for direct chromatographic comparison. The compound that gave rise to the very early smaller peak in the chromatogram has not been identified.



The ketone **7** was also converted to a mixture of **9** and **10** by an alternative route. Sodium borohydride reduction of the carbonyl group of **7** gave a two-component mixture composed of the diastereoisomeric alcohols **5** and **11**. Identification of **5** in the mixture was ascertained by TLC comparison with a sample of authentic material derived from **4**. Clearly then, the other component of the mixture must be the L-idose derivative **11**. The isopropylidene groups of **5** and **11** were then removed by acid-catalyzed hydrolysis to give a mixture readily resolved by microcrystalline cellulose TLC into two compounds. The D-glucose derivative, 6-acetamido-6-deoxy-D-glucose (**12**), was identified as one of the compounds in the mixture by comparison with authentic material obtained from pure **5**. The other spot on the chromatogram must then correspond to 6-acetamido-6-deoxy-L-idose (**13**). Reduction of the aldehydo carbonyl of these two isomers with sodium borohydride gave, as determined by GLC, the same mixture that resulted from **7** by way of compound **8**. The conversion of **7** to the final acetamidodeoxyalditols **9** and **10** by this route was straightforward and without complication. The fact that the same products resulted from **7** by the first sequence, hydrolysis then reduction, supports the premise that the conversion of **7** to **8** proceeded as depicted.

Experimental Section

General Methods. Proton magnetic resonance spectra were recorded using a Varian Model HA-60-IL or HA-100 spectrometer, in deuteriochloroform solution with tetramethylsilane serving as the internal standard, or in deuterium oxide, with chemical shifts measured from the δ 1.23 signal of *tert*-butyl alcohol as an internal standard. The ir spectra were obtained on a Perkin-Elmer Model 337 grating infrared spectrometer and optical rotations were measured with a Perkin-Elmer Model 141 polarimeter at 20°. GLC was carried out on a Beckman GC-5 gas chromatograph fitted with a flame ionization detector, using 0.25 in. o.d. × 6 ft stainless steel columns containing 3% SE-30 on Gas-Chrom Q, 80–100 mesh (Applied Science Laboratories, State College, Pa.). The oven temperature was maintained at 160° and the helium flow rate at 37 ml/min. Silica gel (0.06–0.20 mm, 70–230 mesh, E. Merck, Darmstadt) was used for column chromatographic separations. Precoated silica gel GF and Avicel plates (250 μ, Analtech Inc., Newark, Del.) were used for thin layer chromatography. All melting points were obtained on a Fisher-Johns melting-point apparatus and are uncorrected. Galbraith Laboratories, Inc., Knoxville, Tenn., performed the elemental analyses.

3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-*xylo*-hexofuranos-5-ulose Dimethyl Acetal (1). Crude 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose dimethyl acetal (2.5 g), prepared by the method of Kiely and Fletcher,[7] was purified on a column of silica gel (ca. 150 g) by eluting with benzene–ether (1:10) and collecting 10-ml fractions. Fractions 65–100 contained the chromatographically pure material and were pooled and concentrated in vacuo, yield 1.2 g. To a solution of the syrupy dimethyl acetal (0.55 g) in 5 ml of anhydrous pyridine was added *p*-toluenesulfonyl chloride (0.93 g). The reaction mixture was briefly agitated and after remaining for 5 hr at room temperature, was shown, by TLC to contain no starting material. Enough water was added to dissolve the pyridine hydrochloride and the reaction mixture was left undisturbed for 1 hr. The solution was then poured into 50 ml of ice water, which in turn was extracted with two 30-ml portions of chloroform. The combined chloroform extracts, washed successively with water, aqueous sodium hydrogen carbonate, and water, were then dried (Na_2SO_4). After the solvent was removed in vacuo, a methanol solution of the residue was decolorized (Norit) and concentrated in vacuo at 38° to give an almost colorless, syrupy product (**1**), 0.72 g, 92%: ir (neat) no OH stretch; NMR δ 7.68 and 7.22 (each d, J = 8.0 Hz, $SO_2C_6\mathbf{H}_4CH_3$), 7.34 (s, $CH_2C_6\mathbf{H}_5$), 5.84 (d, $J_{1,2}$ = 3.5 Hz, H-1), 4.63–4.16 (overlapping signals from ring protons, $\mathbf{CH}_2C_6H_5$, and $\mathbf{CH}_2OTs$), 3.96 (d, J_{4-3} = 3.3 Hz, H-3 or H-4), 3.32 and 3.29 [each s, $C(OCH_3)_2$], 2.42 (s, $SO_2C_6H_4\mathbf{CH}_3$), 1.44 and 1.30 [each s, $C(\mathbf{CH}_3)_2$]. The tosylate **1** slowly decomposed at room temperature and was used in the next step without further purification.

