Note

The nitrous acid deamination of 2-amino-2-deoxy-D-mannose hydrochloride to D-glucose*

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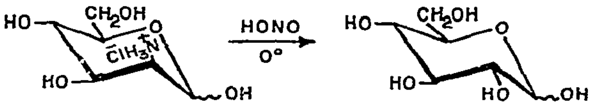
(Received October 21st, 1971)

The reaction of amino sugars with nitrous acid was first studied by Ledderhose[1] in 1880, as he sought to determine the structure of 2-amino-2-deoxy-D-glucose. It is well established[2] that nitrous acid converts 2-amino-2-deoxyaldoses (and their glycosides) into 2,5-anhydrides, with inversion at C-2, when the amino group is equatorially attached in the favored conformation.

Levene[3] observed that treatment of 2-amino-2-deoxy-D-mannose (**1**) with nitrous acid, followed by oxidation with nitric acid, gave (in 9% yield) D-glucaric acid, presumably arising from D-glucose (**2**). The identity and yield of the immediate product of deamination has never been firmly established. Levene also stated that attempted oxidation of **1** to 2-amino-2-deoxy-D-mannonic acid with mercuric oxide gave, instead, 2,5-anhydro-D-glucose[3]. It has been proposed[4] that, at the elevated temperatures employed, deamination occurred through the alternative *1C*(D) conformation, having the amino group equatorially attached and C-2 exposed for rearside attack by O-5.



1 2

In the present study, deamination of 2-amino-2-deoxy-D-mannopyranose (**1**) with sodium nitrite in aqueous acetic acid at 0° gave crystalline α-D-glucose (**2**, 72%). Small proportions of two other products were also detected by paper chromatography, but no mannose was detected. The D-glucose formed was further character-

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*Supported, in part, by the National Institute of General Medicine, National Institutes of Health, U. S. Public Health Service, Grant. No. GM-11976-08 (The Ohio State University Research Foundation Project 1820), and, in part, by the Ligue Nationale Française contre le Cancer.

ized by use of D-glucose oxidase, and by conversion into the crystalline diethyl dithioacetal.

The starting amino sugar **1** has been shown[5] to favor the chair conformation having the amino group axially attached; in water, it exists as a 43:57 mixture of the α-D and β-D pyranose anomers. It is probable that **2** is formed by direct, rearside attack by solvent on an axial diazonium ion derived from **1**. Ying Kin and Williams[6] have suggested that D-glucose may be formed by hydrolysis of an intermediate D-*gluco* 1,2-epoxide formed by attack of the axial 1-hydroxyl group on the diazonium ion, but the low proportion of the α-D anomer (axial 1-OH) that is present in an aqueous solution of **1** at equilibrium militates against this hypothesis in view of the high yield of **2**.

A similar high degree of stereoselectivity has been observed in the deamination of methyl 4-amino-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside[7], wherein an amino group that, presumably, is axially attached undergoes net replacement (with inversion) by a hydroxyl group; but similar deamination of two axial amines, namely, methyl 4-amino-4-deoxy-α-D-galactopyranoside and methyl 3-amino-3-deoxy-β-D-allopyranoside, led to mixtures of several products[6].

EXPERIMENTAL

General methods. — Solutions were evaporated below 30°. Melting points were determined with a Thomas–Hoover "Unimelt" apparatus, and are uncorrected. Optical rotations were determined with a 1-dm polarimeter tube in a Perkin–Elmer Model 141 recording polarimeter. X-Ray powder diffraction data give interplanar spacings in Å for CuKα radiation (camera diameter = 114.59 mm). Relative intensities were estimated visually: m, moderate; s, strong; v, very; w, weak. The three strongest lines are numbered (1, strongest). The R_F values recorded refer to paper chromatograms on Whatman No. 1 paper, developed by the descending technique, with aniline hydrogen phthalate and periodate–benzidine as detection reagents. Ninhydrin was used for the detection of amino sugars.

*Nitrous acid deamination of 2-amino-2-deoxy-*D*-mannopyranose hydrochloride*[5] (**1**). — A solution of **1** (216 mg, 1.0 mmole) in water (10 ml) was maintained at 0° and sodium nitrite (278 mg, 4.0 mmoles) was added in several portions to the magnetically stirred solution. Acetic acid (0.3 ml) was then added dropwise, at such a rate that the temperature of the solution remained at 0°. Stirring was continued for 4 h at 0°, and nitrogen was then bubbled through the solution for 20 min. The solution was de-ionized by passage through a column of Amberlite MB-3 mixed-bed resin and the resin was washed with one bed-volume of distilled water. The effluents were combined, and freeze-dried, to give a pale-yellow syrup (165 mg). Methanol was added to and evaporated from the syrup several times, and, after being kept for several weeks, small, white crystals of α-D-glucose (**2**) formed. These were washed with a small volume of cold methanol; yield 129 mg (72%), m.p. 145–146° (lit.[8] m.p. 146°). This product was indistinguishable from authentic α-D-glucose by X-ray powder diffraction pattern and mixed m.p.; X-ray powder diffraction data: 8.32 w, 7.22 w, 5.93 s (2,2), 5.12 m, 4.65 s (2,2), 4.23 vs (1), 3.81 w, 3.46 m, and 3.11 m.

The deamination was monitored by paper chromatography of the reaction mixture, and no amino sugar was detected after 1.5 h of reaction.

Paper-chromatographic examination of the resultant, de-ionized syrup with three solvent systems (4:1:5 1-butanol–acetic acid–water; 1:2:2 pyridine–ethyl acetate–water; and 4:1:5 1-butanol–ethanol–water) indicated the presence of two minor components (R_F 0.44 and 0.51, in the first solvent). No mannose was detected.

The presence of D-glucose was verified by enzymic assay for D-glucose with Glucostat (Worthington Biochemical Corp., Freehold, New Jersey) and by treatment, by the method of Wolfrom[9], of the syrupy mixture (60 mg) with ethanethiol to give crystalline D-glucose diethyl dithioacetal; yield 129 mg (64%), m.p. 126–127°, $[\alpha]_D^{26}$ $-31°$ (c 1.0, water) (lit.[10] m.p. 127–128°, $[\alpha]_D^{50}$ $-29.8°$ in water).

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