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THE BEHAVIOR OF SOME ALDOSES WITH 2,2-DIMETHOXYPROPANE-*N*,*N*-DIMETHYLFORMAMIDE–*p*-TOLUENESULFONIC ACID. II. At 80°

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ABSTRACT

Four aldohexoses were individually subjected to the reagent mixture and temperature cited in the title; in each case, the 2,2-dimethoxypropane was present in only a small molar excess and the *p*-toluenesulfonic acid was used in trace amounts. D-Mannose (**1**) afforded the known 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**2**) in significantly higher yield than when the reaction was conducted at room temperature. The other three aldoses, however, gave products markedly different from those formed under the milder conditions. 2-Acetamido-2-deoxy-D-mannose (**3**) gave a mixture of products from which methyl 2-acetamido-2-deoxy-2,3-*N*,*O*-isopropylidene-5,6-*O*-isopropylidene-α-D-mannofuranoside (**4**), 2-acetamido-2-deoxy-2,3-*N*,*O*-isopropylidene-5,6-*O*-isopropylidene-D-mannofuranose (**5a**), and methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-α-D-mannofuranoside (**6a**) were isolated. 2-Acetamido-2-deoxy-D-galactose (**11**) gave compounds identified as methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-β-D-galactofuranoside (**12a**) and methyl 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-galactopyranoside (**13a**). 2-Acetamido-2-deoxy-D-glucose (**16**) afforded methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-β-D-glucofuranoside (**17a**) and methyl 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (**18a**). Evidence in support of the structures assigned to these new derivatives is presented.

INTRODUCTION

In the immediately preceding paper[1], we showed that some typical aldohexoses, in dry *N*,*N*-dimethylformamide and in the presence of a trace of *p*-toluenesulfonic acid, react with 2,2-dimethoxypropane (a small molar excess) to give *O*-isopropylidene derivatives in which O-1 is unsubstituted and which, with one exception (D-mannose), are 1,3-dioxanes (not the 1,3-dioxolanes normally formed with other acetonating reagents). That investigation concerned the use of the reagent mixture at room temperature. We now describe some highly contrasting results obtained when the reagent mixture is employed at 80°.

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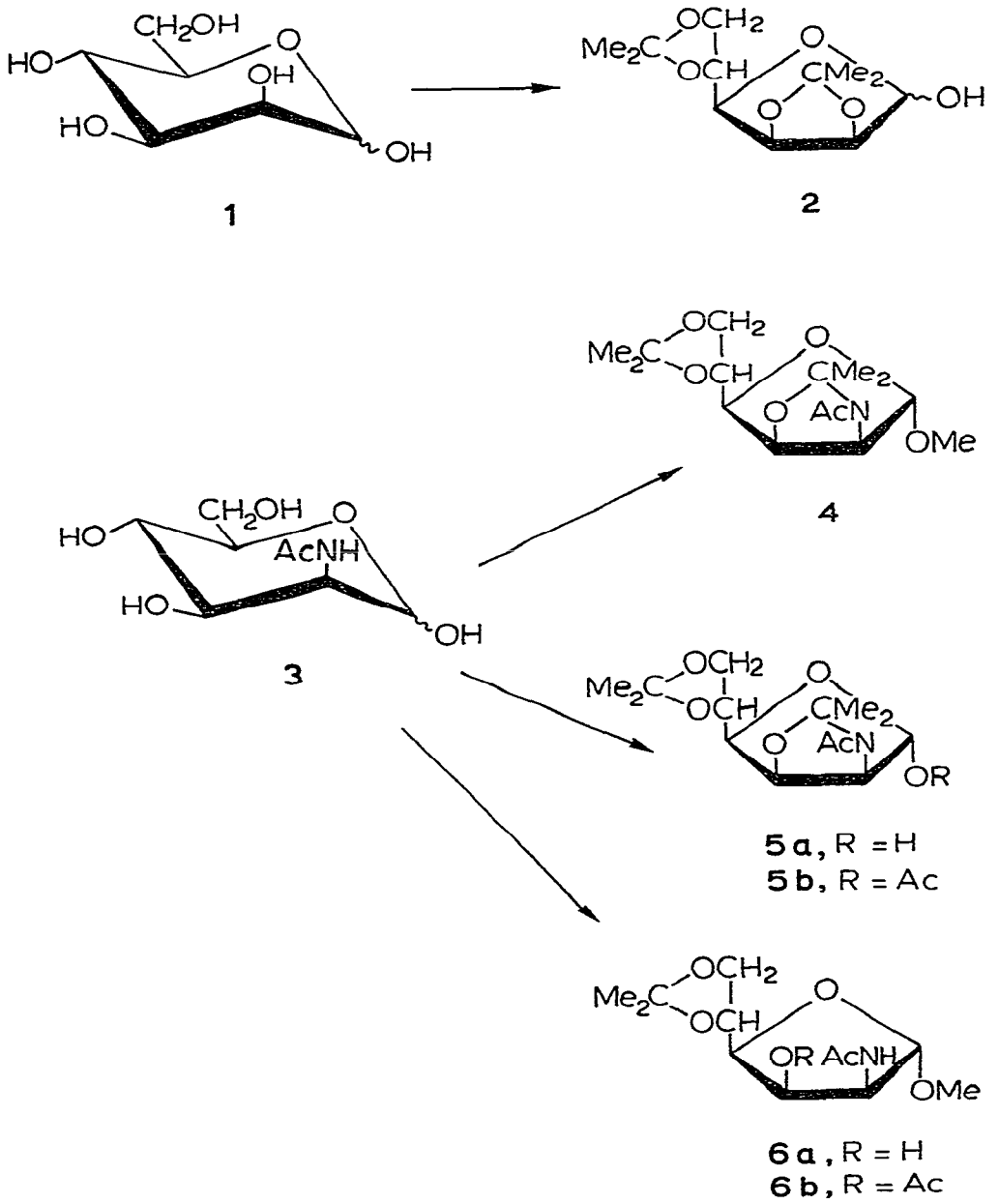
RESULTS

In an initial study with D-mannose (**1**; Scheme I), the more drastic reaction-conditions appeared to lead to a predictable result: the product, namely, 2,3:5,6-di-*O*-



