The Nitrous Acid Deamination of Methyl 4-Amino-4-deoxy-α-D-glucopyranoside

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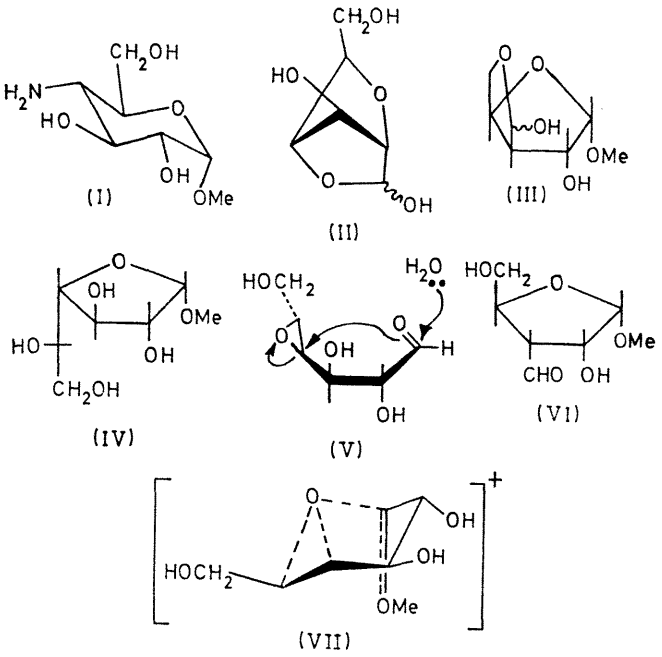
Summary Evidence is presented for the formation of 4,5-anhydro-D-galactose and two other rearrangement products in the deamination of the title compound.

THE continued interest[1-5] in rearrangement reactions of carbohydrate derivatives prompts us to report our results on the deamination of methyl 4-amino-4-deoxy-α-D-glucopyranoside (I). The deamination of glucopyranoside derivatives having an equatorial amine function at positions 2 and 3 were known to proceed with participation of ring oxygen and carbon atoms, respectively, to give the ring-contracted products, (II)[6] and (III).[7]

The deamination of compound (I) was therefore of interest especially in view of the two possible rearrangements involving the ring oxygen and C-2, the participation of the ring oxygen being less favourable than in 2-amino-2-deoxy-D-glucopyranosides due to the lack of a second oxygen atom attached to C-5. Treatment of (I)[8] with aqueous sodium nitrite and acetic acid at a pH of 3—4 gave after deionisation at least six products,† four of which were

† Analysed by paper chromatography and g.l.c.[9]

identified as methyl α-D-glucopyranoside (35%‡), methyl β-L-altrofuranoside (7%‡) (IV), glucose and (III) (15%‡). Each product was characterised by the isolation of a crystalline compound and comparison (mixed m.p. and spectra) with authentic samples. The glucose was shown to be formed from a primary product during deionisation since analysis of the neutralised reaction mixture without deionisation showed that glucose was absent and another compound was present. This compound is formulated as 4,5-anhydro-D-galactose (V), the glucose formation being due to attack of water (or OH^-) on the aldehyde and ring opening of the epoxide as shown. Although a small quantity (1 mg.) of impure (V) was isolated and its conversion into glucose and a trace of altrose under cold acidic (IR 120 ion exchange resin) and basic (aqueous pyridine) conditions was demonstrated, it was very labile and attempts to isolate larger quantities were unsuccessful. Altrose was also detected in the partially decomposed (V) isolated *via* chromatography on sephadex G10, and it arises by ring opening of the epoxide at C-5. Six-membered ring formation is often a minor reaction pathway in irreversible cyclisation reactions.[10,11] Further evidence for the structure of (V) was provided by treatment of the reaction mixture (neutralised and concentrated to dryness) with cold methanolic sodium methoxide followed by the isolation of crystalline methyl α-D-glucofuranoside (3·5%) and its β-anomer (6%), characterised as the tetraphenylcarbamoate derivate. 4,5-Anhydroaldose derivatives have been postulated as intermediates in the rearrangements of various aldose 5-sulphonate derivatives[5,11,12] and of methyl 4-*O*-*p*-nitrobenzenesulphonyl-α-D-glucopyranoside.[3] Attack of methoxide ion on the aldehyde function in (V) is much less stereoselective (furanoside β:α ratio 1·8:1) than in derivatives having the bulky *O*-isopropylidene function at C-2,C-3 (furanoside β:α ratio > 6:1).[11] A similar low stereoselectivity has recently been reported in the reaction of a 2,3-di-*O*-benzylaldose 5-sulphonate derivative with sodium methoxide.[5]



The isolation of (III), characterised by comparison with an authentic sample[2] and as crystalline dibenzoate (m.p 135·5—136·5°) and lactone[2,7] derivatives, was unexpected since a concerted rearrangement involving migration of the atom C-2 periplanar to the diazonium function would give the aldehyde (VI). Since one of the steps in the isolation of (III) involved paper chromatography in a pyridine-containing system it seemed likely that (III) resulted from the epimerisation of (VI). This was supported by the isolation, under cold base-free conditions of a fraction which was predominantly an aldehyde (100 Mc./sec. n.m.r. data: τ 0·27, d, *J* 3 c./sec., D_2O solvent, Me_3COH internal standard) and which on standing at room temperature in aqueous pyridine was converted into (III) τ 4·51 (s, 3-H); 7·32 (t, *J* 7 c./sec., 3H). The isolation of fractions containing (III) also under these conditions demonstrated that the enolisation of (VI) must be unusually easy

The methyl α-D-glucopyranoside (IV), and (V) can be considered to arise from the intermediate oxonium ion (VII) by attack of solvent water at C-4, C-5, and C-1, respectively. The ion (VII) has previously been postulated as an intermediate in the solvolysis of methyl 4-*O*-*p*-nitrobenzenesulphonyl-α-D-glucopyranoside. Major differences between the deamination and solvolysis reactions are the absence of methyl α-D-galactopyranoside from, and the presence of (III) in, the deamination products.

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‡ Yield of isolated compound.

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