Treatment of 1 with Sodium Azide in *N,N*-Dimethylformamide. To a solution of crude **1** (0.723 g) in *N,N*-dimethylformamide (30 ml) was added 1.6 g of sodium azide. The reaction mixture was refluxed for 4 hr, at the end of which time TLC [benzene–ether (1:1)] showed that no starting material was left. The solvent was removed in vacuo (*ca.* 1 mmHg) at 27° and the residue was extracted with chloroform. The combined chloroform extracts were dried (Na_2SO_4) and concentrated in vacuo to give a syrupy residue, which was chromatographed on a column of silica gel (ca. 25 g) by eluting with benzene–ether (9:2) and collecting 6-ml fractions. The pure fractions were pooled and concentrated in vacuo to a yellow

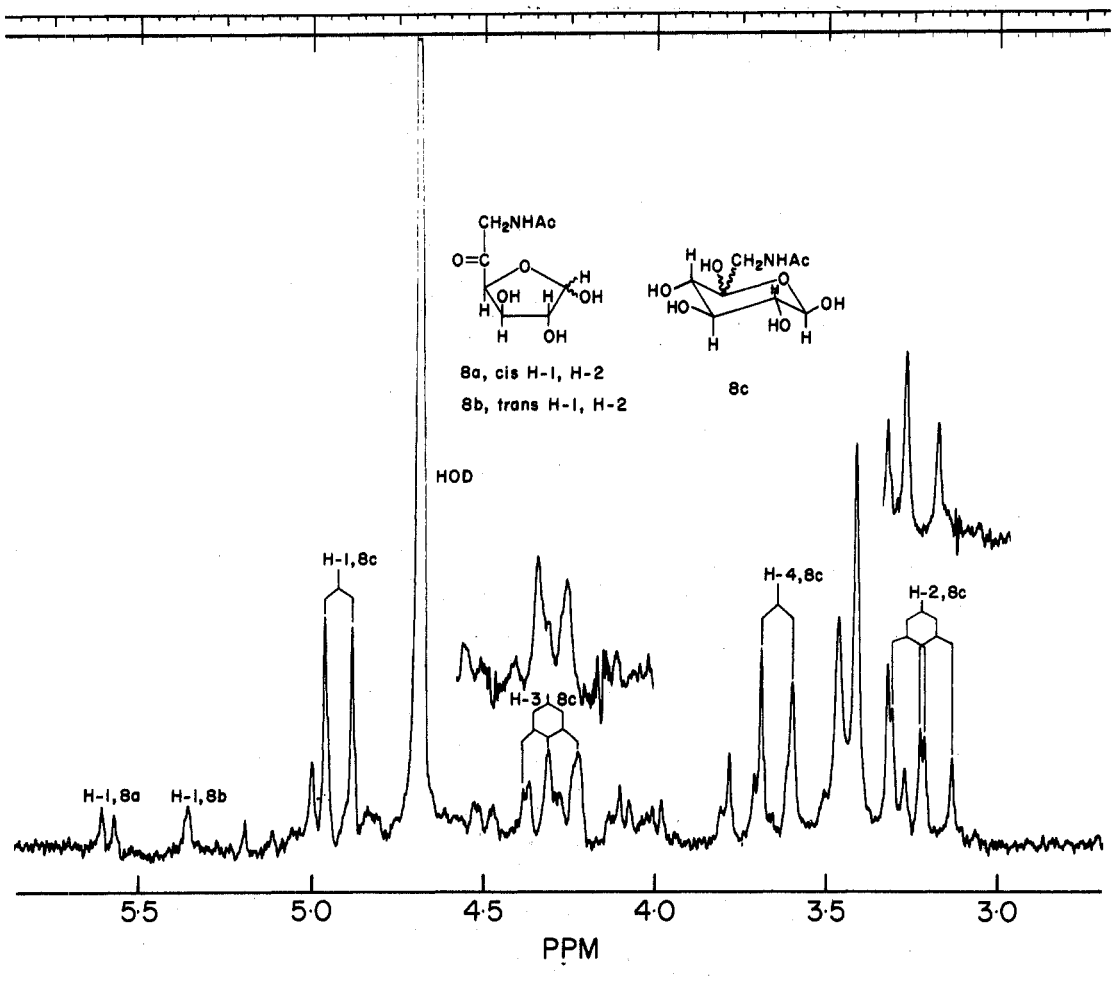


Figure 1. 100-MHz ^1H NMR spectrum of 8 (ring proton region) as a mixture of pyranose and furanose forms with decoupled signals at δ 3.27 and 4.28.

syrup. A solution of this material was decolorized (Norit) and concentrated in vacuo to give 3,6-anhydro-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose dimethyl acetal (**2**) as a colorless syrup, 0.22 g, 63%: $[\alpha]^{20}D$ +46° (*c* 1.17, chloroform); ir (Nujol) no N_3 absorption; NMR δ 5.98 (d, $J_{1,2}$ = 3.5 Hz, H-1), 4.60 (overlapping signals from H-2, H-3, and H-4), 3.95 and 3.57 (each d, J_{gem} = 10 Hz, C-6 protons), 3.42 and 3.30 [each s, $C(OCH_3)_2$], 1.48 and 1.33 [each s, $C(CH_3)_2$].

Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.53; H, 7.46.

6-Azido-6-deoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (4).[9] This compound was prepared by way of the known tosylate 3-*O*-benzyl-1,2-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (**3**).[9,17] Crude 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose[17] (2.11 g) was treated with *p*-toluenesulfonyl chloride (1.5 g) in the standard fashion, and the products separated by silica gel column chromatography. The monotosylate **3** was obtained chromatographically pure in 52% yield (1.65 g).

