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Note

The decomposition of *N*-acetyl-2,3,4,6-tetra-*O*-acetyl-*N*-nitroso-β-D-glucopyranosylamine: a potential new method for the synthesis of glycosides

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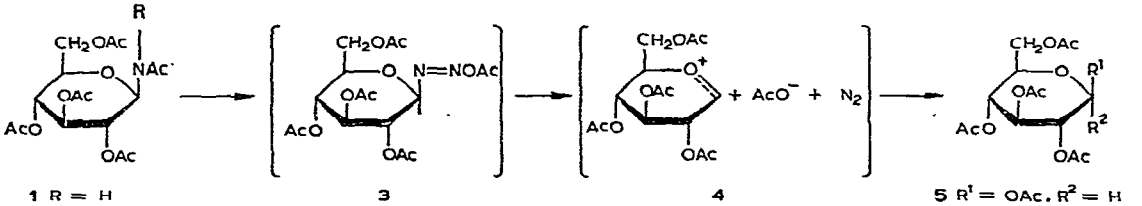
Treatment[1] of a solution of *N*-acetyl-tetra-*O*-acetyl-β-D-glucopyranosylamine (**1**) in pyridine with dinitrogen tetraoxide gave the *N*-nitroso derivative **2**, which was obtained as a chromatographically pure, yellow oil that was unstable at room temperature. The i.r. spectrum of **2** showed the characteristic N=O absorption at 6.56 μm, and the absorption for the nitroso chromophore in the u.v. spectrum was similar to that observed[1] for 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(*N*-nitroso)acetamido-β-D-glucopyranose.

In the n.m.r. spectrum of **2**, the N–H signal was absent and the NAc signal appeared at δ 2.72, showing a downfield shift of 0.7 p.p.m. compared with the NAc signal of **1**. Further, the signals for the anomeric proton and H-2 appeared at lower field.

The decomposition of nitrosamides of primary amines [$RCH_2N(NO)COR'$] involves[2–4] (*1*) rearrangement to a diazoester (RCH_2–N=N–OCOR'); (*2*) cleavage of the diazoester giving a diazoalkane and the acid, or the diazonium ion and the carboxylate anion; and (*3*) elimination of nitrogen and recombination to give the corresponding ester. If the reactions are performed in nonpolar solvents, elimination occurs and olefins are obtained.

When a solution of **2** in dichloromethane–pyridine was refluxed, penta-*O*-acetyl-β-D-glucopyranose (**5**) was formed in high yield; the α-D anomer could not be



1 R = H
2 R = NO

3

4

5 R^1 = OAc, R^2 = H
6 R^1 = H, R^2 = OMe
7 R^1 = OMe, R^2 = H

detected. Presumably, the reaction proceeds *via* the intermediates **3** and **4**. When a solution of **2** in methanol–pyridine was refluxed, methyl tetra-*O*-acetyl-α-D-glucopyranoside (**6**, 75%) and methyl tetra-*O*-acetyl-β-D-glucopyranoside (**7**, 25%) were obtained in almost quantitative yield (g.l.c.). The yields were higher in the preparative reactions when **2** was not isolated.

The reaction of glycosylamines or *N*-acetylglycosylamines with dinitrogen tetraoxide in aprotic solvents, followed by treatment with an alcohol, is a potential new method for the synthesis of glycosides.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer Model 141 polarimeter. N.m.r. spectra were recorded on a Varian HA-100 D spectrometer, i.r. spectra with a Perkin–Elmer 337 spectrometer, and u.v. spectra with a Perkin–Elmer 137 spectrometer. T.l.c. was performed on Silica Gel F_{254} (Merck). G.l.c. was conducted with a Varian model 2700 instrument fitted with a column containing 3% of ECNSS-M on Gas Chrom Q. For g.l.c.–m.s. a Varian CH7 gas chromatograph–mass spectrometer was used.

N-*Acetyl 2,3,4,6-tetra*-O-*acetyl-β*-D-*glucopyranosylamine* (**1**). — Compound **1**, prepared as described by Isbell *et al.*[5], had m.p. 161–162°, $[\alpha]_{578}^{20}$ +17° (*c* 1, chloroform); lit.[5] m.p. 163°, $[\alpha]_D^{20}$ +17°. N.m.r. data: δ 6.79 (d, $J_{NH,1}$ 9.0 Hz, N–H), 5.31 (t, $J_{2,3}$ 9.4 Hz, H-3), 5.29 (t, $J_{NH,1}$ 9.3 Hz, H-1) (collapsed to a doublet when the N–H resonance was irradiated), 5.05 (t, $J_{3,4}$ 9.4 Hz, H-4), 4.92 (t, $J_{1,2}$ 9.5 Hz, H-2), 4.31 (dd, $J_{5,6}$ 4.7, $J_{6,6'}$ 12.5 Hz, H-6), 4.10 (dd, $J_{5,6'}$ 1.9, $J_{6,6'}$ −12.5 Hz, H-6'), 3.86 (o, $J_{4,5}$ 9.0 Hz, H-5), 2.08, 2.06, 2.05, 2.03, and 2.00 (5 s, 15 H, 4 AcO, NAc).

