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Preliminary communication

A facile synthesis of [3,6-di-*O*-acetyl-4-*O*-(chloroacetyl)-1,2-dideoxy-α-D-glucopyrano]-[2,1-*d*]-2-methyl-2-oxazoline for use in oligosaccharide synthesis*

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It has been well documented that 2-methylglyco-[2,1-*d*]-2-oxazolines can be effectively employed as suitable glycosylating agents for the facile preparation of various 1,2-*trans*-2-acetamido-2-deoxy-D-glycopyranosides. Various laboratories[2–4] have reported syntheses of such oxazolines with *O*-benzyl systems as "persistent" protecting groups. However, we have recommended the use of temporary protection by the chloroacetyl group[5] in such oxazolines for similar purposes. Our continuing interest in the chemistry of such valuable intermediates, required for the sequential synthesis of complex sugar molecules, led to the preparation of the title oxazoline.

As reported earlier[5], for the preparation of an oxazoline from 1-*O*-acetyl derivatives of 2-acetamido-2-deoxyaldoses by the anhydrous ferric chloride method, it is essential that the anomeric *O*-acetyl group be *trans* to the 2-acetamido group. Based upon such observations, we attempted the preparation of 2-acetamido-1,3,6-tri-*O*-acetyl-4-(chloroacetyl)-2-deoxy-β-D-glucopyranose (**7**), which could be readily converted into oxazoline **8**.

Okuyama[6] had observed that treatment of 2-acetamido-4,6-*O*-benzylidene-2-deoxy-D-glucopyranose with acetic anhydride–pyridine gives a mixture of compounds **2** and **3** in which the α-D anomer **3** preponderates. However, under similar conditions of acetylation, crystalline 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranose (**1**) gave a 2:3 mixture (from p.m.r. analysis at 100 MHz of a solution in dimethyl sulfoxide-d_6) of acetylated α-D (δ 5.97, $J_{1,2}$ 3.5 Hz, equatorial H-1) and β-D (δ 5.8, $J_{1,2}$ 8 Hz, axial H-1) anomers. The desired β-D-pyranose anomer **2** was isolated from this mixture by fractional recrystallization (yield 27%), m.p. 260°, $[\alpha]_D^{25}$ –17.1° (*c* 1, $HCONMe_2$).

In order to avoid complete removal of the β-*O*-acetyl group from **2** during cleavage of the 4,6-*O*-benzylidene group, hydrolysis in acetic acid (70%) was conducted for 3 h at 50–60°, to give a mixture of two products, **4** and **5**, which was chromatographed on silica gel (using 65:15:2 chloroform–methanol–water) to afford 2-acetamido-1,3-di-*O*-acetyl-2-

*Synthetic Studies in Carbohydrates, Part IX. For Part VIII, see ref. 1.

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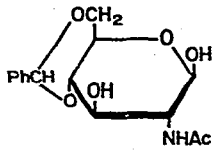

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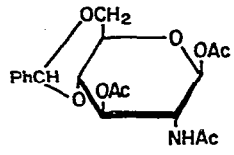

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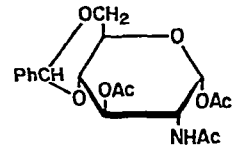

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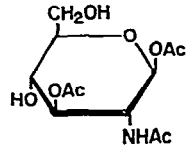

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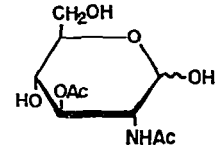

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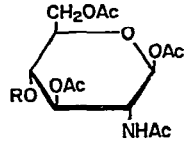
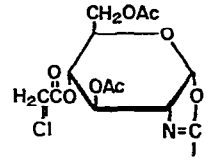


6 R=H



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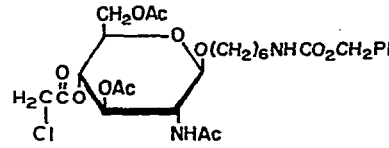
7 R=$\overset{O}{\overset{\|}{C}}CH_2Cl$



