Anomeric Equilibria in Derivatives of Amino Sugars. Nuclear Magnetic Resonance Studies on Acetylated Amino Sugars and Specifically Deuterated Analogs[1-4]

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Acetylation of derivatives of 2-amino-2-deoxy-D-glucose and 2-amino-2-deoxy-D-mannose with acetic anhydride-d_6 permitted definitive assignment of the signal for the *N*-acetyl methyl group in the nuclear magnetic resonance (nmr) spectra of the pyranose pentaacetates of the two amino sugars, and some related derivatives. The anomeric compositions of the mixtures formed by acetylation of the amino sugars, and a number of simple sugars, with acetic anhydride in pyridine, were investigated. Aryl substituents in acetylated sugar derivatives are shown to cause shielding of certain acetyl groups, with the result that, in chloroform-*d*, the nmr signals of these acetyl groups are observed at unusually high field.

In the nmr spectra of poly-*O*-acetylated aldopyranoses, measured in chloroform-*d*, the signal for the 1-acetoxy group may be assigned[5] by comparison of the spectra of a pair of anomers; the signal position is usually to lower field than the signals of the other acetoxy groups, and the signal is observed at lower field when the acetoxy group is axial than when it is equatorial. On this basis, assignments have been made[6] for the 1-acetoxy group of the anomeric 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α- (and β-) D-glucopyranoses (**2** and **13**) and their 2-(2,4-dinitroanilino) analogs **7** and **20**; these assignments are in agreement with anomeric assignments based on the first-order coupling constant observed for the signal of H-1 in each of the derivatives. (See Chart I.)

No firm criteria exist for the assignment of the signals of acetoxy group at other ring positions, although the principle that axial acetoxy groups give signals at lower field than equatorial acetoxy groups appears generally valid,[7-13] and it has been proposed[7-11] that the highest field acetoxy signal is normally that of a primary acetoxy group; these tentative assignments are, however, unreliable[13] as evidence for structure.

The derivatives **2**, **7**, **13**, and **20** all show one of the acetyl group signals at high field (τ ~8.09–8.12). It has been reported[7,14-16] that equatorial acetamido groups given signals in the region τ 8.04–8.10. However, since only two of the four derivatives have acetamido groups, a tentative assignment[6] of the high-field signal in each of the derivatives to the primary acetoxy group,[7-11] rather than the acetamido group, has been made.

Synthesis of specifically deuterated derivatives, and direct comparison by nmr of the deuterated and nondeuterated compounds, provides a completely unambiguous method for assigning specific signals in nmr spectra. In this paper, the deuteration procedure is used for definitive identification of the signals of acetamido methyl groups. It is shown that methods based on comparison of related derivatives are unreliable for assignments of acetyl group signals. Aryl substituents may have a pronounced effect on the chemical shift of individual acetyl group signals in nmr spectra.

Assignment of Acetamido Methyl-Group Signals by Means of Specifically Deuterated Derivatives.—The anomeric 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α- (and β-) D-glucopyranoses (**2** and **13**) were compared by nmr with the corresponding analogs **3** and **14** that had been specifically deuterated in the *N*-acetyl methyl group. The spectrum of **3** was identical with that of **2**, except that the three-proton singlet at τ 8.09 in the spectrum of **2** was absent, and the latter signal can thus be unambiguously assigned to the *N*-acetyl methyl group in **2**. Similarly, the spectrum of **14** was identical with that of **13**, except that a three-proton singlet at τ 8.09 in the spectrum of **13** was absent in the spectrum of **14**. The signal at τ 8.09 is thus identified as that of the *N*-acetyl methyl group in each of these compounds. The specifically deuterated **3** and **14** were prepared by acylating 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrochloride[17,18] (for **3**) or its β-D anomer[18,19] (for **14**) with acetic anhydride-d_6 in pyridine. No O → N acyl migration occurred under the reaction conditions. If migration had occurred, the intensity of the three-proton singlet for the 1-*O*-acetyl group would have been diminished or the signal would have disappeared altogether. Furthermore, acetylation of 2-acetamido-2-deoxy-α-D-glucopyranose (**26**) with acetic anhydride-d_6 gave the tetra-*O*-trideuterioacetylated analog **29** of **2**, whose nmr spectrum showed only one signal, a three-proton singlet at τ 8.09, in the region where acetyl group signals are observed. This signal most be that of the *N*-acetyl methyl group, since

(1) Previous paper in this series: D. Horton, J. S. Jewell, and Kerstin D. Philips, *J. Org. Chem.*, **31**, 4022 (1966).

(2) A preliminary report of part of this work has been given: D. Horton, Abstracts, 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965, p 5D.

(3) Supported in part by Grants-in-Aid No. 19187 and 170200 from The Ohio State University Development Fund.

(4) Funds for purchase of the nmr spectrometer were provided by the National Science Foundation, Washington, D. C.

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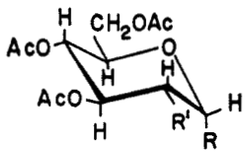
CHART I



1 R = −OAc R′ = −OAc

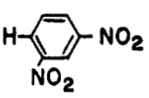
2 R = −OAc R′ = −NHAc

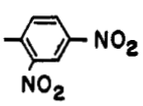
3 R = −OAc R′ = −NHCOCD$_3$

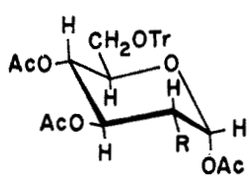
4 R = −Cl R′ = −NHAc

5 R = −Cl R′ = −NHCOCD$_3$

6 R = −OAc R′ = −NHCO$_2$CH$_2$Ph

7 R = −OAc R′ = 

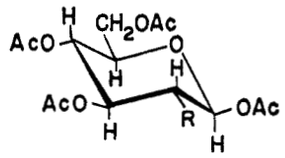
8 R = −Br R′ = 



9 R = −OAc

10 R = −NHAc

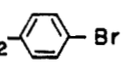
11 R = −NHCOCD$_3$

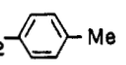


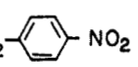
12 R = −OAc

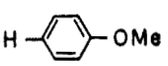
13 R = −NHAc

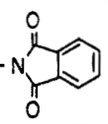
14 R = −NHCOCD$_3$

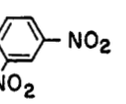
15 R = 

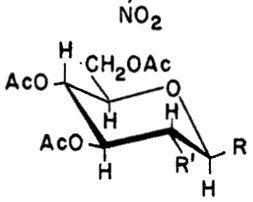
16 R = 

17 R = 

18 R = 

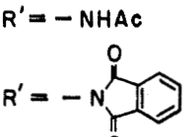
19 R = 

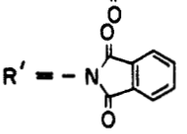
20 R = 



21 R = −OCHMe$_2$ R′ = −NHAc

22 R = −OCMe$_3$ R′ = −NHAc

23 R = −Br R′ = 

24 R = −Cl R′ = 

25 R = −SAc R′ = −NHAc

there is no driving force for N → O acetyl migration[20] in pyridine solution. (See Chart II.)