To a solution of **3** (1.6 g) in acetone (12 ml) was added 2 g of sodium azide in water (9 ml). After the reaction mixture was refluxed for 3 days, TLC [benzene–ether (1:1)] showed no unreacted starting material. The solvent was evaporated in vacuo and the residue was extracted with acetone (30 ml). Concentration of this solution in vacuo gave the organic product still contaminated with inorganic salts. This material was then successively extracted with acetone and chloroform to give the slightly yellow, chromatographically pure, syrupy **4**[9] (1.03 g, 86% from **3**), ir (neat) 2.87 (OH) and 4.74 μm (N_3). Saeki and Ohki described the conversion of **3** to **4** with sodium azide in methyl sulfoxide solution.[9]

Chromic Acid Oxidation of 4. Jones reagent (3 ml), prepared according to the method of Djerassi et al.,[4] was added to an ice-cold solution of **4** (1.8 g) in acetone (65 ml). The temperature of the reaction mixture was maintained at 0–5° and additional reagent (3-ml aliquots) was added after 1 and 2 hr, and again after 4 hr (2-ml aliquot). The reaction mixture, diluted with ether (400 ml), was washed with three 50-ml portions of water or until the organic layer was colorless. The ether solution was then dried ($MgSO_4$) and concentrated in vacuo to give a syrupy mixture (1.5 g) consisting mainly of the ketone **6**. The analytical sample of **6** was prepared by chromatographing a portion of the crude product (0.15 g) on a column of silica gel (8 g) with benzene–ether (92:8): yield 0.120 g of pure **6**; $[\alpha]^{20}D$ −121° (*c* 1.24, chloroform); ir (neat) 4.74 (N_3) and 5.75 μm (C=O); NMR δ 7.32 (m, $CH_2C_6H_5$), 6.07 (d, $J_{1,2}$ = 3.5 Hz, H-1), 4.77, 4.63, and 4.32 (each d, J = 3.5 Hz, three remaining ring protons), 4.66 and 4.45 (each d, estimated J_{gem} = 11 Hz, $CH_2C_6H_5$), 4.23 (s, CH_2N_3), 1.51 and 1.44 [each s, $C(CH_3)_2$].

