

The Nitrous Acid Deamination of Methyl 2-Amino-2-deoxy- α -D-glucopyranoside, 2-Amino-2-deoxy-1,3,4,6-tetra-*O*-acetyl- β -D-glucopyranose and 2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosylamine in Glacial Acetic Acid

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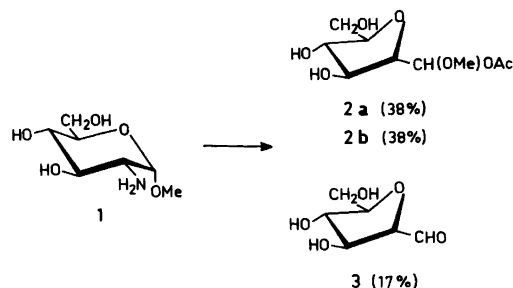
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The deamination of carbohydrate amines has been reviewed by Williams.¹ In hexopyranoses, rearrangement by participation of an atom antiperiplanar to the nitrogen atom of the amine often predominates, especially when the amino group is equatorial. Most studies on deamination of carbohydrates have been performed in water or water-containing solvents.

Nitrous acid deamination of polyfunctional amines usually results in complex mixtures owing to the high reactivity of the carbonium ion that is generated by heterolysis of the diazonium ion. Rearrangement reactions generally increase with the polarity of the solvent used.² We now report on

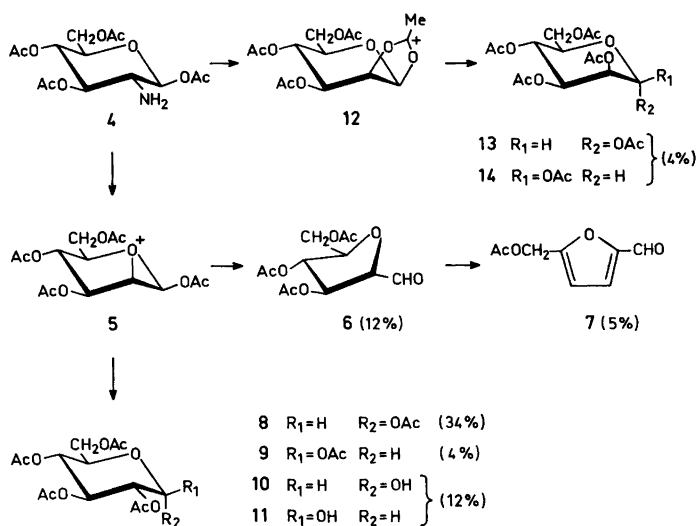
the deamination of 2-amino-2-deoxy-D-glucose and D-glucosylamine derivatives in a non-aqueous solvent (anhydrous acetic acid).



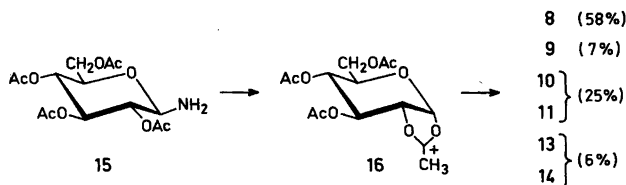
Scheme 1. Treatment of methyl 2-amino-2-deoxy- α -D-glucopyranoside (1) with sodium nitrite in anhydrous acetic acid.

Treatment of methyl 2-amino-2-deoxy- α -D-glucopyranoside (1) with sodium nitrite in anhydrous acetic acid yielded the two anomers of 1-*O*-acetyl-2,5-anhydro-1-*O*-methyl-D-mannose (2a and 2b) and 2,5-anhydro-D-mannose (3) in the proportions 2:2:1 (Scheme 1). No ring-contraction products involving participation of C-4 as observed for the corresponding reaction in water³ were obtained. The formation of mixed acetals of 3 has been observed on brominolysis of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo- α -D-glucopyranoside in acetic acid.⁴

Deamination of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy- β -D-glucopyranoside (4) resulted in a more



Scheme 2. Deamination of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy- β -D-glucopyranoside (4).