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (**4**) was compared by nmr with the analog (**5**) that had been specifically deuterated in the *N*-acetyl methyl group. The signal of the acetamido methyl group in **4** was thus shown to be a three-proton singlet at τ 7.99. The deuterated derivative **5** was prepared by selective *N*-acetylation of 2-amino-2-deoxy-D-glucose with acetic anhydride-d_6, to give 2-deoxy-2-trideuterioacetamido-α-D-glucopyranose (**27**), followed by treatment of the latter with acetyl chloride.

The signal of the acetamido methyl group in 2-acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-6-*O*-trityl-α-D-glucopyranose[21] (**10**) was identified as the three-proton singlet at τ 8.08, since the latter signal was absent in the corresponding derivative (**11**) that had been deuterated specifically in the *N*-acetyl methyl group. It is noteworthy that, in substance **10**, the signal of the *N*-acetyl methyl group is not the highest field, acetyl group-signal; another three-proton singlet is observed at τ 8.28. Similarly, in 1,2,3,4-tetra-*O*-acetyl-6-*O*-trityl-α-D-glucopyranose (**9**), the signal of one of the acetyl groups is observed at exceptionally high field.

In the case of the D-*manno* analogs **30** and **32** of **2** and **13**, the signal of the *N*-acetyl methyl group was assigned by acetylation of 2-acetamido-2-deoxy-β-D-mannopyranose (**34**) monohydrate with acetic anhydride-d_6. The crystalline β-D pentaacetate **32** can be prepared[22-24] in about 55% yield by acetylation of 2-

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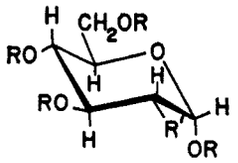
CHART II

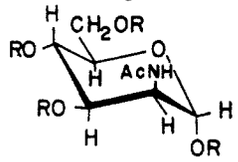


26 R = H R′ = NHAc

27 R = H R′ = $NHCOCD_3$

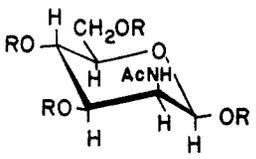
28 R = $COCD_3$ R′ = $NHCOCD_3$

29 R = $COCD_3$ R′ = NHAc



30 R = Ac

31 R = $COCD_3$



32 R = Ac

33 R = $COCD_3$

34 R = H

amino-2-deoxy-D-mannose hydrochloride[22] or the *N*-acetyl derivatives,[24] in pyridine, with a large excess of acetic anhydride. In the present work, the acetylation was performed by treating anomerically pure[1] 2-acetamido-2-deoxy-β-D-mannopyranose (**34**) in pyridine with a slightly more than stoichiometric proportion of acetic anhydride-d_6, to give crystalline 2-acetamido-2-deoxy-1,3,4,6-tetra-*O*-trideuterioacetyl-β-D-mannopyranose (**33**). The nmr spectrum of the latter showed a three-proton singlet at τ 7.92, which can be assigned to the acetamido methyl group, since there is no driving force for N → O acetyl migration[20] under the basic reaction conditions used in the preparation of **33**.

The mother liquors from the preparation of **33** contained some of the α-D anomer **31**, and indicated that a limited amount of mutarotation had occurred during the acetylation. The signal for the *N*-acetyl methyl group in **31** was observed at τ 7.96. The anomers **31** and **33** thus resemble the anomeric 2-acetamido-2-deoxy-D-mannopyranoses[1] in that the signal of the *N*-acetyl methyl group has a different chemical shift according to the anomeric disposition. In the D-*manno* series the 2-acetamido group is axial in the favored conformation. In the D-*gluco* series (where the acetamido group is equatorial in the favored conformation) there is no observed difference between anomers in the chemical shift of the *N*-acetyl methyl group.

The nondeuterated analogs **30** and **32** of **31** and **33** showed nmr signals for the *O*-acetyl groups that overlapped the positions of the signals for the *N*-acetyl group. The signal for the *N*-acetyl group cannot, therefore, be observed independently in the spectrum of **32**.

Relative Chemical Shifts of Signals of Acetyl Groups.—The definitive assignment of the signal at τ 8.09 to the equatorial acetamido group, and the signal at τ 7.92–7.96 to the axial acetamido group, in the peracetylated 2-amino-2-deoxy-D-gluco- (and D-manno-) pyranoses accords with assignments proposed for acetylated inosamine derivatives, and acetylated derivatives of some amino sugars from antibiotics.[15,16,25]

It can be seen (Table I) that many derivatives that do not contain an acetamido group, nevertheless, exhibit signals near or above τ 8.10. In each case where this is observed, an aryl group is present. It is evident, therefore, that an aryl group in the molecule causes shielding of one or more of the acetyl groups, with the result that the signals of these acetyl groups are observed at unusually high field. Particularly large upfield shifts are observed when the trityl group is present. The effect is reminiscent of the large upfield shifts

TABLE I

CHEMICAL SHIFTS OF ACETYL METHYL PROTONS

Compd	Chemical shifts,[a] τ (integral, protons)
1	7.82 (3), 7.92 (3), 7.98 (6), 7.99 (3)
2	7.81 (3), 7.93 (3), 7.98 (6), 8.09[b] (3)
3	7.81 (3), 7.93 (3), 7.98 (6)
4	7.92 (3), 7.96 (6), 7.99[b] (3)
5	7.92 (3), 7.96 (6)
6	7.94 (3), 8.01 (3), 8.10 (1.5), 8.15 (1.5)
7	7.71 (3), 7.89 (3), 7.94 (3), 8.12[c] (3)
8	7.89 (3), 7.93 (3), 8.15 (3)
9	7.84 (3), 7.92 (3), 8.03 (3), 8.27 (3)
10	7.84 (3), 7.97 (3), 8.08[b] (3), 8.27 (3)
11	7.84 (3), 7.97 (3), 8.27 (3)
12	7.90 (3), 7.93 (3), 7.97 (6), 7.98 (3)
13	7.89 (3), 7.93 (3), 7.97 (6), 8.09[b] (3)
14	7.89 (3), 7.93 (3), 7.97 (6)
15	7.92 (3), 7.97 (3), 8.10 (3), 8.16 (3)
16	7.92 (3), 7.98 (3), 8.15 (3), 8.18 (3)
17	7.90 (3), 7.94 (3), 8.10 (3), 8.14 (3)
18	7.94 (3), 8.00 (3), 8.02 (3), 8.16 (3)
19	7.90 (3), 7.94 (3), 8.01 (3), 8.12 (3)
20	7.81 (3), 7.93 (3), 8.00 (3), 8.09 (3)
21	7.90 (3), 7.94 (6), 8.02 (3)
22	7.99 (3), 8.00 (6), 8.10 (3)
23	7.85 (3), 7.95 (3), 8.12 (3)
24	7.88 (3), 7.97 (3), 8.13 (3)
25	7.60[d] (3), 7.93 (3), 7.94 (6), 8.08 (3)
26	7.96 (3)
27[e,f]	
28[f]	
29	8.09[b] (3)
31	7.96[b] (3)
32	7.92 (9), 7.93 (3), 8.00 (3)
33	7.92[b] (3)
34[e]	7.92 (3)

[a] Measured at 60 Mcps in chloroform-*d*, unless otherwise stated. [b] Identified by deuterium labeling as the signal of the acetamido methyl protons. [c] Given incorrectly as 8.02 in ref 6. [d] Signal of *S*-acetyl methyl protons. [e] Measured in deuterium oxide. [f] No acetyl signals observed.