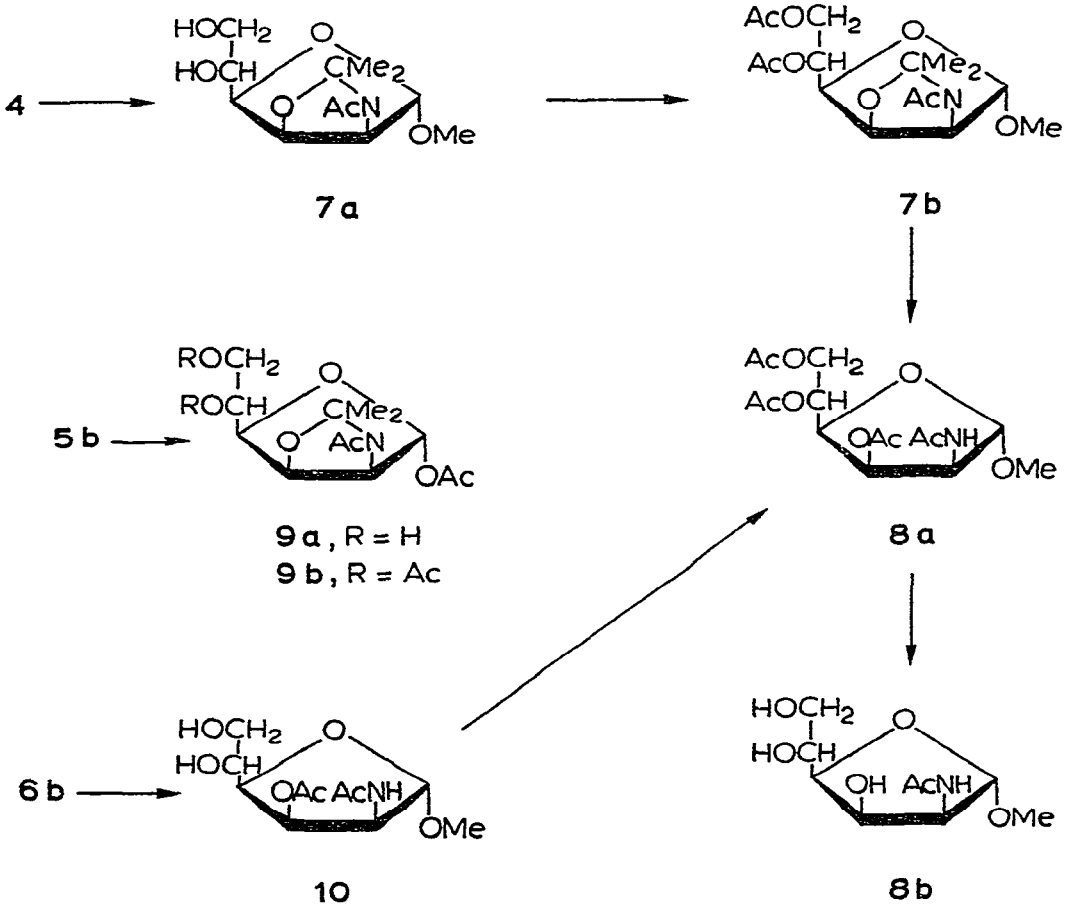
Scheme I

isopropylidene-D-mannofuranose (**2**), which had been isolated in 54% yield after the use of the milder conditions, was now obtained in 74% yield.

However, 2-acetamido-2-deoxy-D-mannose (**3**) appeared to give none of the 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-D-mannopyranose found earlier, but, under the severer conditions, afforded a mixture from which, by column chromatography, three pure (but amorphous) products were isolated. One of these, obtained in 49% yield, had the elemental composition and spectral properties of a methyl acetamido-deoxy-diisopropylidene-hexoside. Although the acetyl group was still present, the nitrogen atom was clearly trisubstituted, and the n.m.r. spectrum showed a pair of three-proton peaks that, by their chemical shift, were well differentiated from a second pair—the two isopropylidene groups; a low-field, one-proton singlet suggested a furanoid structure having a *trans* disposition of the groups at C-1 and C-2. Assuming retention of the D-*manno* configuration, structure **4** is consistent with these data. Brief treatment of the compound with 60% acetic acid at 50° converted it in high yield into a crystalline product; the spectral characteristics and elemental composition of this showed that one isopropylidene group had been lost. The nitrogen atom was still trisubstituted, and the compound consumed 0.94 molar equivalents of periodate; it was concluded that the 5,6-*O*-isopropylidene group had been lost and, in view of its low-field doublet ($J_{1,2}$ 1.0 Hz), structure **7a** (see Scheme II) appeared to be appropriate. The n.m.r. spectrum of the glycoside shows the two, three-proton, isopropylidene signals which appeared at lower field in the spectrum of **4**; it would be expected that the *N*,*O*-isopropylidene group would be more deshielded than the *O*-isopropylidene one. Acetylation of the monoisopropylidene derivative gave a crystalline di-acetate having a composition and spectral properties consistent with structure **7b**; heating of this derivative in 60% acetic acid for 6 h at 95–98° afforded a syrupy product that, on acetylation, gave a crystalline derivative. Here, the second isopropylidene group had been lost, and the acetamido group was unsubstituted. The *O*-methyl signal was still present in the n.m.r. spectrum, and a low-field singlet showed the retention of anomeric configuration; hence, the compound has structure **8a**. Finally, de-*O*-acetylation gave a crystalline glycoside, the properties of which clearly identified it as the known methyl 2-acetamido-2-deoxy-α-D-mannofuranoside[2] (**8b**).

A second product from the isopropylidenation of 2-acetamido-2-deoxy-D-mannose was obtained in 16% yield; its i.r. spectrum showed the amide proton to be substituted, and its n.m.r. spectrum included two well-separated pairs of three-proton doublets. Although a low-field singlet bespoke an α-D-mannofuranose ring, no signals, attributable to an aglycon were evident; structure **5a** was tentatively assigned to this product. Acetylation introduced a single acetyl group and gave a crystalline product but, apparently, caused only one significant change in the n.m.r. spectrum—a downfield shift of the singlet attributed to the anomeric proton. This observation supported the view that it was OH-1 that was free in the parent compound, depicted by **5a**, and permitted consideration of **5b** as its acetate. Hydrolysis of **5b** with 60% acetic acid for 3 h at 46–50° gave, in high yield, a crystalline product; for this, only the lower-field, isopropylidene signals remained, and reduction of periodate confirmed the loss

of the *O*-isopropylidene group. All of the spectral features were in harmony with structure **9a**; the tri-*O*-acetyl derivative served to characterize the compound further, and provided spectral data consistent with structure **9b**.