Scheme 3. Deamination of 2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosylamine (15).

complicated reaction mixture, which was investigated by ^1H NMR, GLC and sugar analysis. Part of the product was not deaminated, most probably because of acetyl migration to nitrogen. The main products were acetates of D-glucopyranose (8, 9, 10 and 11) and some mannopyranose derivatives (13 and 14). Ring-contracted products, namely 3,4,6-tri-*O*-acetyl-2,5-anhydro-D-mannose (6) and its product formed on elimination of acetic acid (7),⁵ 5-(acetoxymethyl)-2-furaldehyde, were also formed. Yields are depicted within parentheses in Scheme 2. The formation of β -D-glucopyranose pentaacetate (9) may be accounted for by postulating an attack of acyl ion (or acetic acid) upon the oxonium ion 5. The α -anomer (8) obtained in high yield is probably an anomerization product. Tetraacetates, with free hydroxyl group on C-1, (10 and 11) were also formed, probably by hydrolysis of 8 and 9 by water formed in the diazotation reaction. The formation of small amounts of D-mannopyranosyl pentaacetates indicates either a direct attack of acetyl ion (or acetic acid) upon the diazonium ion derived from 4 or on C-1 of the acetoxonium ion 12.

The low yield of ring-contraction products on deamination of 4 is due both to the solvent and to the presence of an acetoxyl group on C-1. Similar results have been observed previously.³

On deamination of 2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosylamine (15) in anhydrous acetic acid, mainly acetates of D-glucopyranose (8, 9, 10 and 11) were formed probably *via* attack on C-1 of the diazonium ion derived from 15 or on the acetoxonium ion 16 (Scheme 3). The formation of small amounts of D-mannose derivatives (13 and 14) may be accounted for by an attack of acyl ion (or acetic acid) on C-2 of 16.

Experimental. General methods. Melting points are uncorrected. Concentrations were carried out under reduced pressure at bath temperatures not exceeding 40°C. NMR spectra were recorded in D_2O , CDCl_3 or acetone (d_6) at 30°C using a JEOL FX 90 Q instrument. TLC and column chromatography were performed on silica gel F₂₅₄ (Merck) and silica gel 60 (Merck), respectively. Optical rotations were determined with a Perkin

Elmer 141 polarimeter. For GLC a Packard 427 instrument and glass capillary columns (25 m \times 0.3 mm) coated with OV-225 were used.

Deamination of methyl 2-amino-2-deoxy- α -D-glucopyranoside (1). Compound 1 (800 mg) was dissolved in glacial acetic acid (80 ml) and sodium nitrite (3.0 g) was added gradually. The reaction mixture was stirred at room temperature for 1 h and filtered. The filtrate was evaporated to give a syrup (780 mg) which showed two major spots on TLC; the anomeric forms of 2,5-anhydro-1-acetyl-1-methoxy-D-mannose (2a and 2b). Fractionation on a silica gel column (3 \times 50 cm) irrigated with ethyl acetate–methanol (9:1 v/v) afforded pure fractions of 2a (123 mg) and 2b (82 mg) along with fractions containing a mixture of 2a and 2b (370 mg).

Compound 2a, $[\alpha]_{578}^{20} + 55.5^\circ$ (c 0.93, CH_3OH), was a syrup which was homogeneous on TLC and GLC. ^1H NMR (acetone- d_6): δ 5.82 (d, 1 H, $J_{1,2}$ 5.9 Hz, H-1), 4.01–4.17 (m, 2 H, H-3, H-4), 3.80–3.93 (m, 2 H, H-2, H-5), 3.63–3.71 (m, 2 H, H-6, H-6'), 3.42 (s, 3 H, OMe) and 2.09 (s, 3 H, Ac). Acetylation of 2a yielded a syrup (2a'), $[\alpha]_{578}^{20} + 46.3^\circ$ (c 0.52, CHCl_3), lit.⁴ $[\alpha]_{\text{D}} + 49.4^\circ$. ^1H NMR (CDCl_3): δ 5.90 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 5.36 (t, 1 H, $J_{2,3}$ 3.7 Hz, $J_{3,4}$ 3.0 Hz, H-3), 5.16 (t, 1 H, $J_{4,5}$ 2.8 Hz, H-4), 4.19–4.21 (m, 3 H, H-5, H-6, H-6'), 4.13 (dd, 1 H, H-2), 3.49 (s, 3 H, OMe), 2.13 (s, 3 H, Ac) and 2.09 (s, 9 H, 3 Ac).