N-*Acetyl-2,3,4,6-tetra*-O-*acetyl*-N-*nitroso-β*-D-*glucopyranosylamine* (**2**). — To a solution of **1** (3 g, 7.7 mmol) in anhydrous pyridine (30 ml) at 0°, a solution of dinitrogen tetraoxide (3 g, 32.6 mmol) in dichloromethane (15 ml) was added during 15 min at 0°. Excess of dinitrogen tetraoxide was removed with nitrogen at 0°, dichloromethane (25 ml) was added, and the solution was washed at 0° with hydrochloric acid (4M, 50 ml) and water (3 × 100 ml). The solution was dried ($MgSO_4$), and concentrated at 0° to give **2** as a chromatographically pure, yellow oil (2.25 g, 70%), $[\alpha]_{578}^{24}$ +46° (*c* 2.6, dichloromethane), R_F 0.85 (3:1 ethyl acetate–light petroleum); $\lambda_{max}^{CHCl_3}$ 3.31, 5.73 (C=O) and 6.56 (N=O) μm; λ_{max}^{EtOH} 392 (ε 36), 409 (53), and 428 (55) nm. N.m.r. data: δ 5.70 (2 H, H-1,2), 5.18 (2 H, H-3,4), 4.18 (d, 2 H, $J_{5,6}$ 2.8 Hz, H-6,6'), 3.80 (sex, H-5), 2.72 [s, 3 H, N(NO)Ac], and 2.10, 2.06, 2.00, 1.90 (4 s, 12 H, 4 AcO).

Decomposition reactions of **2**. — (*a*) A solution of **1** (1.3 g) in pyridine (20 ml) was treated with dinitrogen tetraoxide (1.5 g) in dichloromethane (10 ml) at 0°. The reaction was monitored by t.l.c. After 30 min, the mixture was purged with nitrogen for 1 h at 0°, in order to remove excess of dinitrogen tetraoxide. More (15 ml) dichloromethane was added and the solution was refluxed overnight, then cooled, washed with 4M hydrochloric acid (2 × 50 ml) and water (3 × 50 ml), dried ($MgSO_4$), and concentrated. The product was crystallized from ethanol to yield penta-*O*-acetyl-

β-D-glucopyranose (**5**, 0.75 g), m.p. 135°, $[\alpha]_{578}^{24}$ +4° (*c* 1, chloroform); lit.[7] m.p. 132–134°, $[\alpha]_D$ +4°. The yield, determined by g.l.c. using penta-*O*-acetyl-β-D-galactopyranose as an internal standard, was 65%.

(*b*) The reaction was performed as described in (*a*), except that methanol (50 ml) instead of dichloromethane was added after the removal of excess of nitrogen tetraoxide. The solution was refluxed for 8 h, and then processed as described in (*a*) to give a quantitative yield (g.l.c.) of a mixture of methyl 2,3,4,6-tetra-*O*-acetyl-α- and -β-D-glucopyranoside (**6** and **7**) in the ratio 3:1 (g.l.c.).

In a preparative experiment, **1** (3 g) was dissolved in pyridine (30 ml), and dinitrogen tetraoxide (3 g) in dichloromethane (25 ml) was added. The rest of the reaction was then performed as described above. The product mixture (2.9 g) was suspended in dry methanol (30 ml) and deacetylated by the addition of M methanolic sodium methoxide (9 ml). The mixture was neutralised with Dowex-50(H^+) resin and concentrated to dryness, and the residue was fractionated on a column of Dowex 1-X (HO^-) resin (200–400 mesh)[6]. The separation was followed polarimetrically, and recrystallisation from ethanol of the products in the appropriate fractions yielded methyl α-D-glucopyranoside (825 mg), m.p. 164°, $[\alpha]_{578}^{24}$ +157° (*c* 2.5, water) (lit.[7] m.p. 165–166°, $[\alpha]_D^{20}$ +158°), and methyl β-D-glucopyranoside (270 mg), m.p. 108°, $[\alpha]_{578}^{24}$ −31° (*c* 1.8, water) (lit.[7] m.p. 110°, $[\alpha]_D^{20}$ −32°).

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