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deoxy-β-D-glucopyranose† (4) in 75% yield; $[\alpha]_D^{25}$ +9.6° (*c* 1, $HCONMe_2$); it softens at 85°. The absence of a tertiary benzylidene proton signal [at δ 5.68 for 2 in Me_2SO-d_6] from its p.m.r. spectrum indicated complete removal of the benzylidene group. [The second product, namely, 2-acetamido-3-*O*-acetyl-2-deoxy-D-glucopyranose (5), isolated from the column as a by-product, had m.p. 173–175° (from ethyl acetate), and showed mutorotation; and its p.m.r. spectrum showed the presence of only one *O*-acetyl group in the molecule.] Structure 4 was supported by the fact that, on reaction with benzaldehyde and

†Compound 4 may also be prepared by acetylation of 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-D-glucopyranose, followed by removal of the isopropylidene group. It may be mentioned that acetylation under the usual conditions yields the α anomer as the major product, as reported by Hasegawa and Fletcher[7]. We attempted the acetylation by dissolving in pyridine at ~100°, followed by addition of acetic anhydride, and the desired 2-acetamido-1,3-di-*O*-acetyl-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranose was isolated in low yield (~20%).

anhydrous zinc chloride, this compound furnished the starting material (2), thereby suggesting that an *O*-acetyl group did not migrate to hydroxyl groups at C-4 or C-6 during removal of the benzylidene group.

Treatment of a solution of 4 in pyridine with acetic anhydride (1 mol) at 0° gave compound 6 as the major product, owing to the relative ease of acetylation of the primary hydroxyl group as compared with the sterically hindered, secondary hydroxyl group at C-4. Separation by column chromatography on silica gel, with elution with 9 : 1 chloroform–methanol, provided pure compound 6, which was recrystallized from ethyl acetate, m.p. 162°, $[\alpha]_D^{24}$ −37.8° (*c* 1, $CHCl_3$). As expected, this did not give a trityl ether on treatment with chlorotriphenylmethane under the usual conditions. Condensation of compound 6 with chloroacetic anhydride in anhydrous pyridine for 10 h at 0° produced the desired compound 7 in 41% yield, m.p. 158° (chloroform–ether), $[\alpha]_D^{24}$ −6.9° (*c* 1, $CHCl_3$).

Finally, brief treatment of 7 with anhydrous ferric chloride in dichloromethane[8] gave the title oxazoline, which was isolated as a colorless syrup (yield 87%). T.l.c. indicated the absolute purity of the syrupy product; $[\alpha]_D^{22}$ +20.1° (*c* 1, $CHCl_3$); ν_{max}^{neat} 1675 cm^{-1} (C=N); p.m.r. data ($CDCl_3$): δ 1.1, 1.2, and 1.15 (3-proton singlets, 2 OAc and Me), 4.12 (s, 2 H, $ClCH_2CO$), and 6.02 (d, 1 H, $J_{1,2}$ 7 Hz, H-1). The glycosylating capability of this oxazoline was examined with 6-(benzyloxycarbonylamino)-1-hexanol, under the usual reaction-conditions[5], to give 9 in 47% yield; 9 had m.p. 115°, $[\alpha]_D^{20}$ −9.9° (*c* 1, $CHCl_3$), and the expected i.r. and ^{1}H-n.m.r. spectra.

Very recently, Kiso and Anderson[9,10] reported the direct, ferric chloride glycosylation of alcohols[9] and protected sugar acceptors[10] by 2-acetamido-2-deoxy-β-D-glucopyranosyl acetate. Our compound 7 and the previously reported 2-acetamido-1,3,4-tri-*O*-acetyl-6-*O*-(chloroacetyl)-2-deoxy-β-D-glucopyranose[5] under their conditions may provide another simple method for the sequential synthesis of oligosaccharides.

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