Anal. Calcd for $C_{16}H_{19}N_3O_5$: C, 57.65; H, 5.75; N, 12.61. Found: C, 57.46; H, 5.64; N, 12.30.

6-Acetamido-6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (7) from 5. Hydrogenolysis of the azide **4** (1.8 g), in acetic acid (100 ml), at 2 atm of hydrogen with 10% palladium on carbon (1.6 g) was complete after 18 hr as seen by TLC [ether–methanol (9:1)]. The mixture was filtered and the filtrate, then diluted with an equal volume of acetic anhydride, was kept at room temperature for 3 hr. The solution, after dilution with water (100 ml), was concentrated in vacuo (ca. 1 mmHg) at 38° and the residue was triturated with ethyl acetate to give **5** (0.245 g). A second fraction of **5** (0.320 g) was recovered by addition of petroleum ether to the ethyl acetate wash, yield 38% from **4**. Recrystallization of the crude product from ethyl acetate–petroleum ether gave pure **5**, mp 162–163° (lit.[10] mp 164–165°).

Acetone (25 ml) was added to crude **5** (0.245 g) and the mixture was stirred vigorously for several minutes until dissolution was almost complete. Jones reagent (0.65 ml) was added to the cooled (−5°) solution, the reaction mixture was maintained at −5° for 1 hr and warmed to 5°, and a second aliquot of reagent (0.35 ml) was added to it. After an additional 9 hr, 6 hr at 5° and 3 hr at 25°, the reaction mixture contained no starting material as detected by TLC [ether–methanol (9:1)]. Excess acid was neutralized with sodium hydrogen carbonate and the reaction mixture was concentrated. The blue residue was extracted with benzene (100 ml) and then benzene–methanol (100 ml, 9:1) and the combined extracts

were concentrated to a blue oil. This material was chromatographed on a column of silica gel (ca. 20 g) with ether–methanol (95:5) and the 20-ml fractions containing the major component (7) were pooled and concentrated: yield of 7, 0.092 g (38% from 5 or 15% from 4); mp 114–115°; $[\alpha]^{20}D$ −102° (c 0.419, chloroform); ir (KBr) 5.75 (ketone C=O), 6.05 (acetamido C=O), and 6.45 μm (NH); NMR ($CDCl_3$) δ 6.72 (t, J_{NH,CH_2} = 5.0 Hz, NH, exchanged in D_2O), 6.12 (d, $J_{1,2}$ = 3.5 Hz, H-1), 4.8–4.5 (unresolved signals from ring protons), 4.28 (d, J_{NH,CH_2} = 5.0 Hz, C-6 protons, changed to s after addition of D_2O), 2.07 (s, NHAc), 1.50 and 1.35 [each s, $C(CH_3)_2$]; NMR (D_2O) δ 6.12 and 4.98 (each d, $J_{1,2}$ = 3.5 Hz, H-1 and H-2), 4.63 (HOD and remaining ring protons), 4.25 (s, C-6 protons), 2.05 (s, NHAc), 1.48 and 1.37 [each s, $C(CH_3)_2$].

Anal. Calcd for $C_{11}H_{17}NO_6$: C, 50.96: H, 6.61; N, 5.40. Found: C, 50.75; H, 6.52; N, 5.25.

6-Acetamido-6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (7) from 6. Crude 6 (1.45 g) in acetic acid (80 ml) was agitated for 18 hr at 2 atm of hydrogen with 10% palladium on carbon. The suspension, after being diluted with acetic anhydride (40 ml) and left to stand at room temperature for 2 hr, was seen by TLC [ether–methanol (9:1)] to contain one major product. The suspension was filtered, and the filtrate, after dilution with water (40 ml), was kept at 0° for 3 hr. The aqueous acetic acid was removed by lyophilization and the syrupy residue was chromatographed on a column of silica gel (ca. 60 g) with ether–methanol (95:5) to give white, crystalline 7, mp 113–114°, yield 0.47 g (33% from 4).