(25) H. Agahigian, G. D. Vickers, M. H. von Saltza, J. Reid, A. I. Cohen, and H. Gauthier, *J. Org. Chem.*, **30**, 1085 (1965).

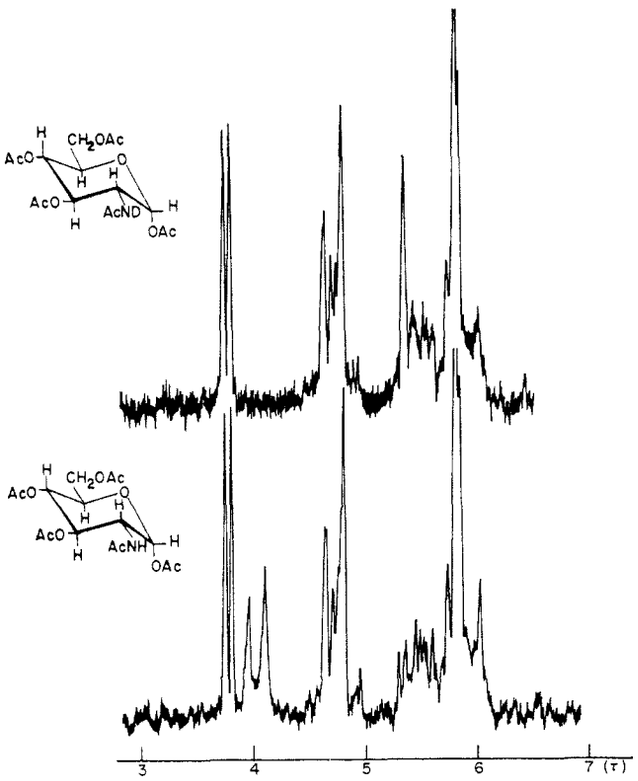


Figure 1.—The low-field portion of the nmr spectrum of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose (**2**) in chloroform-*d* at 60 Mcps, before and after deuteration.

of acetyl group signals observed when the nmr spectra of acetylated sugars are measured in benzene, rather than in chloroform.

It is known[26] that groups near an aromatic nucleus experience either shielding or deshielding, according to whether they are perpendicular to, or parallel to, the plane of the ring. The use of molecular models suggest some reasonable positional assignments to the high-field signals,[16] but detailed discussion of these assignments is reserved until data on specific deuteration at individual acetoxy groups are compiled. Firm assignments by the latter method will provide a means for determining the favored spatial disposition of the aryl substituent groups.

Preparation of Derivatives.—Most of the compounds used in this study were prepared by standard methods in the literature, or by simple adaptations thereof, and details are given in the Experimental Section.

The *t*-butyl glycoside derivative **22** was obtained in modest yield by a modified[27,28] Königs–Knorr reaction, with mercuric cyanide as the condensing agent, in benzene solution.

2-Acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-6-*O*-trityl-α-D-glucopyranose[21] (**10**) was obtained anomerically pure, and in essentially quantitative yield, by treating 2-acetamido-2-deoxy-α-D-glucopyranose (**26**) in pyridine with an equivalent of chlorotriphenylmethane for 4 days at room temperature, followed by treatment with an excess of acetic anhydride; the 2-trideuterioacetamido analog **11** was similarly prepared, starting from **27**. The procedure is a useful preparative method for **10** because the formation of the β-D anomer and a 1,6-di-*O*-trityl derivative under these conditions is negligible. In contrast, a mixture of products is obtained[21] when the reaction mixture is heated. Substance **10** showed a great propensity for the formation of solvates.

2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-mannopyranose (**30**), encountered as a side product in the preparation of its anomer **32**, was obtained, following Levene,[22] by anomerization of **32** in acetic anhydride containing zinc chloride. Darkening of the solution precluded observation of the equilibrium by polarimetry, but nmr measurements revealed that, at equilibrium, about 80% of **30** was present; no acyclic or furanose forms could be detected. The α-D anomer **30** was recognized by the appearance of a doublet, τ 3.98, $J_{1,2}$ = 1.7 cps, assigned to H-1 of **30**. Separation of **30** from the remaining β-D anomer **32** in the mixture was not achieved.

Analysis of Nmr Spectra.—The ring-proton regions of the spectra[2,6,29] of the anomeric pentaacetates **2** and **13** of 2-amino-2-deoxy-D-glucopyranose are closely similar to those of the anomeric pentaacetates of D-glucopyranose,[13] and the spectrum of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-mannopyranose[2,29] (**32**) is similar to that of β-D-mannopyranose pentaacetate.[13] An exception is noted, however, in the chemical shift of the H-2 signal, which is observed about 0.7 ppm to higher field for the 2-acetamido derivatives than for the 2-acetoxy analogs. The H-2 signal is readily located in the spectra, even when the multiplet is poorly resolved, because the signal changes in appearance when the sample is deuterated, owing to removal of coupling between H-2 and the NH proton (Figure 1); the coupling of H-2 with deuterium on the nitrogen atom is of much smaller magnitude. Details of the assignments are given in the Experimental Section.

The anisotropy of the aryl substituents affects the chemical shifts, not only of certain acetyl groups, but also those of certain ring protons. Preparation of suitable aryl derivatives of sugars may constitute a useful technique for obtaining a first-order interpretation of the signals of the ring protons, without the necessity for measurements at higher field strengths. An example is provided in the spectrum of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-6-*O*-trityl-α-D-glucopyranose (**10**) (Figure 2). When the spectrum is compared with that of the 6-*O*-acetyl analog **2** at the same field strength (Figure 1), it can be seen that the trityl group causes considerable shielding of the H-6 protons, so that a first-order interpretation, as the AB portion of an ABXY system, can readily be made. Since the AX and BX first-order coupling constants can be measured, and since the H-5 signal is readily recognized, it is possible to determine the approximate coupling of H-5 with H-4. The latter is very useful in assignments[12] of configuration and conformation. The H-2 signal in the spectrum of **10** is readily assigned, because the signal, originally a multiplet, appears after deuteration as a broadened quartet.

