Simple Syntheses of Glycofuranosylamines derived from D-Xylose, D-Mannose, and L-Rhamnose, Intermediates in the Preparation of some *N*-Glycofuranosyl Uracils†

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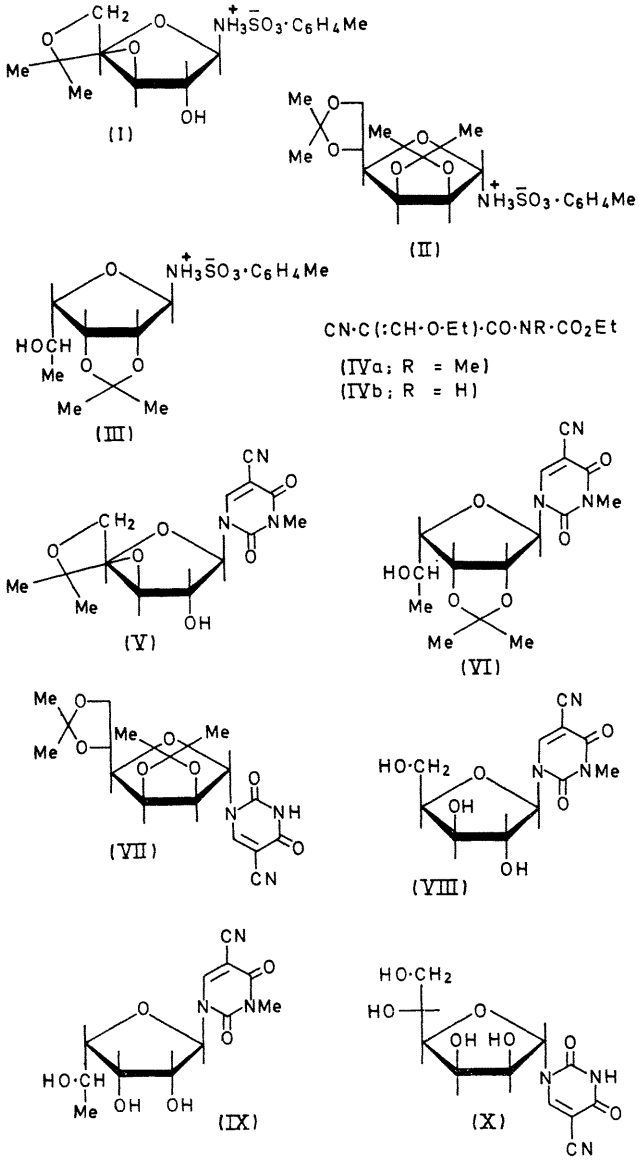
Summary 3,5-*O*-Isopropylidene-D-xylofuranosylamine, 2,3-*O*-isopropylidene-L-rhamnofuranosylamine, and 2,3:5,6-di-*O*-isopropylidene-D-mannofuranosylamine have been prepared in high yield as toluene-*p*-sulphonates by reaction of the corresponding pyranosylamines with acetone, 2,2-dimethoxypropane, and toluene-*p*-sulphonic acid; the glycofuranosylamines have been used to prepare pyrimidine nucleosides.



† Patent applied for.

WE recently recorded the preparation of 2,3-*O*-isopropylidene-β-D-ribofuranosylamine toluene-*p*-sulphonate in high yield by reaction of the readily available D-pyranosylamine with acetone, 2,2-dimethoxypropane, and toluene-*p*-sulphonic acid, and shown that it may be used for syntheses of 5-aminoimidazole (and hence purine) and pyrimidine nucleosides.[1] We have examined the generality of the reaction, in particular to see if it could be extended to the preparation of glycofuranosylamines from pyranosylamines whose structures might be expected to favour formation of furanose configurations including those (like xylose) where the derived cyclic acetal is a six-membered ring. We now report that the reaction may be extended to include syntheses of glycofuranosylamines derived from D-xylose, D-mannose, and L-rhamnose.

Reaction of the readily available (from the sugar and methanolic ammonia) D-xylopyranosylamine,[2,3] D-mannopyranosylamine,[3] or L-rhamnopyranosylamine[2] with acetone 2,2-dimethoxypropane, and toluene-*p*-sulphonic acid in a manner similar to that for D-ribopyranosylamine,[1] gave in excellent yields, 3,5-*O*-isopropylidene-β-D-xylofuranosylamine toluene-*p*-sulphonate (I) which crystallised directly from the reaction mixture after 5 min and had m.p. 121° (decomp.), $[\alpha]_D^{20}$ −16·1° (*c* 1 in Me_2SO); 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosylamine toluene-*p*-sulphonate (II) which separated, after addition of ether, as a crystalline solid, m.p. 132—134° (decomp.) $[\alpha]_{578}^{16}$ +6·2° (*c* 1 in Me_2SO); and 2,3-*O*-isopropylidene-α-L-rhamnofuranosylamine toluene-*p*-sulphonate (III) which also separated as a crystalline solid, m.p. 143° (decomp.) $[\alpha]_{578}^{20}$ +13·6° (*c* 0·1 in Me_2SO), after addition of ether.

The structural assignments were confirmed by elemental analyses, formation of acetone (identified as its 2,4-dinitrophenylhydrazone) on acid hydrolysis, and reaction with the linear ethoxyacryloyl derivative (IVa)[4] in the case of the xylo- and rhamno-furanosylamines to give corresponding uracil derivatives (V), m.p. 220—222° (decomp.) and (VI), m.p. 272° (decomp.), respectively, or in the case of the mannofuranosylamine with compound (IVb)[5] to afford the uracil (VII), m.p. 85°. The isopropylidene groups in each of the compounds (V), (VI), and (VII) could be removed by heating with dilute aqueous acid to give the corresponding uracils (VIII), m.p. 197° (decomp.), $[\alpha]_D^{20}$ −72° (*c* 0·5 in H_2O) (IX), m.p. 142° (decomp.), $[\alpha]_{857}^{20}$ −86·5° (*c* 0·1 in H_2O), and (X), m.p. 218° (decomp.), $[\alpha]_D^{20}$ +60° (*c* 0·5 in H_2O). The structures of the latter uracils were further confirmed by elemental analyses, and mass and u.v. absorption spectra (characteristic of 1-substituted 5-cyanouracils).[6] Periodate titration studies of the uracils gave for (VIII) 1·15 mol. periodate (no formic acid), for (IX) 0·95 mol. periodate (no formic acid), and for the mannofuranosyl derivative (X) a characteristic, variable, pH-dependent, over-(non-Malapradian) oxidation with consumption of *ca.* 4 mol. of periodate and formation of formic acid as a result

of intermediate formation of hydroxymalondialdehyde [7] In addition, in each case the furanoses were compared with, and shown to differ from, the corresponding pyranosyl uracils obtained in high yield by similar condensations of the acryloyl derivatives (IVa and b) with the appropriate pyranosylamines using a greatly improved preparative procedure which involved dimethyl sulphoxide as a solvent and isolation of the products as sodio-derivatives where appropriate The latter preparations are an extension of our previously recorded syntheses [4]

In all cases a *trans*-arrangement is assumed to exist between the sugar 2′-hydroxy-group and the uracil ring leading to α-configurations for the rhamnose and mannose derivatives and a β-configuration for the xylose derivatives Reasons for assignments according to the *trans*-rule have been given previously[8] and the rule has never yet been violated in this type of synthesis Nevertheless further work to establish configurations rigorously, and work on other glycosylamines is in progress

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