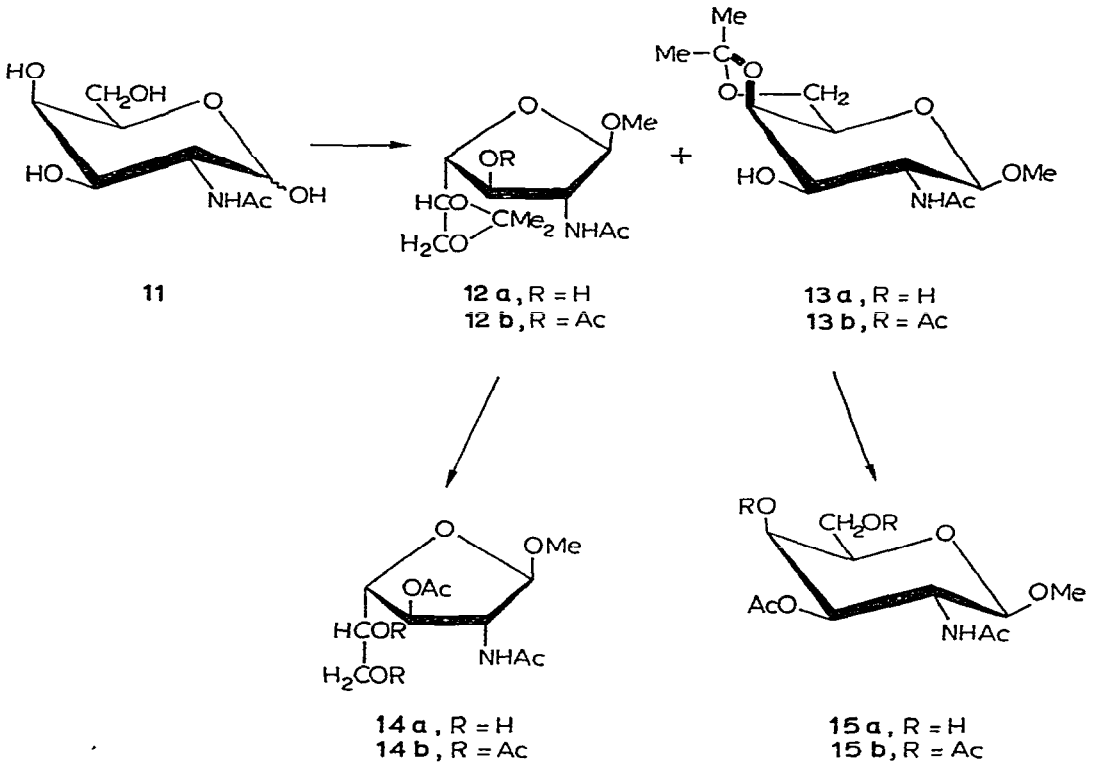


Scheme II

A third product from the isopropylidenation of 2-acetamido-2-deoxy-D-mannose had spectral features which showed it to be a methyl glycoside, but a low-field doublet of 3.0 Hz did not immediately permit assignment of ring size or anomeric configuration. The acetamido group was unsubstituted, and the twin peaks for an isopropylidene group came at relatively high field, characteristic of *O,O*-attachment. Acetylation gave a crystalline monoacetate having $J_{1,2}$ 2.5 Hz; the isopropylidene group was then removed under conditions found effective for the cleavage of *O,O*-isopropylidene groups. The resulting crystalline diol showed a singlet at τ 5.12 (H-1); acetylation converted this diol into methyl 2-acetamido-3,5,6-tri-*O*-acetyl-2-deoxy-α-D-mannofuranoside (**8a**), permitting assignment of structure **6a** to the primary product

of isopropylidenation, and structures **6b** and **10** to the compounds derived therefrom (assuming the absence of acyl migration in the conversion of **6b** into **10**).

The isopropylidenation of 2-acetamido-2-deoxy-D-galactose (**11**) by the trio of reagents at 80° gave a mixture from which a syrup (53% yield) and a crystalline product (24% yield) were isolated by column chromatography. Spectral observations showed the syrupy product to be a methyl glycoside having a free acetamido group, a high-field isopropylidene group, and an H-1 signal appearing as a singlet—all suggestive of structure **12a**, namely, methyl 2-acetamido-5,6-*O*-isopropylidene-β-D-galactofuranoside. Acetylation gave a syrupy monoacetate without changing the chemical shift or character of the signal from H-1. The milder of the two hydrolytic conditions then removed the isopropylidene group, to give a crystalline diol that consumed one mole-equivalent of periodate and possessed spectral characteristics compatible with those for methyl 2-acetamido-3-*O*-acetyl-2-deoxy-β-D-galactofuranoside (**14a**). The



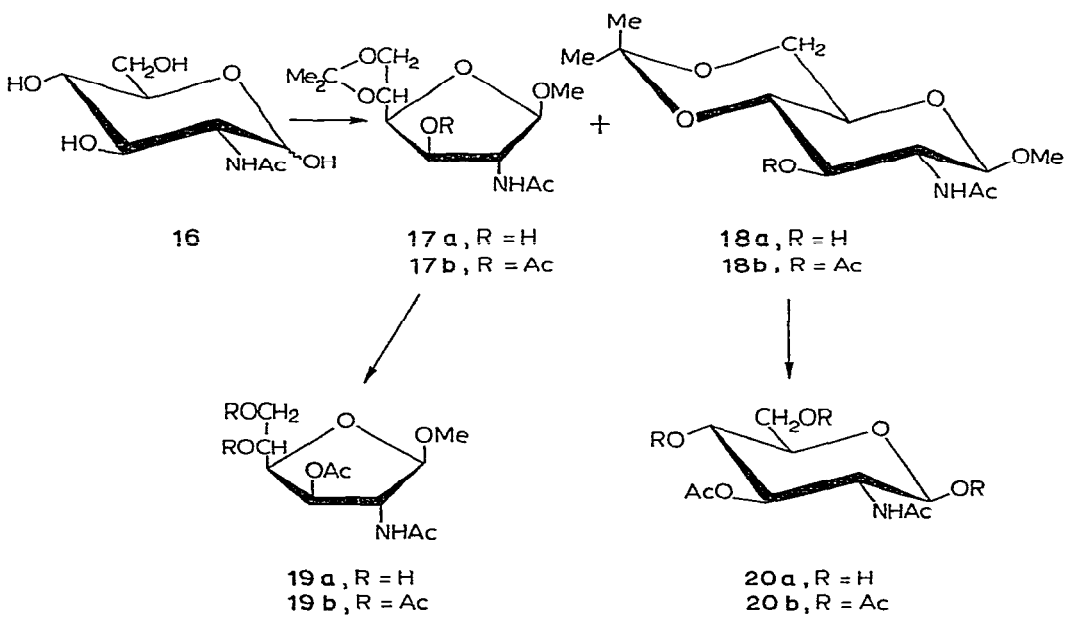
Scheme III

two hydroxyl groups were acetylated to give a crystalline product having an elemental composition and properties consonant with structure **14b**, namely, methyl 2-acetamido-3,5,6-tri-*O*-acetyl-2-deoxy-β-D-galactofuranoside. It was concluded that the syrupy, preponderant product from the isopropylidenation of 2-acetamido-2-deoxy-

D-galactose (**11**) is methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-β-D-galactofuranoside (**12a**).

The crystalline product from the isopropylidenation of **11** was also a methyl glycoside having the acetamido function unaltered and bearing an isopropylidene group which gave its two three-proton signals at relatively high field. A monoacetate of it was also crystalline, but its spectral features appeared to provide no additional structural information. Cleavage of the isopropylidene group from the monoacetate gave a crystalline diol that failed to reduce periodate; acetylation of the diol led to a crystalline ester having a melting point identical with that reported[3] for methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranoside (**15b**). Although the specific rotation found for this compound differed substantially from that reported by the earlier authors[3], the elemental composition and spectral characteristics of the compound supported the structure and configuration assigned. It was then evident that the crystalline product derived by isopropylidenation of **11** is methyl 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-galactopyranoside (**13a**); the acetate of this compound may be written as **13b**, and the hydrolysis product from this, as **15a**. Although, in principle, an acyl migration might have occurred during the removal of the isopropylidene group from **13b**, the relatively mild conditions employed for the hydrolysis appear to render this possibility rather remote.

