The Nitrous Acid Deamination of Methyl 4-Amino-4-deoxy-α-D-galactopyranoside and 3-Amino-3-deoxy-β-D-allopyranoside

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Summary Rearrangements are important reaction pathways in the deamination of the pyranoside amines (II) and (IV).

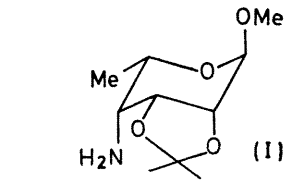
THERE is considerable current interest[1-5] in rearrangement reactions of pyranose derivatives, and the recently reported[4] deamination of methyl 4-amino-4-deoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (I) is interesting in that it proceeds predominantly *without* rearrangement. We report analogous reactions in which rearranged products are formed from two monocyclic pyranosides each containing an axial amino-group.

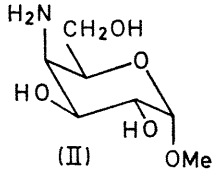
Methyl 4-amino-4-deoxy-α-D-galactopyranoside[6] (II), on deamination with sodium nitrite in dilute acetic acid solution, gave as major product a uloside (III) ν_{max} 1723 cm^{-1}, which was isolated pure in 17% yield† by preparative paper chromatography. The uloside gave a crystalline 2,4-dinitrophenylhydrazone and the structure (III) was indicated by the n.m.r. spectrum: $J_{1,2}$ 4·4, $J_{2,4a}$ 1·3, $J_{4,4'}$ 14·6, $J_{4a,5}$ 11·6, $J_{4e,5}$ 3·5: the 4-H axial proton resonates at lower field than 4-H equatorial, in agreement with the results of Overend and his co-workers.[7] The (^4J) long-range coupling (1·3 Hz) between axial protons 2-H and 4-H is interesting since the bonds through which it occurs do not

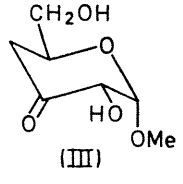
† The low yield resulted from the necessity to elute a narrow zone from the paper chromatograms to avoid contamination from adjacent zones. A second sample of the uloside (III), containing traces of two minor products, was isolated in 41% yield. All new compounds isolated had satisfactory elemental and/or spectral analyses.

have the planar W orientation commonly associated[8] with ^4J. Methyl α-D-glucopyranoside and α-D-galactopyranoside were minor products, which were isolated crystalline in 9% and 2% yields, respectively, and identified by comparison with authentic samples. There were at least three other unidentified products, the predominant one of which had reducing properties.

Deamination of methyl 3-amino-3-deoxy-β-D-allopyranoside[9] (IV) gave a mixture which contained at least seven products. G.l.c. and paper-chromatographic analysis showed that two products predominated, one of these being methyl β-D-glucopyranoside. Attempts to isolate the other major product by silica gel chromatography, followed by paper chromatography of an acetone extract of the product


(I)


(II)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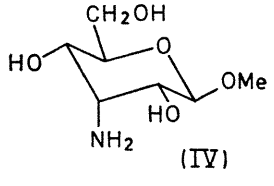
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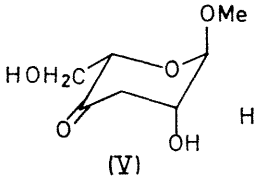
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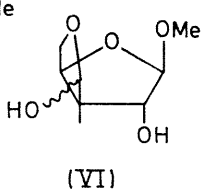
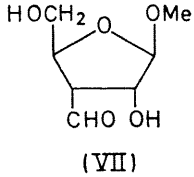

(VI)


(VII)

mixture, gave a mixture of two ulosides in 7% yield [ν_{max} 1720 cm^{-1}, unsymmetrical; τ (pyridine) 6·8—7·3 (m, CH_2·CO)]. Repeated fractionations on paper were unsuccessful in providing the major uloside in pure form, and it was established by n.m.r. and paper chromatography that the uloside was rearranging to give an isomeric uloside. The latter was obtained pure by preparative paper chromatography and its n.m.r. spectrum ($J_{1,2}$ 2·5, $J_{2,3}$ 4·5 and 5·0, $J_{3,3'}$ 17·0) indicates the structure (V), the C-5 epimer of the expected 4-uloside. Difficulties in the purification of hexopyranosid-2- and -4-uloses have been reported previously.[10] Thus the major uloside product, the precursor of (V), is tentatively identified as the C-5 epimer of (V). A ring-contracted product, methyl 3-formyl-3-deoxy-β-D-xylofuranoside (VI), was also isolated unexpectedly in 5% yield. The n.m.r. spectrum of the xyloside was similar to that of the known α-anomer,[5,11] and the presence of a five-membered-ring hemiacetal was established by bromine oxidation to a γ-lactone (ν_{max} 1750 cm^{-1}). The structure of the xyloside was proved by sequential sodium borohydride reduction and acid hydrolysis to 3-hydroxymethyl-D-xylose, which was identical (n.m.r., g.l.c., paper chromatography) with the product similarly obtained from the α-anomer. Ring contractions normally occur in the deamination of equatorial amines,[5] and the preferred conformation of the 3-amino-3-deoxyalloside is most likely to be that shown (IV), in which the amino-group is axial. Since the xyloside (VI) is a relatively minor product it may arise from a small proportion of a conformation in which the C-5/C-4/C-3/N bonds are coplanar. Two such conformations[12] are C_4^1 and $B^{0,3}$. Twist boats such as S_5^3 are also possibilities if some deviation from coplanarity is permitted in the transition state for the rearrangement. However, all of these conformations would give the ring-contracted aldehyde (VII), and epimerisation at C-3 is necessary to account for the observed product (VI). Evidence has been presented for an analogous epimerisation of the α-anomer of (VII) in the deamination of methyl 4-amino-4-deoxy-α-D-glucopyranoside.[5] Chromatography of the alloside deamination products on Dowex AG1-X2 (OH)[13] gave a crystalline glycoside mixture (32%) which was shown by n.m.r. and g.l.c.[14] to contain methyl β-D-glucopyranoside (29·5%) and methyl β-D-allopyranoside (2·5%). The glucoside was obtained pure by recrystallisation, and further confirmation of the alloside was obtained by the identification of allose and 1,6-anhydroallose after acid hydrolysis of the mixture.

The deamination of 2-amino-2-deoxy-D-mannose which gives mainly D-glucose,[15] an unrearranged product, would appear to be anomalous compared with the above results. However, we have shown that the glucose is formed stereospecifically (no mannose could be detected by g.l.c.) and we suggest that the glucose may arise from 1,2-anhydroglucose which can be formed by participation of the anomeric hydroxy-group in the α-anomer of 2-amino-2-deoxy-D-mannose.

The fusion of a second ring to the pyranose ring, as in the taloside (I), clearly renders the rearrangement pathways much less favourable.

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