A Simple Synthesis of Azidodeoxy-sugars *via* Chlorodeoxy-sugars

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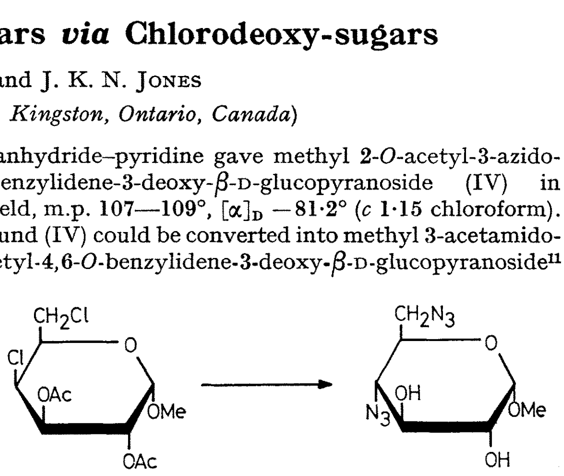
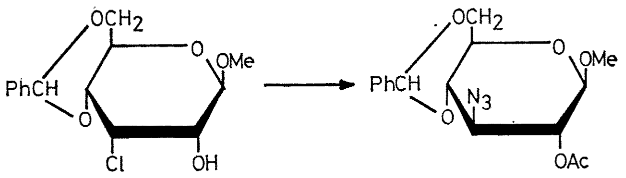
THE reaction of sulphuryl chloride with carbohydrates containing free hydroxy-groups has been extensively studied,[1] and has been shown to give fully substituted derivatives containing both chlorodeoxy- and chlorosulphate ester groups. The chlorodeoxy-groups are formed by bimolecular displacement by chloride ion of certain of the chlorosulphonyloxy-groups.[2] Some conformational aspects of the substitution reactions have been discussed.[3] The ready availability of chlorodeoxy-sugars by reaction with sulphuryl chloride and by other methods[4] should make these compounds valuable intermediates in the synthesis of other sugar derivatives, such as deoxy- and aminodeoxy-sugars of biological interest. This potential utility has been, however, relatively unexplored. We have previously used chlorodeoxy-sugars in the preparation of 4,6-dideoxy-3-*O*-methyl-D-*xylo*-hexose (D-chalcose)[5] and other deoxy-sugars,[6] and some displacements of primary chloro-groups in carbohydrate derivatives have been reported by other workers.[7] We report now some examples of displacement of chloro-groups in hexopyranosides with azide ion; not only is the chloro-group at C-6 readily displaced, but substitution on ring carbons occurs also.

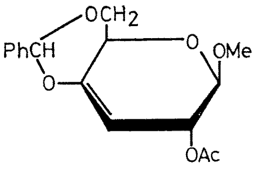
The displacement reactions were performed in *NN*-dimethylformamide at 120—130° with a twofold excess of sodium azide. Methyl 2,3-di-*O*-acetyl-4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside (I)[8] (prepared *via* a sulphuryl chloride reaction with methyl α-D-glucopyranoside[9]) gave after 12 hr. a syrupy product, which was de-*O*-acetylated to give crystalline methyl 4,6-diazido-4,6-dideoxy-α-D-glucopyranoside (II)[10] in 90% yield. With methyl 4,6-*O*-benzylidene-3-chloro-3-deoxy-β-D-allopyranoside (III)[2,4] (prepared by the reaction of sulphuryl chloride with methyl 4,6-*O*-benzylidene-β-D-glucopyranoside[2]†) a crystalline product was isolated after 1 hr., and was shown to consist of two components by t.l.c. Treatment of the product with acetic anhydride–pyridine gave methyl 2-*O*-acetyl-3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside (IV) in 60% yield, m.p. 107—109°, $[\alpha]_D$ −81·2° (*c* 1·15 chloroform). Compound (IV) could be converted into methyl 3-acetamido-2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside[11]



(I) (II)



(III) (IV)



(V)

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† In the present work compound (III) was obtained in crystalline form and had m.p. 129—130°.

by hydrogenation over Adams' catalyst and acetylation of the reduced product. Also isolated from the acetylation of the original mixture was a crystalline compound which was assigned the structure of methyl 2-*O*-acetyl-4,6-*O*-benzylidene-β-D-*erythro*-hex-3-enopyranoside (V), m.p. 130—131°, $[\alpha]_D$ — 164° (*c* 1·05 chloroform); λ_{max} (Nujol) 5·78 (OAc), 5·91 μm. (C=C); τ 4·67 (q, vinylic H); the same compound could be obtained, as the sole product, by heating the chlorodeoxy-sugar (III) in *NN*-dimethylformamide at reflux temperature with sodium benzoate, followed by treatment of the mixture with acetic anhydride–pyridine.‡

The displacement of chloro-groups in sugars and reduction of the resultant azido-derivatives constitutes a convenient, high-yielding procedure for synthesis of amino-sugars.

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‡ *Added in proof.* Since submitting this communication, we have noted a report on the displacement of the chloro-group in compound (III) with azide ion (S. Hanessian and N. R. Plessas, *J. Org. Chem.*, 1969, **34**, 1045). In that work, however, the formation of an unsaturated derivative was not reported.

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