Isopropylidenation of 2-acetamido-2-deoxy-D-glucose (**16**) led to the isolation,



Scheme IV

through chromatography, of two syrupy products. One of these, obtained in a yield of 34%, had an unsubstituted amide group, an isopropylidene group that gave n.m.r. signals at relatively high field, a methoxyl group, and an anomeric proton giving a low-field singlet; these observations pointed to its being methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-β-D-glucofuranoside (**17a**). On acetylation, the syrup gave a crystalline monoacetate having the composition and properties expected of **17b**. Removal of the isopropylidene group from the monoacetate was accomplished by heating at 50–55° with 60% aqueous acetic acid, to give, in high yield, a crystalline diol (**19a**) that reduced periodate. Further acetylation of **19a** afforded a crystalline end-product having the elemental composition of a methyl acetamido-tri-acetyl-deoxy-hexoside. In addition to the evidence already presented, compounds **17b**, **19a**, and **19b** were all found to be levorotatory, and both **17b** and **19b** showed a $J_{1,2}$ value of 2.0 Hz; designation of the end product as methyl 2-acetamido-3,5,6-tri-*O*-acetyl-2-deoxy-β-D-glucofuranoside (**19b**), and of its precursors as **18a**, **18b**, and **19a**, therefore seems justified.

The second, amorphous product from the isopropylidenation of **16** was obtained in 20% yield; it gave a crystalline acetate that was clearly a methyl 2-acetamido-*O*-acetyl-2-deoxy-*O*-isopropylidenehexoside. The isopropylidene group was selectively hydrolyzed from this ester to give a crystalline, periodate-stable diol; subsequent acetylation afforded another crystalline product having properties that matched those reported[4] for methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (**20b**). It is evident, then, that the second product from the isopropylidenation of **16** is methyl 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (**18a**).

DISCUSSION

Although the present investigation has been restricted to a very limited number of aldoses, it appears that the elevated temperature employed gives results that are, in general, qualitatively different from those earlier noted when the trio of reagents was used at room temperature. Under the more drastic conditions, furanose structures are much more frequently encountered, and methoxyl transfer, to give methyl glycosides, occurs generally. Attention is drawn to the fact that the methoxyl group in all of these glycosides is *trans* to the function at C-2; the significance of this observation must await future investigation. Particularly interesting is the formation of *N*,*O*-isopropylidene derivatives in the case of 2-acetamido-2-deoxy-D-mannose; as far as we are aware, such heterocyclic moieties, which are *N*-acyl-2,2-dimethyloxazolidines, have not hitherto been encountered in the carbohydrate field. In an accompanying paper[5], the preparation of *N*,*O*-isopropylidene derivatives of some *N*-acylinosamines is described. That this heterocyclic system is of potential utility for the synthesis of specifically substituted amino sugar and amino cyclitol derivatives need not be emphasized.

EXPERIMENTAL

General methods. — See Ref. 1.

2,3:5,6-Di-O-isopropylidene-D-mannofuranose (**2**). — A stirred solution of D-mannose (**1**) (4.0 g, 22.2 mmoles) in dry *N,N*-dimethylformamide (100 ml) was heated to 80°, and 2,2-dimethoxypropane (12 ml, 97 mmoles, 4.4 moles/mole of **1**) and *p*-toluenesulfonic acid monohydrate (50 mg) were added. The mixture was stirred for 1 h at 80°, by which time, the starting material was no longer detectable on t.l.c. in 30:1 chloroform–methanol. The mixture was cooled and treated with Amberlite IR-45 ion-exchange resin to remove the acid; the resin was filtered off, and the filtrate was evaporated *in vacuo* (55–60° bath). The crystalline residue was recrystallized from hexane to give 3.38 g of product; m.p. 122° and $[\alpha]_D^{20}+16°$ (*c* 1.0, ethanol). Chromatography of the mother liquor on a column of silicic acid (30 g) with chloroform yielded a further 890 mg of the product, raising the total to 4.27 g (74%). The n.m.r. and i.r. spectra of the product were identical with those of an authentic specimen[6,7] of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**2**); a mixed m.p. was undepressed.

Isopropylidenation of 2-acetamido-2-deoxy-D-mannose (**3**). — A solution of 2-acetamido-2-deoxy-D-mannose (**3**) monohydrate (4.0 g, 16.7 mmoles) in dry *N,N*-dimethylformamide (100 ml) was warmed to 80° and stirred, while 2,2-dimethoxypropane (12 ml, 5.8 moles/mole of **3**) and *p*-toluenesulfonic acid monohydrate (50 mg) were added; stirring was continued for 1 h at 80°. The mixture was cooled and treated with Amberlite IR-45 ion-exchange resin to remove the acid; the resin was filtered off and washed with dry *N,N*-dimethylformamide. The filtrate and washings were combined, and evaporated *in vacuo* (55–60° bath) to a syrup that was chromatographed on a column of silicic acid (100 g) with chloroform and then with 30:1 chloroform–methanol. The chloroform eluate yielded methyl 2-acetamido-2-deoxy-2,3-*N,O*-isopropylidene-5,6-*O*-isopropylidene-α-D-mannofuranoside (**4**): wt. 2.6 g (49%). The chloroform eluate also gave 2-acetamido-2-deoxy-2,3-*N,O*-isopropylidene-5,6-*O*-isopropylidene-D-mannofuranose (**5a**): wt. 820 mg (16%). The chloroform–methanol eluate afforded methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-α-D-mannofuranoside (**6a**): wt. 550 mg (12%). These three products are characterized in the sections immediately following.

Methyl 2-acetamido-2-deoxy-2,3-N,O-isopropylidene-5,6-O-isopropylidene-α-D-mannofuranoside (**4**). — This compound, obtained as a syrup, had $[\alpha]_D^{20}-7°$ (*c* 1.0, chloroform); the i.r. spectrum of neat **4** showed absorption at 1660 (AcN) and 850 cm^{-1} (Me_2C), and its n.m.r. spectrum included signals at τ 5.0 (singlet, H-1), 6.63 (3 H, MeO), 7.91 (3 H, AcN), 8.54 and 8.60 (both 3 H, *O,O*-CMe_2), and 8.37 and 8.46 (both 3 H, *O,N*-CMe_2).

Anal. Calc. for $C_{15}H_{25}NO_6$: C, 57.13; H, 7.99; N, 4.44. Found: C, 57.05; H, 8.08; N, 4.58.