Compound 2b, $[\alpha]_{578}^{20} + 33.2^\circ$ (c 0.81, methanol) was obtained as a syrup and was homogeneous on TLC and GLC. ^1H NMR (acetone- d_6): δ 5.87 (d, 1 H, $J_{1,2}$ 7.0 Hz, H-1), 4.05–4.22 (m, 2 H, H-3, H-4), 3.80–3.98 (m, 2 H, H-2, H-5), 3.68 (m, 2 H, H-6, H-6'), 3.42 (s, 3 H, OMe), and 2.09 (s, 3 H, Ac). Acetylation of 2b yielded 2b' which was also obtained as a syrup and had $[\alpha]_{578}^{20} + 41.1^\circ$ (c 0.73, CHCl_3), lit.⁴ $[\alpha]_{\text{D}} + 46.3^\circ$. ^1H NMR (CDCl_3): δ 5.86 (d, 1 H, $J_{1,2}$ 5.9 Hz, H-1), 5.43 (t, 1 H, $J_{2,3}$ 3.0 Hz, $J_{3,4}$ 3.0 Hz, H-3), 5.12 (dd, 1 H, $J_{4,5}$ 4.8 Hz, H-4), 4.11–4.26 (m, 3 H, H-5, H-6, H-6'), 4.10 (dd, 1 H, H-2), 3.48 (s, 3 H, OMe), 2.12 (s, 3 H, Ac), 2.10 (s, 3 H, Ac), and 2.09 (s, 6 H, 2 Ac).

Compound 1 (20 mg) was dissolved in glacial acetic acid (2.5 ml) and sodium nitrite (120 mg) was added. The reaction mixture was stirred for 1 h at room temperature. After evaporation to dryness

myo-inositol (3 mg) was added as internal standard and the reaction mixture was treated with pyridine and hydroxylamine hydrochloride followed by acetic anhydride. In this reaction 2a and 2b were acetylated and 3 transformed into the acetylated nitrile. The reaction mixture was evaporated and analyzed by GLC. The yield of 2a, 2b and 2,5-anhydro-D-mannose (3) was 38, 38 and 17%, respectively. The detector responses for acetylated 2a, 2b and 3 as nitrile were determined relative to *myo*-inositol and were found to be 0.55, 0.50 and 0.39, respectively.

Deamination of 2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (4). Compound 4 (40 mg) was dissolved in anhydrous acetic acid (6 ml) and sodium nitrite (250 mg) was added together with 1,2,3,4-tetra-O-acetyl-β-D-xylopyranoside as internal standard. The reaction mixture was stirred at room temperature for 1 h, then concentrated to dryness, extracted with chloroform (3 × 5 ml) and filtered. The filtrate was divided into three parts.

The first part was dissolved in CDCl₃ and analyzed by ¹H NMR spectroscopy. Doublets at δ 5.72 (*J*_{1,2} 7 Hz) and δ 6.32 (*J*_{1,2} 4 Hz) in the relative proportions 1:9 were attributed to the anomeric protons of 9 and 8, respectively.

The first part was also analyzed by GLC showing α- and β-D-glucose pentaacetate (8 and 9, 34 and 4%, respectively) and 5-(acetoxymethyl)-2-furaldehyde (7, 5%).

The second part was concentrated to dryness and treated with an excess of sodium borohydride (20 mg) in aqueous methanol.⁴ After 18 h at room temperature, the reaction mixture was treated with an excess of acetic acid. The reaction mixture was concentrated to dryness, codistilled with methanol (3 × 10 ml) and acetylated. GLC revealed the presence of 1,3,4,6-tetra-O-acetyl-2,5-anhydro-D-mannitol (12%).

In the third part, the components were deacetylated.⁶ Sugar analysis⁷ revealed the presence of D-mannose (4%) and D-glucose (50%).

In the preparative experiment compound 4 (200 mg) was dissolved in glacial acetic acid (30 ml) and sodium nitrite (1.25 g) was added. The reaction mixture was stirred at room temperature (1 h), concentrated to dryness and extracted with chloroform (3 × 50 ml). The extract was filtered and concentrated to a small volume. Separation on a silica gel column (3 × 25 cm) with chloroform-methanol (20:1, v/v) yielded 7, 10 mg. The ¹H NMR spectrum was in accordance with literature values. ¹³C NMR (CDCl₃). δ: 177.75 (CHO), 170.27 (CH₃C=O), 152.96 (C-2), 121.32 (C-3), 112.49 (C-4), 155.48 (C-5), 57.80 (C-6), 20.61 (CH₃C=O). M.S. had *inter alia* peaks at *m/e* 43 (100), 79 (23), 97 (18), 109 (22), 126 (62) and 168 (2).

Deamination of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylamine (15). Compound 15 (40 mg) was deaminated in the presence of 1,2,3,4-tetra-O-acetyl-β-D-xylopyranose (10 mg) and analyzed as described above. The reaction mixture contained 58% of 8 and 7% of 9. Sugar analysis of the deacetylated reaction mixture yielded 6% D-mannose and 90% D-glucose, indicating the presence of 6% of 13 and 14 and 25% of 10 and 11 in the original reaction mixture.

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