6-Acetamido-6-deoxy-D-*xylo*-hexos-5-ulose (8). An acid form cation exchange resin (0.3 ml, AG 50W-X2, 200–400 mesh, Bio-Rad Laboratories, Richmond, Calif.) was added to an aqueous solution (1.5 ml) of 7 (10 mg). The reaction mixture was then maintained at 45°, without stirring, for 18 hr. Microcrystalline cellulose TLC [ethyl acetate–pyridine–water (2:1:2) upper phase[18]], in conjunction with the ammoniacal silver nitrate spray reagent,[19] showed that the hydrolysate was composed of a single reducing sugar (8), R_f 0.41. The resin was removed by filtration and after the aqueous wash (0.5 ml) was added to the filtrate. The filtrate was concentrated to a gum by freeze drying: ir (KBr) 2.97 (OH), 5.75 (ketone C=O), and 6.05 μm (acetamido C=O). A solution of the residual gum in deuterium oxide was prepared and after 1 hr at room temperature the solvent was removed by freeze drying. This process was repeated twice more in order to minimize the HOD peak in the NMR spectrum of the material: NMR (D_2O) δ 5.60 (d, J = 4.0 Hz, H-1, 8a), 5.37 (s, H-1, 8b), 4.93 (d, J = 8.0 Hz, H-1, 8c), 4.69 (HOD), 4.28 (m over a q, H-3, 8c, and unassigned signals), 3.65 (d, J = 9.2 Hz, H-4, 8c), 3.48 and 3.40 (each s, H-6 protons), 3.27 (d of d, $J_{1,2}$ = 8.0 and $J_{2,3}$ = 9.2 Hz, H-2, 8c), and 2.09, 2.06, and 2.03 (each s, NHAc, in the ratio of 1:5.5:8.7). Additional unresolved signals were observed at δ 5.11, 4.93 (under the H-1 signal of 8c), 4.28, 4.11, and 3.80, but no signal was observed for an aldehyde proton. Lowering the temperature of the probe from the normal operating temperature (32°) to 7.5° shifted the HOD peak from δ 4.69 to δ 5.0, but no additional signals were seen at the higher frequency. Results from the decoupling experiments are described in the discussion section.

Compounds 9 and 10 from 7. Sequence A, by Way of 8. Sodium borohydride (13 mg) was added to the hydrolysate from 7 and the reaction mixture was left to stand at room temperature for 18 hr. The aqueous solution was treated with an acid form cation exchange resin until hydrogen evolution ceased, the resulting mixture was filtered, and the filtrate and aqueous washings were freeze dried. After the boric acid was removed from the residue as its volatile trimethyl ester, the remaining material was treated with a trimethylsilylating reagent[20] (800 μl). This reaction was brought almost to boiling and then left at room temperature for 2 hr. A sample of the mixture was analyzed by GLC giving a chromatogram with two major peaks (ratio ~ 9:1), retention times of 12.4 and 6.3 min, respectively. The larger peak was unsymmetrical and increased in size when the mixture was cochromatographed with the trimethylsilyl derivative of authentic 9.

Sequence B, by Way of 12 and 13. Sodium borohydride (15 mg) was added to a solution of 7 (13.5 mg) in water (1 ml). The reaction mixture was kept at room temperature for 1 day and then worked up by the procedure described in sequence A. Silica gel TLC [ether–methanol (9:1)] showed a mixture of two components, R_f 0.35 and 0.20. The component of higher R_f value gave a spot indistinguishable from that of 6-acetamido-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (5). An authentic sample of the L-idose derivative 11 was not available for TLC comparison. The protecting isopropylidene groups were then removed from the two compounds in the mixture by resin-catalyzed acid hydrolysis. The hydrolysate contained two reducing sugars of R_f 0.33 and 0.43, as determined by microcrystalline cellulose TLC using the previously mentioned ethyl acetate–pyridine–water system. The component of R_f 0.33 gave a spot identical with that from 6-acetamido-6-deoxy-D-glucose (12), obtained by acid hydrolysis of pure 5. The mixture was then treated with sodium borohydride and the reduction products were analyzed by GLC. The resulting chromatogram was essentially the same as that obtained via sequence A.

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References and Notes

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