Methyl 2-acetamido-2-deoxy-2,3-N,O-isopropylidene-α-D-mannofuranoside (**7a**) *from* **4**. — A solution of **4** (600 mg) in 60% aqueous acetic acid (22 ml) was held at 50° while the progress of the reaction was monitored by t.l.c.; after 3 h, **4** was no longer

detectable. The solution was concentrated *in vacuo* to a crystalline mass, which was recrystallized from ether to give **7a**: wt. 454 mg (87%), m.p. 102°, $[\alpha]_D^{20}+5.5°$ (*c* 1.0, methanol). In aqueous solution at room temperature, **7a** was found to consume 0.94 mole-equivalent of sodium metaperiodate during 24 h. I.r. data (Nujol mull): 3300 (OH), 1640 (AcN), and 825 cm^{-1} (*N,O*-CMe_2); n.m.r. data (60 MHz, methanol-d_4): τ 5.03 (doublet, 1 H, H-1, $J_{1,2}$ 1.0 Hz), 6.63 (MeO), 7.91 (AcN), and 8.41 and 8.49 (*N,O*-CMe_2); (100 MHz, methyl sulfoxide-d_6): τ 5.56 (triplet, J_{CH_2OH} 12 Hz) and ~5.3 (CHOH, not resolved)

Anal. Calc. for $C_{12}H_{21}NO_6$: C, 52.35; H, 7.69; N, 5.09. Found: C, 52.38; H, 7.93; N, 4.90.

*Methyl 2-acetamido-5,6-di-*O*-acetyl-2-deoxy-2,3-*N,O*-isopropylidene-α-*D*-mannofuranoside* (**7b**) *from* **7a**. — A sample of **7a** (360 mg) was treated with pyridine (10 ml) and acetic anhydride (3 ml), and the solution was kept overnight at room temperature. It was then evaporated *in vacuo* to a syrup which was crystallized from ether–hexane to give 330 mg of **7b**. Chromatography of the mother liquor on a column of silicic acid (20 g) with 50:1 chloroform–methanol afforded a further 90 mg of **7b**, raising the total yield to 420 mg (89%). Recrystallized from ether, the product was obtained as colorless needles: m p. 111°, $[\alpha]_D^{20}+8°$ (*c* 1.0, chloroform); i.r. absorption (Nujol mull) at 1750, 1250–1225 (ester), 1660 (AcN), and 835 cm^{-1} (Me_2C); n.m.r. signals at τ 5.08 (singlet, H-1), 6.62 (MeO), 7.92 (9 H, AcN and AcO), and 8.38 and 8.49 (*N,O*-CMe_2).

Anal. Calc. for $C_{16}H_{25}NO_8$: C, 53.47; H, 7.01; N, 3.90. Found: C, 53.70; H, 7.32; N, 3.89.

*Methyl 2-acetamido-3,5,6-tri-*O*-acetyl-2-deoxy-α-*D*-mannofuranoside* (**8a**). — A solution of compound **7b** (150 mg) in 60% aqueous acetic acid (15 ml) was heated for 6 h at 95–98° and then evaporated *in vacuo* to a syrup which was chromatographed on a column of silicic acid (10 g) with 50.1 chloroform–methanol, to give 30 mg of chromatographically homogeneous product. This was acetylated by heating with a mixture of pyridine (3 ml) and acetic anhydride (0.5 ml) for 30 min at 50°. The acetylation product was recrystallized from ether to give 32 mg (21%) of **8a**: m.p. 135–136°, $[\alpha]_D^{20}+125°$ (*c* 1.0, chloroform); i.r. absorption (Nujol mull) at 3300 (NH), 1750 and 1225–1220 (ester), and 1650 and 1540 cm^{-1} (amide); n.m.r. signals at τ 5.16 (singlet, H-1), 6.61 (MeO), 7.92 (3 H), 7.93 (3 H), and 8 00 (6 H); (AcO and AcN).

Anal. Calc. for $C_{15}H_{23}NO_9$: C, 49.86; H, 6.42; N, 3.88. Found: C, 49.86; H, 6.72; N, 3.85.

*Methyl 2-acetamido-2-deoxy-α-*D*-mannofuranoside* (**8b**) *from* **8a**. — The tri-*O*-acetyl derivative (**8a**, 25 mg) was dissolved in 10 ml of methanol presaturated with anhydrous ammonia, and the solution was kept overnight at room temperature. Evaporation of the solution *in vacuo* at 90° afforded a crystalline residue in quantitative yield; recrystallization from ethanol gave fine needles; m.p. 178°, $[\alpha]_D^{20}+130°$ (*c* 1.0, ethanol), and $[\alpha]_D^{20}+143°$ (*c* 1.0, water); lit.[2] m.p. 177–178° and $[\alpha]_D^{24}+141°$ (*c* 1.3, water).

*2-Acetamido-1-*O*-acetyl-2-deoxy-2,3-*N,O*-isopropylidene-5,6-*O*-isopropylidene-α-*D*-mannofuranose* (**5b**).—2-Acetamido-2-deoxy-2,3-*N,O*-isopropylidene-5,6-*O*-iso-

propylidene-D-mannofuranose (**5a**) proved to be amorphous. The i.r. spectrum of the compound (neat) showed absorption at 3400 (OH), 1660 (AcN), and 850–860 cm^{-1} (Me_2C); its n.m.r. spectrum included a singlet at τ 4.60 (H-1) and other signals at 7.85 (AcN), 8.55 and 8.61 (*O,O*-CMe_2), and 8.37 and 8.43 (*N,O*-CMe_2). A solution of a sample (750 mg) of the product in a mixture of pyridine (5 ml) and acetic anhydride (3 ml) was kept overnight at room temperature, and then evaporated *in vacuo*; the residue was chromatographed on a column of silicic acid (30 g) with 50:1 chloroform–methanol, to give 740 mg (87%) of **5b**. After recrystallization from ether, the product was obtained as colorless needles, m.p. 124°, $[\alpha]_D^{20}+3°$ (*c* 1.0, chloroform); i.r. absorption (Nujol mull) at 1740 and 1220 (ester), 1670 (AcN), and 860 cm^{-1} (Me_2C); n.m.r. signals at τ 3.78 (singlet, H-1), 7.84 (6 H, AcN and AcO), 8.54 and 8.60 (*O,O*-CMe_2), and 8.33 and 8.42 (*N,O*-CMe_2).

Anal. Calc. for $C_{16}H_{25}NO_7$: C, 55.97; H, 7.34; N, 4.08. Found: C, 55.81; H, 7.60; N, 4.01.

*2-Acetamido-1-*O*-acetyl-2-deoxy-2,3-*N,O*-isopropylidene-α-*D*-mannofuranose* (**9a**). — A solution of **5b** (300 mg) in 60% aqueous acetic acid (15 ml) was kept for 3 h at 46–50°; it was then evaporated *in vacuo* to a syrup which was crystallized from ether to give **9a**: wt. 232 mg (88%). After recrystallization from ether, the product was obtained as colorless needles, m.p. 122°, $[\alpha]_D^{20}+12°$ (*c* 1.0, methanol). The product reduced 1.0 mole-equivalent of aqueous sodium metaperiodate during 24 h. Its i.r. spectrum (Nujol mull) showed absorption at 3500–3300 (OH), 1750, 1250–1220 (ester), 1650 (AcN) and 830 cm^{-1} (Me_2C). The n.m.r. spectrum of the compound in methanol-d_4 included signals at τ 3.78 (singlet, H-1), 7.96 (AcO), 7.92 (AcN), and 8.38 and 8.46 (Me_2C); (in methyl sulfoxide-d_6 at 100 MHz) τ 5.54 (triplet, J_{CH_2OH} 12 Hz).