The spectrum of 1,2,3,4-tetra-*O*-acetyl-6-*O*-trityl-α-D-glucopyranose (**9**) can be analyzed in the same manner as that of **10**, except that the H-2 signal could not

(26) C. E. Johnson, Jr., and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).
(27) B. Helferich and K. F. Wedemeyer, *Ann.*, **563**, 139 (1949); *cf.* B. Lindberg, *Acta Chem. Scand.*, **3**, 151 (1949).
(28) M. L. Wolfrom, W. A. Cramp, and D. Horton, *J. Org. Chem.*, **29**, 2302 (1964).
(29) T. D. Inch, J. R. Plimmer, and H. G. Fletcher, Jr., *ibid.*, **31**, 1825 (1966).

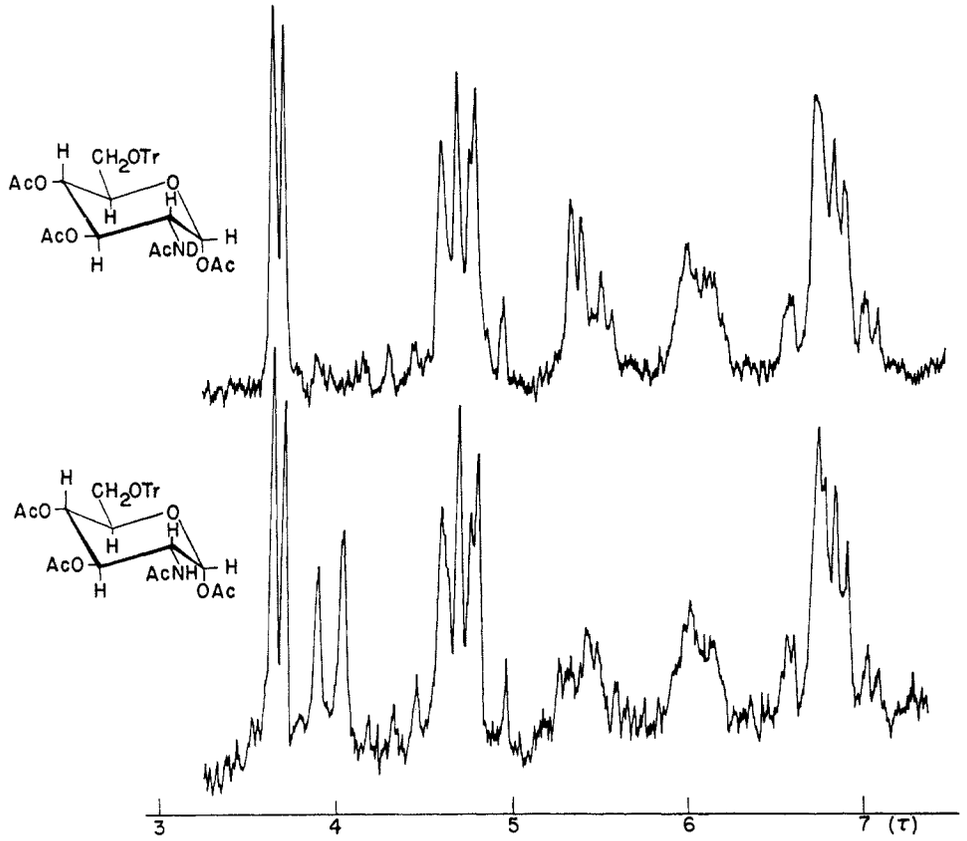


Figure 2.—The low-field portion of the nmr spectrum of 2-acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-6-*O*-trityl-α-D-glucopyranose (**10**) in chloroform-*d* at 60 Mcps, before and after deuteration.

be specifically identified; it was observed, as expected, at considerably lower field.

The spectrum of methyl 3,4,6-tri-*O*-acetyl-2-[(benzyloxycarbonyl)amino]-2-deoxy-α-D-glucopyranoside (**6**) suggests that there is hindered rotation about the NCO bond at room temperature, since the signal for the methoxyl group, and also the signal for one of the acetyl groups, appear split, indicating that slowly interconverting rotomers may be involved. Details of this phenomenon, with **6** and some related derivatives will be the subject of a separate report.[30]

Acetylation Experiments.—It has been noted that acetylation of 2-acetamido-2-deoxy-β-D-mannose monohydrate with acetic anhyidride in pyridine at room temperature gave the β-D pentaacetate **32**, together with about 20% of the α-D anomer **30**. Under similar conditions of acetylation, a 9:11 mixture of **30** and **32** was formed from crystalline 2-amino-2-deoxy-D-mannose hydrochloride. The latter has been shown[31] to be a co-crystallized mixture of anomers.

Acetylation of crystalline β-D-mannopyranose with acetic anhydride–pyridine gave a 1:3 mixture of the pentaacetates of the α-D and β-D anomers, whereas acetylation of a syrup, prepared by rapid evaporation of a solution of D-mannose at mutarotational equilibrium, gave a 7:3 mixture of the acetylated α-D- and β-D-pyranose anomers. The latter composition is close to that of the pyranose anomers at equilibrium.[32,33]

Similar results were observed upon acetylation of syrups prepared by rapid evaporation of equilibrated aqueous solutions of D-galactose, D-glucose, D-xylose, and 2-amino-2-deoxy-D-glucose hydrochloride. Acetylation of the crystalline α-D-pyranose anomers of the latter sugars with acetic anhydride–pyridine gave essentially only the α-D-pyranose pentaacetates, except in the case of D-galactose. D-Ribose, either as the crystalline β-D-pyranose form, or after mutarotation, gave a mixture, mainly of the pyranose tetraacetates, with the β-D anomer preponderating. A detailed discussion of these data will be presented[30] in comparison with results on sugars of other configurations.

Experimental Section[34]

2-Deoxy-2-trideuterioacetamido-α-D-glucopyranose (27).—2-Amino-2-deoxy-α-D-glucopyranose hydrochloride (2.75 g) was *N*-acetylated[35] with acetic anhydride-d_6 (1.5 ml) to give crystalline **27** in 95% yield, mp 200–202°. Its nmr spectrum in deu-

(30) D. Horton, J. S. Jewell, and Kerstin D. Philips, to be published.

(31) D. Horton, J. S. Jewell, and Kerstin D. Philips, *J. Org. Chem.*, **31**, 3843 (1966).

(32) H. S. Isbell, *J. Res. Natl. Bur. Std.*, **66A**, 233 (1962).

(33) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y., 1965, p 408.

