# The Synthesis of Derivatives of 2,3,4,6-Tetra-amino-2,3,4,6-tetradeoxy-D-galactose and -D-idose

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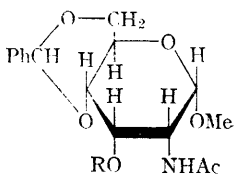
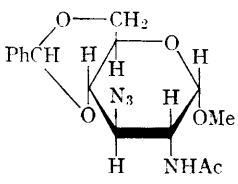
SEVERAL monosaccharides containing one or two amino- or dimethylamino-groups have been isolated from antibiotics[1] and certain micro-organisms and methods for the synthesis of these amino- and diamino-sugars are quite numerous. However, no monosaccharides containing more than two amino-groups have been described and it was therefore of interest to develop methods for the synthesis of polyamino-sugars and to investigate their properties. We now describe the synthesis of two 2,3,4,6-tetra-acetamidohexopyranosides with the D-*galacto*- and D-*ido*-configurations (VII and XIII, respectively).

Methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-allopyranoside (I) was prepared originally by the method of Jeanloz[2] but was later more conveniently obtained, and in higher yield, from methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside[3] by sequential oxidation with dimethyl sulphoxide–acetic anhydride, reduction with sodium borohydride and *N*-acetylation; a reaction sequence involving epimerisation at C-2 during the oxidation. The pyranoside (I) was converted into the 3-*O*-methanesulphonate (II) which underwent a bimolecular replacement reaction with sodium azide in dimethylformamide

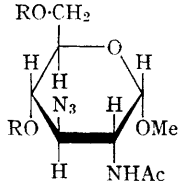
to give, by inversion of configuration at C-3, the 3-azido-glucopyranoside (III) in a yield of 86%. The azide (III) could also be synthesised from methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside (IX)[4] by a brief treatment with sodium azide in boiling dimethylformamide. The yield, however, by this procedure was only 10—30% due to simultaneous de-*N*-acetylation to the epimine (VIII), which could also be isolated from the reaction mixture. The diequatorial ring-opening of the acetylepimine (IX) is analogous to that observed for the *N*-benzoate by Guthrie and Murphy[5] who were unable to characterise a product when they treated



(I) R=H
(II) R=Ms

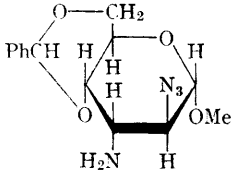


(III)



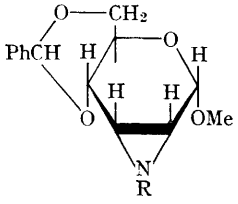
(IV) R=H
(V) R=Ms

R=Ac

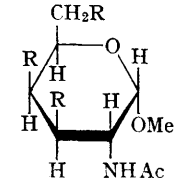


(X)

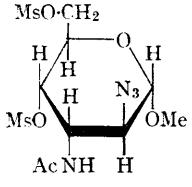
R=H



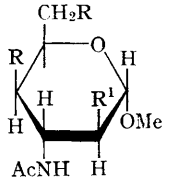
(VIII) R=H
(IX) R=Ac



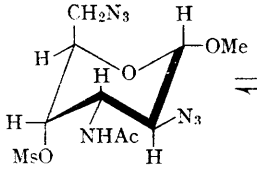
(VI) R=$N_3$
(VII) R=NHAc



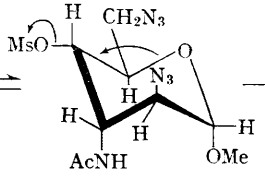
(XI)



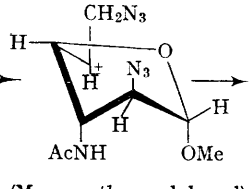
(XII) R=$R^1$=$N_3$
(XIII) R=$R^1$=NHAc
(XIV) R=$PhCO_2$, $R^1$=$N_3$
(XV) R=OH, $R^1$=$N_3$



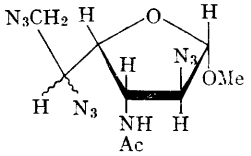
(XVI)



(XVII)



(Ms = methanesulphonyl)



(XVIII)

(IX) with sodium azide in boiling dimethylformamide for 3 hr.

Removal of the 4,6-benzylidene substituent from the azido-glucoside (III) was effected with aqueous acetic acid and the resulting diol (IV) was converted to the 4,6-dimethanesulphonate (V). Both sulphonate residues underwent displacement when (V) was heated with sodium azide in hexamethylphosphoric triamide at 90° and methyl 2-acetamido-3,4,6-triazido-2,3,4,6-tetradeoxy-α-D-galactopyranoside (VI) was isolated in 68% yield. Catalytic reduction of the triazide using Raney nickel gave the corresponding syrupy triamine, which on treatment with acetic anhydride in ethanol gave the highly crystalline tetra-*N*-acetate (VII), m.p. 285° (dec.), $[\alpha]_D$ + 118° (*c* 0·35, $H_2O$).

The corresponding D-idopyranoside was synthesised from methyl 4,6-*O*-benzylidene-2,3-epimino-2,3-dideoxy-α-D-allopyranoside (VIII),[4] which underwent *trans*-diaxial ring-opening with azide to give the 2-azido-altropyranoside (X).[3] *N*-Acetylation followed by acid hydrolysis and methanesulphonylation yielded methyl 3-acetamido-2-azido-2,3-dideoxy-α-D-altropyranoside 4,6-dimethanesulphonate (XI), which underwent displacement of both sulphonate residues during a brief treatment with sodium azide in boiling dimethylformamide to give a triazide in 61% yield. The structure of the triazide was a matter of some doubt, since direct replacement at C-4 in the C1 conformation (XVII) would be sterically hindered by the β-*trans*-axial azide substituent at C-2.[6] In cases where this condition exists ring-contraction has been observed [*i.e.*, (XVII) → (XVIII)] to give a furanoside.[7] The pyranoside structure of our triazide was demonstrated by hydrogenation to a syrupy triamine, which was not oxidised by periodate. Furthermore, the dimethanesulphonate (XI) underwent displacement by benzoate in hexamethylphosphoric triamide to give a dibenzoate (XIV) which afforded a diol on debenzoylation, which again was not oxidised by periodate thus showing it possessed a pyranoside structure (XV). It would seem likely that compound (XVII) must undergo direct replacement at C-4 by changing to the IC conformation (XVI) in which there should be no significant hindrance to direct replacement. Acetylation of the syrupy triamine prepared from the triazide (XII) gave methyl 2,3,4,6-tetra-acetamido-2,3,4,6-tetradeoxy-α-D-idopyranoside (XIII), decomp. 260°, $[\alpha]_D$ + 42° (*c* 0·5, $H_2O$).

All compounds described in this paper had satisfactory analyses and their infrared spectra were in accord with the structures assigned to them.

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