Anal. Calc. for $C_{13}H_{21}NO_7$: C, 51.48; H, 6.98; N, 4.62. Found: C, 51.79; H, 6.90; N, 4.35.

*2-Acetamido-1,5,6-tri-*O*-acetyl-2-deoxy-2,3-*N,O*-isopropylidene-α-*D*-mannofuranose* (**9b**). — The diol **9a** (180 mg) was acetylated with pyridine–acetic anhydride at room temperature, and the product, purified by chromatography on a column of silicic acid (20 g) with 50:1 chloroform–methanol, was obtained as a syrup: wt. 220 mg (95%), $[\alpha]_D^{20}+13°$ (*c* 1.0, chloroform); i.r. absorption (neat) at 1745 and 1225–1220 (ester), 1650 (AcN), and 833 cm^{-1} (Me_2C); n.m.r. signals at τ 3.76 (singlet, H-1), 7.90 (AcN), 7.93 (6 H, AcO) and 7.95 (3 H, AcO), and 8.36 and 8.48 (*N,O*-CMe_2).

Anal. Calc. for $C_{17}H_{25}NO_9$: C, 52.71; H, 6.51; N, 3.62. Found: C, 52.87; H, 6.35; N, 3.35.

*Methyl 2-acetamido-3-*O*-acetyl-2-deoxy-5,6-*O*-isopropylidene-α-*D*-mannofuranoside* (**6b**). — Methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-α-D-mannofuranoside (**6a**) was obtained as a chromatographically homogeneous syrup which showed i.r. absorption (neat) at 3400–3300 (OH, NH), 1650 and 1540 (amide), and 850 cm^{-1} (Me_2C); its n.m.r. spectrum included signals at τ 5.12 (H-1, $J_{1,2}$ 3.0 Hz), 6.65 (MeO), 7.99 (AcN), and 8.60 and 8.65 (Me_2C). A sample (480 mg) of the syrup was acetylated at room temperature with pyridine–acetic anhydride to give, after chromatography on a column of silicic acid (30 g) with 50:1 chloroform–methanol, a crystalline product:

wt. 510 mg (92%). After recrystallization from ether, the acetate **6b** was obtained as colorless needles, m.p. 139–140° and $[\alpha]_D^{20}$ +61.5° (*c* 1.0, chloroform); the i.r. spectrum (Nujol mull) showed absorption at 3350 (NH), 1650 and 1540 (amide), and 870 cm^{-1} (Me_2C); the n.m.r. spectrum included signals at τ 5.16 (H-1, $J_{1,2}$ 2.5 Hz), 6.62 (MeO), 7.88 (AcO), 8.00 (AcNH), and 8.57 and 8.67 (Me_2C).

Anal. Calc. for $C_{14}H_{23}NO_7$: C, 52.99; H, 7.31; N, 4.41. Found: C, 52.99; H, 6.53; N, 4.33.

*Methyl 2-acetamido-3-*O*-acetyl-2-deoxy-α-*D*-mannofuranoside* (**10**). — A solution of compound **6b** (200 mg) in 60% aqueous acetic acid (15 ml) was kept for 2 h at 46–50° and then evaporated *in vacuo* at 50°, giving a crystalline solid. Recrystallization from ether–ethanol afforded 165 mg (94%) of **10**, having m.p. 145–146° and $[\alpha]_D^{20}$ +132° (*c* 1.0, methanol). The i.r. spectrum (Nujol mull) of **10** showed absorption at 3330 (OH, NH), 1750 and 1230 (ester), and 1650 and 1550 cm^{-1} (amide); the n.m.r. spectrum (60 MHz, methanol-d_4) included signals at τ 5.12 (singlet, H-1), 6.63 (MeO), 7.90 (AcO), and 8.10 (AcNH).

Anal. Calc. for $C_{11}H_{19}NO_7$: C, 47.65; H, 6.91; N, 5.05. Found: C, 47.87; H, 7.13; N, 4.79.

A sample of **10** (100 mg) was acetylated with pyridine–acetic anhydride to give 105 mg (80%) of a product having m.p. 135–136° and $[\alpha]_D^{20}$ +125° (*c* 1.0, chloroform); its i.r. and n.m.r. spectra were identical with those of **8a**, and a mixed m.p. with **8a** prepared from **7b** was undepressed.

*Isopropylidenation of 2-acetamido-2-deoxy-*D*-galactose* (**11**). — A solution of **11** (4.0 g, 18.1 mmoles) in dry *N*,*N*-dimethylformamide (100 ml) was heated at 80° and stirred while 2,2-dimethoxypropane (12 ml, 5.4 moles/mole of **11**) and *p*-toluenesulfonic acid monohydrate (50 mg) were added. The mixture was stirred for 1 h at 80°, cooled, and freed of acid by addition of Amberlite IR-45 ion-exchange resin. The suspension was filtered, and the filtrate evaporated *in vacuo* at 50–55° (bath), to give a syrup which was chromatographed on a column of silicic acid (100 g) with 30:1 chloroform–methanol. Methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-β-D-galactofuranoside (**12a**) issued as a faster-moving component, and was obtained as a syrup (2.65 g, 53%). Methyl 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-galactopyranoside (**13a**) appeared as a slower-moving component: wt. 1.2 g (24%). These two products are characterized in the sections following.

*Methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-β-*D*-galactofuranoside* (**12a**). — The syrupy compound, isolated as just described, had $[\alpha]_D^{20}$ −38.5° (*c* 1.0, chloroform); its i.r. spectrum (neat) showed absorption at 3400–3300 (OH, NH), 1650 and 1540 (amide), and 850–840 cm^{-1} (Me_2C); the n.m.r. spectrum included signals at τ 5.12 (singlet, H-1), 6.59 (MeO), 8.03 (AcN), and 8.53 and 8.59 (Me_2C).

Anal. Calc. for $C_{12}H_{21}NO_6$: C, 52.35; H, 7.69; N, 5.09. Found: C, 52.31; H, 8.06; N, 4.86.

*Methyl 2-acetamido-3-*O*-acetyl-2-deoxy-5,6-*O*-isopropylidene-β-*D*-galactofuranoside* (**12b**). — A sample of **12a** (500 mg) was acetylated at room temperature with pyridine–acetic anhydride, and the product was purified by chromatography on a column

of silicic acid (15 g) with 50:1 chloroform–methanol as the eluant. The acetate (**12b**) was obtained as a syrup (wt. 500 mg, 87%) having $[\alpha]_D^{20} -40°$ (*c* 1.0, chloroform); its i.r. spectrum (neat) showed absorption at 3350 (NH), 1670 and 1540 (amide), 1750, 1240–1220 (ester), and 845 cm^{-1} (Me_2C); the n.m.r. spectrum included signals at τ 5.15 (singlet, H-1), 6.61 (MeO), 8.03 (AcN), 7.90 (AcO), and 8.53 and 8.57 (Me_2C).