(34) Melting points were determined with a Thomas–Hoover Unimelt apparatus (Arthur H. Thomas Co., Philadelphia, Pa.). Specific rotations were measured in a 2-dm tube. Infrared spectra were measured with a Perkin-Elmer Infracord infrared spectrometer. Nmr spectra were measured with a Varian A-60 spectrometer. Unless otherwise stated, spectra were measured at about 40° on *ca.* 10% solutions in chloroform-*d*, with tetramethylsilane (τ 10.00) as the internal standard. For spectra measured in deuterium oxide, the internal standard was sodium 4,4-dimethyl-4-silapentane-1-sulfonate (τ 10.00). The recorded first-order coupling constants are the measured peak spacings. Elemental analyses were performed by W. N. Rond. X-Ray powder diffraction data give interplanar spacings, A, for Cu Kα radiation. 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 with Desaga equipment, with silica gel G (E. Merck, Darmstadt, Germany), activated at 110°, as the adsorbent and indication was effected with sulfuric acid.

(35) D. Horton, *Biochem. Prepn.*, **11**, 1 (1966).

terium oxide was identical with that[1] of **26**, exceptth at there was no signal near τ 8.0.

3,4,6-Tri-*O*-acetyl-2-deoxy-2-trideuterioacetamido-α-D-glucopyranosyl Chloride (5).—Substance **27** (1.16 g) was treated with acetyl chloride, by the procedure[36] used for conversion of **26** into **4**, to give **5**, yield 1.07 g, mp 125–127°. The product had an nmr spectrum identical with that[12] of **4**, except that the three-proton singlet at τ 7.99 was absent.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-trideuterioacetamido-α-D-glucopyranose (3).—This product was prepared by an adaptation of the procedure[6] used for preparation of the nondeuterated analog (**2**). To 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrochloride[17,18] (183 mg) was added, in rapid succession, dry pyridine (3.5 ml) and acetic anhydride-d_6 (0.052 ml). After 18 hr at room temperature, the solution was poured into ice and water (25 ml), and after 30 min the mixture was extracted with five 10-ml portions of chloroform. The extract was dried (magnesium sulfate), evaporated, the residue was codistilled several times with toluene, and the crystalline residue was recrystallized from methanol–ether to give **3** having melting point and X-ray powder diffraction pattern indistinguishable from those[6] of a sample of **2**. The nmr spectrum of **3** was identical with that[6] of **2**, except that the three-proton singlet at τ 8.09 in the spectrum of **2** was absent in the spectrum of **3**. The low-field portion of the spectrum of **3** (or **2**), measured before and after deuteration (Figure 1) yielded the following data: τ 3.82 (one-proton doublet, $J_{1,2}$ = 3.5 cps, H-1) (lit.[6] τ 3.82, $J_{1,2}$ = 3.5 cps), 4.04 (one-proton broadened doublet, J = 8.5 cps, shift varies with change in concentration, disappears on deuteration, NH), 4.45–4.95 (two-proton multiplet, H-3,4), 5.51 (one-proton multiplet, collapses on deuteration to broadened quartet, $J_{2,3}$ = ~9 cps, H-2), and 5.70–6.15 (three-proton multiplet, H-5,6,6′).

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-trideuterioacetamido-β-D-glucopyranose (14).—1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride[18,19] was converted into **14** by a procedure essentially the same as that employed in the preceding experiment for preparation of **5**. The nmr spectrum of **14** was identical with that[6,29] of the nondeuterated analog **13**, except that a three-proton singlet at τ 8.09 in the spectrum of **13** was absent in that of **14**. The spectrum of **14** (or **13**) gave the following data: τ 4.27 (one-proton doublet, $J_{1,2}$ = 8.6 cps, H-1) (lit.[6] τ 4.27, $J_{1,2}$ = 8.5 cps), 3.75 (one-proton broadened doublet, J = 9.5 cps, shift varies with concentration, disappears on deuteration, NH), 4.58–5.11 (two-proton multiplet, H-3,4), 5.58 (one-proton multiplet, multiplicity diminished on deuteration, H-2), 5.70–5.95 (two-proton multiplet, H-6,6′), and 6.14 (one-proton multiplet, width ~18 cps, H-5).

2-Acetamido-2-deoxy-1,3,4,6-tetra-*O*-trideuterioacetyl-α-D-glucopyranose (29).—Treatment of crystalline 2-acetamido-2-deoxy-α-D-glucopyranose (**26**, 100 mg) with pyridine (0.2 ml) and acetic anhydride-d_6 (2 ml) for 18 hr at room temperature, followed by processing as described for **3** gave crystalline **29**, having melting point and X-ray powder diffraction pattern indistinguishable from those of **2**. The nmr spectrum of **29** was identical with that of **2**, except that only one signal, a three-proton singlet at τ 8.09, was observed in the acetyl group region. Acetylation of **27** similarly gave **28**.

2-Acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-6-*O*-trityl-α-D-glucopyranose (10).—A mixture of 2-acetamido-2-deoxy-α-D-glucopyranose[35] (**26**, 45 g) and chlorotriphenylmethane (57.5 g) in dry pyridine (400 ml) was shaken at room temperature until a clear solution was obtained (4 days), and then acetic anhydride (100 ml) was added with cooling. After the initial reaction had moderated, the solution was kept for 2 days at room temperature and then poured into ice and water (2 l.). The precipitated solid was filtered, washed with water, and dried, yield 117 g (99%). The nmr spectrum of the product showed that it contained no detectable proportion of the β-D anomer.[37] Recrystallization from chloroform gave a gelatinous, microcrystalline product that upon drying at 56° had mp 156–157°, $[\alpha]^{20}D$ +106° (*c* 1, chloroform) [lit.[21] mp 154–156°, $[\alpha]D$ +97° (*c* 1.2, chloroform)]; R_f 0.2 (3:1 chloroform–ether); λ_{max}^{KBr} 5.70 (OAc), 6.02, 6.50 (NHAc), 13.2–13.4, and 14.25 μ (aryl); nmr data (see Figure 2), τ 2.43–2.91 (15-proton multiplet, trityl), 3.69 (one-proton doublet, $J_{1,2}$ = 3.5 cps, H-1), 4.10 (one-proton broadened doublet, J = 9 cps, shift varies with concentration, disappears on deuteration, NH), 4.47–4.98 (two-proton multiplet, H-3,4), 5.47 (one-proton multiplet, changes on deuteration to broadened quartet, $J_{2,3}$ = ~10 cps, H-2), 6.10 (one-proton multiplet, width ~18 cps, H-5), 6.68 (one-proton quartet, $J_{5,6}$ = 2.8 cps, $J_{6,6'}$ = 11 cps, H-6), and 6.98 (one-proton quartet, $J_{5,6}$ = 4 cps, H-6′); X-ray powder diffraction data, 14.98 m, 10.92 s (2), 9.03 vw, 8.12 vw, 7.12 m, 6.39 w, 5.53 w, 5.07 s (1,1), 4.22 s (1,1), and 3.76 m.

Anal. Calcd for $C_{33}H_{35}NO_9$: C, 67.22; H, 5.98; N, 2.38. Found: C, 67.26; H, 6.10; N, 2.18.

The *N*-trideuterioacetylated analog **11** was prepared, starting from **27**, by exactly the same procedure. The nmr spectrum of **11** was identical with that of **10**, except that the three-proton singlet at τ 8.09 in the spectrum of **10** was absent in the spectrum of **11**.