Anal. Calc. for $C_{14}H_{23}NO_7$: C, 52.99; H, 7.31; N, 4.41. Found: C, 52.74; H, 7.50; N, 4.32.

*Methyl 2-acetamido-3-*O*-acetyl-2-deoxy-β-*D*-galactofuranoside* (**14a**). — A solution of compound **12b** (250 mg) in 60% aqueous acetic acid (15 ml) was heated for 3 h at 46–50° and evaporated *in vacuo* at 40° to a syrup which was crystallized from its solution in ether–hexane. Recrystallization from ether–ethanol gave needles: wt. 180 mg (83%), m.p. 142–143°, $[\alpha]_D^{20} -95°$ (*c* 1.0, methanol). In 42mM sodium metaperiodate at room temperature, the compound consumed 1.0 molar equivalent of oxidant in 24 h. The i.r. spectrum of the product (Nujol mull) showed absorption at 3300–3200 (NH, OH), 1750 and 1240 (ester), and 1650 and 1540 cm^{-1} (amide); in methanol-d_4, the 60-MHz n m.r. spectrum of the compound included signals at τ 5.16 (singlet, H-1), 6.65 (MeO), 7.95 (AcO), and 8.06 (AcN); in methyl sulfoxide-d_6, the 100-MHz, n.m.r. spectrum included a triplet centered at τ 5.36 (J_{CH_2OH} 12 Hz) and an unresolved multiplet at ~5.05 that was ascribed to the secondary hydroxyl group and its coupling with H-5.

Anal. Calc. for $C_{11}H_{19}NO_7$: C, 47.65; H, 6.91; N, 5.05. Found: C, 47.40; H, 7.13; N, 4.82.

*Methyl 2-acetamido-3,5,6-tri-*O*-acetyl-2-deoxy-β-*D*-galactofuranoside* (**14b**). — Compound **14a** (100 mg) was acetylated with pyridine–acetic anhydride at room temperature to give **14b**, which was crystallized from ether: wt. 117 mg (90%), m.p. 129°, $[\alpha]_D^{20} -47°$ (*c* 1.0, chloroform). The i.r. absorption spectrum of the compound (Nujol mull) showed bands at 3240 (NH), 1750 and 1240–1220 (ester), and 1630 and 1550 cm^{-1} (amide); the n.m.r. spectrum included signals at τ 5.15 (singlet, H-1), 6.62 (MeO), 7.86 (3 H), 7.92 (3 H), 7.94 (3 H), and 8.00 (3 H) (AcO and AcN).

Anal. Calc. for $C_{15}H_{23}NO_9$: C, 49.86; H, 6.42; N, 3.88. Found: C, 49.79; H, 6.70; N, 3.78.

*Methyl 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-*D*-galactopyranoside* (**13a**). — From its solution in ether, **13a** was obtained as colorless crystals, m.p. 107–109°, $[\alpha]_D^{20} +17°$ (*c* 1.0, methanol). The i.r. spectrum of the compound (Nujol mull) showed absorption at 3330 (OH, NH), 1650, 1550 (amide), and 877 cm^{-1} (Me_2C); the n.m.r. spectrum included signals at τ 6.48 (MeO), 7.99 (AcN), and 8.46 and 8.64 (Me_2C).

Anal. Calc. for $C_{12}H_{21}NO_6$: C, 52.35; H, 7.69; N, 5.09. Found: C, 52.43; H, 7.87; N, 4.90.

*Methyl 2-acetamido-3-*O*-acetyl-2-deoxy-4,6-*O*-isopropylidene-β-*D*-galactopyranoside* (**13b**). — Compound **13a** (350 mg) was acetylated with pyridine–acetic anhydride at room temperature, and the product (**13b**) was crystallized from ether solution: wt. 360 mg (89%), m.p. 161–161.5°, $[\alpha]_D^{20} +31.5°$ (*c* 1.0, chloroform); i.r. absorption (Nujol mull) at 3330 (NH), 1750 and 1250–1220 (ester), 1650 and 1550 (amide), and

880 cm^{-1} (Me_2C); n.m.r. signals at τ 6.50 (MeO), 7.90 (AcO), 8.00 (AcN), and 8.48 and 8.67 (Me_2C).

Anal. Calc. for $C_{14}H_{23}NO_7$: C, 52.99; H, 7.31; N, 4.41. Found: C, 52.77; H, 7.50; N, 4.27.

Methyl 2-acetamido-3-O-acetyl-2-deoxy-β-D-galactopyranoside (**15a**). — A solution of compound **13b** (300 mg) in 60% aqueous acetic acid (15 ml) was warmed for 2 h at 46–50°; it was then evaporated *in vacuo* (40° bath) to a crystalline residue. Recrystallized from ethanol–ether, the product was obtained as needles; wt. 252 mg (96%), m.p. 215–216°, $[\alpha]_D^{20} -9°$ (*c* 1.0, methanol). The compound failed to reduce sodium metaperiodate in aqueous solution at room temperature during 24 h. Its i.r. spectrum (Nujol mull) showed absorption at 3420–3350 (OH, NH), 1700 and 1240–1230 (ester), and 1640 and 1550 cm^{-1} (amide); the n.m.r. spectrum (methanol-d_4, 60 MHz) included signals at τ 6.54 (MeO), and 7.97 and 8.03 (AcO and AcN).

Anal. Calc. for $C_{11}H_{19}NO_7$: C, 47.65; H, 6.91; N, 5.05. Found: C, 47.42; H, 7.00; N, 4.78.

Methyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranoside (**15b**). — Compound **15a** (100 mg) was acetylated with pyridine–acetic anhydride, and the product was crystallized from ethanol–ether to give 115 mg (88%) of **15b** as needles, m.p. 216–217° and $[\alpha]_D^{20} -39°$ (*c* 1.0, chloroform); lit.[3] m.p. 216–217° and $[\alpha]_D^{23} -17 \pm 1°$ (chloroform). The i.r. spectrum of the compound showed absorption at 3300 (NH), 1750 and 1260–1220 (ester), and 1650 and 1560 cm^{-1} (amide); the n.m.r. spectrum included signals at τ 5.37 (doublet, $J_{1,2}$ 7.0 Hz), 6.50 (MeO), 7.84 (3 H, axial AcO), 7.95 and 8.00 (3 H, equatorial AcO), and 8.03 (equatorial AcN). The elemental composition of the compound fell within acceptable limits.

Isopropylidenation of 2-acetamido-2-deoxy-D-glucose (**16**). — A solution of 2-acetamido-2-deoxy-D-glucose (**16**) (4.0 g, 18.1 mmoles) in dry *N,N*-dimethylformamide (100 ml) was heated to 80° and stirred while 2,2-dimethoxypropane (12 ml, 5.4 moles/mole of **16**) and *p*-toluenesulfonic acid monohydrate (50 mg) were added. The mixture was stirred for 1 h at 80°, cooled and treated with Amberlite IR-45 ion-exchange resin to remove the acid; the suspension was filtered, and the filtrate was evaporated *in vacuo* at 50–55° to a syrup which was chromatographed on a column of silicic acid (100 g) with chloroform and then with 30:1 chloroform–methanol. The chloroform eluate contained 1.2 g of material which was not further investigated. The chloroform–methanol eluate yielded methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-β-D-glucofuranoside (**17a**) (1.7 g, 34%) and methyl 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (**18a**) (1.0 g, 20%); both were syrupy; further data on them follow.