Recrystallization of **10** from Skellysolve B[38] gave product having the same X-ray powder diffraction pattern as that crystallized from chloroform. Recrystallization of **10** from ethyl acetate–Skellysolve B gave a solvate as fine needles: X-ray powder diffraction data, 14.73 s (4), 10.92 s (3), 8.98 w, 7.66 vw, 7.04 s (2), 6.33 w, 5.50 w, 5.07 m, 4.88 w, 4.67 vw, 4.21 vs (1), and 3.75 m. The nmr spectrum of the solvate showed that it contained 2 moles of ethyl acetate/3 moles of **10**, and no petroleum ether. The solvate was stable on prolonged drying at 100°, but was converted into a glassy nonsolvated form at 110°. The solvate softened at 120°, and finally melted completely at the melting point of the nonsolvated form.

Recrystallization of **10** from dichloromethane–cyclohexane gave a second solvate, as fine needles: X-ray powder diffraction data, 14.60 s (2), 10.92 vs (1), 9.03 w, 7.73 vw, 7.12 s (4), 6.37 m, 5.57 m, 5.07 s (3,3), 4.90 vw, 4.67 vw, 4.23 s (3,3), and 3.77 m.

Anomerization of 2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-mannopyranose (32).—A sample[24] of **32** gave the following nmr data: τ ~3.5 (one-proton broadened doublet, J = 9 cps, shift varies with concentration, disappears on deuteration, NH), 4.10 (one-proton doublet, $J_{1,2}$ = 1.6 cps, H-1), ~4.85 (two-proton multiplet, H-3,4), 5.21 (one-proton broad doublet, collapses on deuteration ot broad singlet, width at half-height 6 cps, H-2), ~5.80 (two-proton multiplet, H-6,6′), and 6.16 (one-proton octet, width 18 cps, H-5).

A solution of **32** (65 mg) in acetic anhydride (0.40 ml) containing zinc chloride (~5 mg) was kept at 70°, and the progress of the anomerization was followed by observing the appearance, in the nmr spectrum, of a narrow doublet, assigned to H-1 of **30**, approximately 8 cps downfield from the H-1 signal of **32**. The two peaks were of equal intensity after 25 min. After 48 hr, the solution was poured into water and the product (R_f 0.20 in 3:1 chloroform–ether) was isolated by extraction with chloroform and evaporation of the dried (magnesium sulfate) extract, with codistillation with toluene. The nmr spectrum of the product showed two narrow doublets, total integral one proton, at τ 4.10 ($J_{1,2}$ = 1.6 cps, H-1 of **32**) and 3.98 ($J_{1,2}$ = 1.7 cps, H-1 of **30**), in the ratio 1:4. Two broadened doublets, total integral one proton, were observed at τ 3.53 (J = 9 cps, NH of **32**) and 3.18 (J = 9 cps, NH of **30**), having relative intensities of 1:4. The positions of the latter signals varied with the concentration of the sample, and the signals disappeared on deuteration.

The anomers were not separable by thin layer chromatography.

2-Acetamido-2-deoxy-1,3,4,6-tetra-*O*-trideuterioacetyl-β-D-mannopyranose (33) and Its α-D Anomer (31).—To crystalline 2-acetamido-2-deoxy-β-D-mannopyranose (**34**) monohydrate[1] (100 mg) was added, in rapid succession, pyridine (1.0 ml) and acetic anhydride-d_6 (0.29 ml), and the mixture was kept for 18 hr at room temperature. Ice (25 g) was added, and after 30 min the mixture was extracted with three 25-ml portions of chloroform. The combined extracts were dried (magnesium sulfate), evaporated, and the syrupy residue was codistilled several times with toluene, yield 170 mg (97%). Crystallization from methanol–ether gave 2-acetamido-2-deoxy-1,3,4,6-tetra-*O*-trideuterioacetyl-β-D-mannopyranose (**33**), yield 60 mg, which had melting point and $[\alpha]D$ identical with that of the nondeuterated analog **32**. The nmr spectrum was identical with that of **32**, except that the only signal in the τ 7.8–8.1 region was a three-proton singlet, τ 7.92 (NAc).

(36) D. Horton, *Org. Syn.*, **46**, 1 (1966).

(37) If the reaction mixture was heated during the tritylation step, the reaction led to formation of some of the β-D anomer of **10**. The latter could be detected and its proportion could be determined by observation in the nmr spectrum of a doublet at τ 4.25, $J_{1,2}$ = 8.5 cps, for H-1 of the β-D anomer.

(38) Petroleum ether (bp 30–60°) from Skelly Oil Co., Kansas City, Mo.

The nmr spectrum of the mother liquor indicated the presence of some of the α-D anomer **31** (τ 7.96, NAc; τ 3.98, $J_{1,2}$ = 1.7 cps, H-1), corresponding to approximately 20% of the original syrupy product.

Acetylation Experiments.—Samples of crystalline sugars (100 mg) were stirred with a mixture of pyridine (3 ml) and acetic anhydride (1 ml) for 12 hr at room temperature. Syrupy samples of the same sugars, prepared by rapid evaporation of aqueous solutions that had been allowed to reach mutarotational equilibrium, were acetylated similarly. Each reaction mixture was poured into ice and water, the product was extracted with dichloromethane, the extract was washed with water, sodium hydrogen carbonate solution, and the dried (magnesium sulfate) extract was evaporated. The nmr spectrum of each product was measured (chloroform-*d*), and the approximate proportion of the anomeric forms present was determined from the intensities of the signals for the H-1 proton. The chemical shifts and first-order coupling constants for the H-1 signals were in good agreement with data measured for pure reference compounds, and with literature values.[13]

Crystalline α-D-glucopyranose gave the α-D-pyranose pentaacetate as the only detected product (τ 3.68, $J_{1,2}$ = 3.5 cps, equatorial H-1); the syrupy sugar gave a 7:13 mixture of the α-D- and β-D-pyranose pentaacetates (τ 4.24, $J_{1,2}$ = 7.0 cps, axial H-1 of β-D anomer). Similarly, crystalline α-D-xylopyranose gave the α-D-pyranose tetraacetate (τ 3.75, $J_{1,2}$ = 3.4 cps, equatorial H-1), whereas the syrupy sugar gave a 7:13 mixture of α-D- and β-D-pyranose tetraacetates (τ 4.26, $J_{1,2}$ = 6.2 cps, axial H-1 of β-D anomer). Crystalline β-D-mannopyranose gave a 1:3 mixture of the α-D-pyranose pentaacetate (τ 3.93, $J_{1,2}$ = 1.6 cps, equatorial H-1) and β-D-pyranose pentaacetate (τ 4.09, $J_{1,2}$ = 1.0 cps, axial H-1), and the syrupy sugar gave the anomers in 13:7 proportion. Crystalline 2-amino-2-deoxy-D-mannose hyrochloride,[31] which dissolved only slowly in the acetylation reagent, gave a mixture of the α-D- and β-D-pyranose pentaacetates in 9:11 proportion; the syrupy sugar gave the anomers in similar proportion.

Crystalline α-D-galactopyranose gave the α-D-pyranose pentaacetate (τ 3.64, $J_{1,2}$ = ~1.5 cps, equatorial H-1) as the main product; the syrupy product gave the α-D and β-D pyranose pentaacetates in 3:7 proportion (τ 4.23, $J_{1,2}$ = 7.5 cps, axial H-1). The product from cystalline α-D-galactopyranose showed signals for the α-D- and β-D-pyranose anomers (relative proportion 10:1) together with signals, in relative proportion 4:1, having τ 3.25 (broad singlet) and 3.75 (J = 6.2 cps), probably arising from other tautomeric pentaacetates.

In the case of β-D-ribopyranose, a mixture of pyranose tetraacetates was formed (τ 3.92, $J_{1,2}$ = 2.9 cps, H-1 of α-D-pyranose form; τ 3.99, $J_{1,2}$ = 4.8 cps, H-1 of β-D-pyranose form); from the crystalline sugar the α:β ratio was 1:4, and from the syrup the ratio was 1:2. The product from the crystalline sugar showed no signals in the region τ 3.0–3.75; a weak signal at τ 3.54 was observed in the product from the syrup.

Preparation and Characterization of Acetylated Pyranose Derivatives.—α-D-Glucopyranose pentaacetate (**1**) and its β-D anomer **12** were prepared by standard methods. Appropriate procedures from the literature were used for other known compounds, and the anomeric purity was verified by nmr in each case.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-(and β-) D-glucopyranose,[6] (**7** and **20**) show nmr signals at low field for the NH and aryl protons. Exchange of the NH proton did not occur when the samples in chloroform-*d* were treated with deuterium oxide, even during several days, but subsequent addition of a trace of tri-*n*-butylamine caused rapid exchange. The signals at τ 1.47 (in **7**) and 1.47 (in **20**) were thus assigned definitively to the NH proton, and the signals at τ 2.81 (in **7**) and 2.72 (in **20**) were, therefore, assigned to H-6′ of the aryl moiety. Similarly in substance **8**, the signals at τ 2.85 and 1.23 were assigned to H-6′ and the NH proton, respectively, reversing the earlier[12] tentative assignment.

1,2,3,4-Tetra-*O*-acetyl-6-*O*-trityl-α-D-glucopyranose[39] (**9**) gave the following nmr data: τ 2.45–2.93 (15 proton multiplet, trityl), 3.81 (one-proton doublet, $J_{1,2}$ = 2.0 cps, H-1), 4.35–4.84 (three-proton multiplet, H-2,3,4), 6.12 (one-proton multiplet, width ~18 cps, H-5), 6.69 (one-proton quartet, $J_{5,6}$ = ~2 cps, $J_{6,6'}$ = ~10 cps, H-6), and 6.97 (one-proton quartet, $J_{5,6'}$ = 4 cps, H-6′).

(39) B. Helferich and W. Klein, *Ann.*, **450**, 219 (1926).

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(*p*-methoxybenzylideneamino)-β-D-glucopyranose[19] (**18**) showed signals at τ 1.86 (one-proton singlet, H of aldimine), 2.38 and 3.11 (four protons, two doublets of A_2B_2 system, J = 8.5 cps, aryl), 4.08 (one-proton doublet, $J_{1,2}$ = 8.0 cps, H-1), 4.56 and 4.92 (triplets, two protons, H-3,4), 5.64–6.20 (three-proton multiplet, H-5,6,6′) 6.58 (one-proton triplet, H-2), and 6.20 (three-proton singlet, OMe).

Isopropyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside[28] (**21**) showed a pair of doublets at τ 8.85 and 8.94, J = 6 cps, total integral six protons (CMe_2), indicating nonequivalence of the isopropyl methyl groups.

2-Acetamido-3,4,6-tri-*O*-acetyl-1-*S*-acetyl-2-deoxy-1-thio-β-D-glucopyranose[40] (**25**) showed signals at τ 3.76 (one-proton doublet, J = 10 cps, NH), 4.4–5.0 (three-proton multiplet, H-1,3,4), and 5.38–6.30 (four-proton multiplet, H-2,5,6,6′).

The derivatives **15**, **16**, and **17** were prepared[18] crystalline by treatment of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride[19] with the appropriate arylsulfonyl chlorides in pyridine: nmr data for **15**, τ 2.30 (four-proton broadened singlet, aryl), 4.00 (1-proton doublet, J = 9 cps, disappears on deuteration, NH), 4.30 (one-proton doublet, $J_{1,2}$ = 8.5 cps, H-1), 4.5–5.2 (two-proton multiplet, H-3,4), and 5.7–6.5 (four-proton multiplet, H-2,5,6,6′); nmr data for **16**, τ 2.23 and 2.70 (four protons, two doublets of A_2B_2 system, J = 8.5 cps, aryl), 4.12 (one-proton doublet, J = 9 cps, disappears on deuteration, NH), 4.30 (one-proton doublet, $J_{1,2}$ = 8.5 cps, H-1), 4.7–5.15 (two-proton multiplet, H-3,4), 5.7–6.5 (four-proton multiplet, H-2,5,6,6′), and 7.59 (three-proton singlet, Me); nmr data for **17**, τ 1.45 and 1.92 (four protons, two doublets of A_2B_2 system, J = 8.5 cps, aryl) and 4.28 (one-proton doublet, $J_{1,2}$ = 8 cps, H-1).

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose[41] (**19**), mp 91–94°, showed signals at τ 2.11 (four proton singlet, aryl), 3.42 (one-proton doublet, $J_{1,2}$ = 8.5 cps, H-1), 4.02 and 4.74 (one-proton triplets, H-3,4), and 5.15–6.15 (four-proton multiplet, H-2,5,6,6′). Treatment of **19** with hydrogen bromide in acetic acid[41,42] gave as the apparent equilibrium product the β-D 1-bromide (**23**): nmr data, τ 2.1 (four-proton multiplet, aryl), 3.52 (one-proton doublet, $J_{1,2}$ = 9.5 cps, H-1),[12] 4.17, 4.71, and 5.33 (one-proton triplets, H-3,4,2), ~5.7 (two-proton multiplet, H-6,6′), and ~6.05 (one-proton multiplet, H-5). Treatment of **19** (or **23**) with hydrogen chloride in acetic acid gave, as the apparent equilibrium product, the β-D 1-chloride[43] (**24**): mp 148–149°; nmr data, τ 3.77 (one-proton doublet, $J_{1,2}$ = 9.5 cps, H-1), 4.17, 4.75, and 5.48 (triplets, three protons, H-3,4,2), and 6.00 (H-5).