Methyl 2-acetamido-3-O-acetyl-2-deoxy-5,6-O-isopropylidene-β-D-glucofuranoside (**17b**). — The methyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-β-D-glucofuranoside (**17a**), obtained as just described, showed i.r. absorption (neat) at 3500–3350 (NH, OH), 1650 and 1550 (amide), and 850 cm^{-1} (Me_2C); its n.m.r. spectrum included signals at τ 5.11 (singlet, H-1), 6.59 (MeO), 7.99 (AcN), and 8.54 and 8.61 (Me_2C). A sample of **17a** (1.6 g) was acetylated with pyridine–acetic anhydride, and the product

was chromatographed on a column of silicic acid (30 g) with 50:1 chloroform–methanol to give 1.7 g (92%) of **17b**; after recrystallization from ether, **17b** was obtained as fine prisms, m.p. 93°, $[\alpha]_D^{20} -28°$ (*c* 1.0, chloroform); i.r. absorption (Nujol mull) at 3330 (NH), 1750 and 1220 (ester), 1640 and 1550 (amide), and 850 cm^{-1} (Me_2C); n.m.r. signals at τ 5.12 (doublet, H-1, $J_{1,2}$ 2.0 Hz), 6.60 (MeO), 7.90 (AcO), 7.99 (AcN), and 8.60 and 8.66 (Me_2C).

Anal. Calc. for $C_{14}H_{23}NO_7$: C, 52.99; H, 7.31; N, 4.41. Found: C, 52.72; H, 7.46; N, 4.24.

Methyl 2-acetamido-3-O-acetyl-2-deoxy-β-D-glucofuranoside (**19a**). — A solution of compound **17b** (300 mg) in 60% aqueous acetic acid (15 ml) was kept for 80 min at 50–55°; it was then evaporated *in vacuo* at 40–50° to give a crystalline residue. After recrystallization from ethanol–ether, **19a** was obtained as needles: wt. 232 mg (89%), m.p. 127–128°, $[\alpha]_D^{20} -63°$ (*c* 1.0, methanol); i.r. absorption (Nujol mull) at 3330, 3500 (NH, OH), 1750 and 1270–1250 (ester), and 1650 and 1550 cm^{-1} (amide); n.m.r. signals (methanol-d_4, 60 MHz) appeared at τ 6.65 (MeO), 7.92 (AcO), and 8.02 (AcN). The compound consumed 0.95 mole-equivalent of 42mM sodium metaperiodate during 24 h at room temperature.

Anal. Calc. for $C_{11}H_{19}NO_7$: C, 47.65; H, 6.91; N, 5 05. Found: C, 47.61; H, 7.00; N, 4.85.

Methyl 2-acetamido-3,5,6-tri-O-acetyl-2-deoxy-β-D-glucofuranoside (**19b**). — Compound **19a** (100 mg) was acetylated with pyridine–acetic anhydride at room temperature, and the product was purified by chromatography on a column of silicic acid (10 g) with 50:1 chloroform–methanol. Compound **19b** was obtained as a syrup: wt. 120 mg (92%), $[\alpha]_D^{20} -26°$ (*c* 1.0, chloroform); i.r. absorption (neat) at 3250 (NH), 1750 and 1270–1240 (ester), and 1670 and 1570 cm^{-1} (amide); n.m.r. signals at τ 5.06 (doublet, H-1, $J_{1,2}$ 2.0 Hz), 6.56 (MeO), 7.91 (3 H), 7.94 (3 H), 7.98 (3 H) and 7.99 (3 H) (AcO and AcN).

Anal. Calc. for $C_{15}H_{23}NO_9$: C, 49.86; H, 6.42; N, 3.88. Found: C, 49.86; H, 6.71; N, 3.65.

Methyl 2-acetamido-3-O-acetyl-2-deoxy-4,6-O-isopropylidene-β-D-glucopyranoside (**18b**). — Syrupy **18a**, prepared as already described, showed i.r. absorption (neat) at 3500–3300 (NH, OH), 1660 and 1550 (amide), and 855 cm^{-1} (Me_2C). A portion of **18a** (1.0 g) was acetylated with acetic anhydride–pyridine, and the product was purified by chromatography on a column of silicic acid (30 g) with 50:1 chloroform–methanol. The **18b** thus obtained was crystallized from ether–ethanol: wt. 865 mg (75%), m.p. 197–198°, $[\alpha]_D^{20} -75°$ (*c* 1.0, chloroform); i.r. absorption (Nujol mull) at 3300 (NH), 1740 and 1240 (ester), 1660 and 1540 (amide), and 860 cm^{-1} (Me_2C); n.m.r. signals at τ 6.51 (MeO), 7.90 (AcO), 8.02 (AcN), and 8.50 and 8.61 (Me_2C).

Anal. Calc. for $C_{14}H_{23}NO_7$: C, 52.99; H, 7.31; N, 4.41. Found: C, 53.05; H, 7.55; N, 4.49.

Methyl 2-acetamido-3-O-acetyl-2-deoxy-β-D-glucopyranoside (**20a**). — A solution of compound **18b** (135 mg) in 60% aqueous acetic acid (15 ml) was kept for 70 min at 65–70° and then evaporated *in vacuo* to give a crystalline product which was

recrystallized from ethanol as needles: wt. 100 mg (85%), m.p. 162–164°, $[\alpha]_D^{20} -67°$ (*c* 0.5, methanol). Dissolved in 42mM sodium metaperiodate, a sample of the compound did not change the concentration of the oxidant during 24 h at room temperature. The i.r. spectrum of the compound (Nujol mull) showed absorption at 3500–3200 (OH, NH), 1710 and 1260–1240 (ester), and 1660 and 1575 cm^{-1} (amide); n.m.r. signals (methanol-d_4, 60 MHz) at τ 6.53 (MeO), 7.98 (AcO), and 8.11 (AcN); (methyl sulfoxide-d_6, 100 MHz) at τ 4.73 (doublet, J_{CHOH} 6 Hz) and 5.40 (triplet, J_{CH_2OH} ~12 Hz).

Anal. Calc. for $C_{11}H_{19}NO_7$: C, 47.65; H, 6.91; N, 5.05. Found: C, 47.88; H, 6.69; N, 5.03.

*Methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranoside* (**20b**). — A sample of **20a** (50 mg) was acetylated with pyridine–acetic anhydride to yield, from ethanol–ether, 56 mg (86%) of **20b**: m.p. 159–160°, $[\alpha]_D^{20} -30°$ (*c* 1.0, chloroform); lit.[4] m.p. 160°, $[\alpha]_D^{23} -20°$ (*c* 1, chloroform).

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