Methyl 3,4,6-tri-*O*-acetyl-2-[(benzyloxycarbonyl)amino]-2-deoxy-α-D-glucopyranoside[44] (**6**), mp 105–106°, prepared by acetylation of methyl 2-[(benzyloxycarbonyl)amino]-2-deoxy-α-D-glucopyranoside[45] with acetic anhydride in pyridine, showed signals at τ 2.67 (five-proton singlet, Ph), 6.52 and 6.62 (singlets, three protons, Me), and the signal for the acetyl group at highest field was observed as a doublet (Table I).

***t*-Butyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside** (**22**).—A solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride[36] (**4**, 4.0 g) in benzene (75 ml) was shaken for 15 min with molecular sieve,[46] and then *t*-butyl alcohol (3 ml) and mercuric cyanide (3.6 g) were added and the mixture was shaken for 2 days at room temperature. Water (50 ml) was added, the mixture was shaken, and the aqueous phase was extracted twice with 30-ml portions of dichloromethane. The combined organic layers were extracted twice with 10-ml portions of water, and the dried (magnesium sulfate) organic layer was evaporated to give a solid residue. Recrystallization from dichloromethane–ether gave **22** as fine needles, yield 1.2 g (27%), mp 203.0–203.5°, $[\alpha]^{22}D$ +5.1 ± 0.5° (*c* 4.4, chloroform), λ_{max}^{KBr} 6.01 and 6.51 μ (NHAc), nmr data, τ 8.78 (nine-proton singlet, CMe_3).

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Anal. Calcd for $C_{18}H_{29}NO_9$: C, 53.59; H, 7.25; N, 3.49. Found: C, 53.70; H, 7.02; N, 3.69.

Registry No.—**1**, 604-68-2; **2**, 7784-54-5; **3**, 10026-53-6; **4**, 3068-34-6; **5**, 7772-75-0; **6**, 7772-76-1; **7**, 7784-55-6; **8**, 3068-36-8; **9**, 10028-44-1; **10**, 10026-54-7; **11**, 10026-55-8; **12**, 604-69-3; **13**, 7772-79-4; **14**, 7772-80-7; **15**, 7772-81-8; **16**, 7772-82-9; **17**, 10043-45-5; **18**, 7597-81-1; **19**, 10022-13-6; **20**, 10060-23-8; **21**, 7772-85-2; **22**, 7772-86-3; **23**, 10028-45-2; **24**, 7772-87-4; **25**, 10043-46-6; **26**, 10036-64-3; **27**, 7772-881-5; **2**-d_1, 7772-89-6; **29**, 7772-90-9; **30**, 4539-83-7; **31**, 7772-92-1; **32**, 6730-10-5; **33**, 7772-93-2; **34**, 7772-94-3; **10**-d_1, 7772-95-4.

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Anomalous Rearrangement of Oxidized Xanthate Derivatives of D-Mannose and D-Mannitol[1a]

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Xanthation of 2,3:5,6-di-*O*-isopropylidene-D-mannose followed by coupling with iodine at 0° gave crystalline bis(1-*S*-carbonyl-2,3:5,6-di-*O*-isopropylidene-1-thio-D-mannofuranose) disulfide (II) while none of the expected bis(*O*-thiocarbonyl) disulfide derivative could be isolated. Compound II decomposed on standing in different organic solvents to carbonyl sulfide and crystalline bis(2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl) disulfide (IV). The structure of IV was proved by its independent synthesis and by its conversion to 1,4-anhydro-D-mannitol. Xanthation of 2,3:5,6-di-*O*-isopropylidene-D-mannitol (VI) followed by coupling with iodine gave the corresponding bis(*O*-thiocarbonyl) disulfide derivative (VII). On standing in pyridine, VII decomposed to elemental sulfur, carbon disulfide, VI, and a high-melting, crystalline compound which was shown to be bis-(2,3:5,6-di-*O*-isopropylidene-D-mannitol) orthocarbonate (VIII).

The synthesis of bis(*O*-thiocarbonyl) disulfide derivatives of sugars[2] and simple alkanediols[3] was reported recently. Under the proper conditions, these derivatives undergo rearrangement–fragmentation to give either thionocarbonates or *S*-alkyl dithiocarbonates. The rearrangement appears to be a good method for preparing certain thionocarbonates and *S*-alkyl dithiocarbonates otherwise difficult to obtain. Because such derivatives of sugars have utility as intermediates in the preparation of unsaturated[4] and deoxy sugars,[5] further studies of these rearrangements with carbohydrates seemed warranted. In determining the nature of the rearrangement of the bis(*O*-thiocarbonyl) disulfide derivative at position C-1 of D-mannose and D-mannitol, the anomalous behavior of these derivatives was established.

When 2,3:5,6-di-*O*-isopropylidene-D-mannose (I) was treated with carbon disulfide and sodium hydroxide at 25° and then treated with iodine, the expected bis-(*O*-thiocarbonyl) disulfide derivative was formed in low yield. Attempts to improve the yield by modification of the xanthation conditions failed. Interestingly, when the xanthation was carried out at 25° and then allowed to stand at 0° for 1 hr, followed by oxidative coupling, none of the expected product formed. Instead, a rearrangement occurred between the thiocarbonyl sulfur atom and the oxygen atom at C-1 to give the crystalline bis(1-*S*-carbonyl-2,3:5,6-di-*O*-isopropylidene-1-thio-D-mannofuranose) disulfide (II) as the only sugar derivative which contained sulfur (Scheme I). Product II was isolated in about 13% yield while most of the remaining I was recovered unchanged. In an attempt to prepare the corresponding 1-*S*-carbonyl-*S*-methyl derivative, no rearrangement occurred and only the *S*-methyl dithiocarbonate product was isolated.

A rearrangement of sulfur and oxygen in a sugar derivative was reported previously by Freudenberg and Wolf,[6] who found that on pyrolysis of 1,2:5,6-di-*O*-isopropylidene-3-*O*-[(methylthio)thiocarbonyl]-α-D-glucofuranose, isomerization occurred to give the *S*-carbonyl-3-thio derivative.

The structure of II was formulated on the basis of experimental evidence. Elemental and molecular weight analyses agreed with the proposed structure. The infrared spectrum showed carbonyl absorption at 5.85 and 6.15 μ. The ultraviolet spectrum had an absorption maximum at 235, whereas compounds containing the bis(*O*-thiocarbonyl) disulfide group have maxima near 240 and 285 mμ.[7] Reductive desulfurization of II with Raney nickel gave 1,4-anhydro-2,3:5,6-di-*O*-isopropylidene-D-mannitol which on acid hydrolysis gave the known, crystalline 1,4-anhydro-D-mannitol (III). It was thought that alkali treatment of II would form the corresponding mercaptide which on oxidation should yield bis(2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl) disulfide (IV). Indeed, IV resulted when II was refluxed in aqueous acetone containing barium hydroxide, but no oxidant was required. Also, II gave IV on warming for a short time or even on standing at 25° in different organic solvents. In

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