# Synthesis of Carbohydrate Furoxan Derivatives

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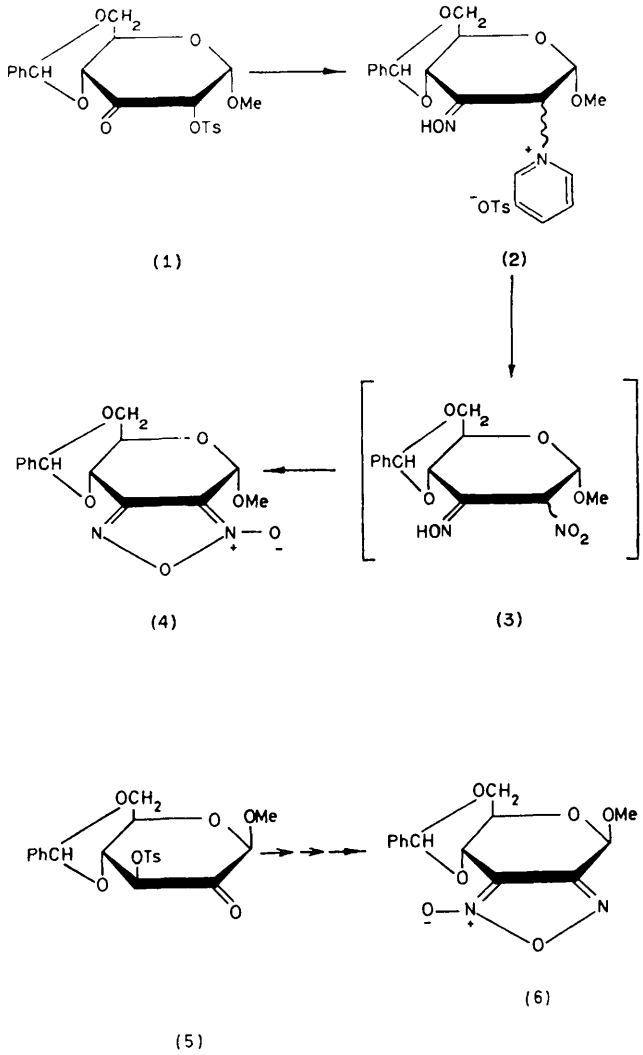
*Summary* A route to carbohydrate furoxan derivatives has been developed which involves treatment of a carbohydrate α-keto toluene-*p*-sulphonate with hydroxylamine hydrochloride in aqueous pyridine, followed by treatment of the resultant oximino-pyridinium salt with sodium nitrite.

THERE is considerable interest in the synthesis of carbohydrate derivatives containing heterocyclic bases, since the new compounds may exhibit therapeutically useful properties. We report the preparation of the first examples of a new class of compounds, namely, carbohydrate derivatives of 1,2,5-oxadiazole 2-oxides (furoxans). Several methods have been used to prepare furoxans,[1] including steroidal[2] furoxans.

It has been shown[3] that treatment of methyl 4,6-*O*-benzylidene-2-*O*-toluene- *p*-sulphonyl-α-D-*ribo*-hexopyranosid-3-ulose (1) with hydroxylamine hydrochloride in aqueous pyridine affords in high yield the pyridinium toluene-*p*-sulphonate (2). Compound (2) readily undergoes substitution reactions at C-2 with a variety of nucleophiles. A mixture of (2) (2·0 g), sodium nitrite (4 g), pyridine (6 ml), tetrahydrofuran (50 ml), and water (50 ml) was heated at reflux temperature for 5 h. The product was crystallized from methanol to give methyl 4,6-*O*-benzylidene-α-D-*erythro*-hexopyranosido[2,3:3′,4′]furoxan (4),†

† All new compounds gave satisfactory elemental analyses. T.l.c. was performed with Silica Gel G as the adsorbent. Structural assignments were supported by u.v., i.r., n.m.r., and mass spectral data.




yield 657 mg (58%), m.p. 169—170°, $[\alpha]_D^{25}$ + 130° (*c* 1·0, chloroform); $\lambda_{max}$ (ethanol) 210 ($\epsilon$ 11,000) and 262 nm (8100) (furoxan[4]); $\nu_{max}$ (chloroform) 1640 (C=N), 1480—1460 (O–N→O), 1390 cm.$^{-1}$ (N–O); *m/e* 306 $(M)^{+}$, 290 $(M - 16)^{+}$ (diagnostic for *N*-oxide[5]).

The conversion of the salt (2) into the furoxan derivatives (4) is considered to occur by an initial replacement of pyridine in compound (2) by nitrite ion to give a 2-*C*-nitro-derivative (3), which then affords the furoxan derivative (4), presumably by way of the *aci*-nitro-form. In the present experiment, the formation of only one furoxan derivative was detected; moreover, no isomerization was observed to occur on heating the compound. However, the formulation of the furoxan derivative as a 2′-*N*-oxide (4) should be regarded as tentative.

To a solution of methyl 4,6-*O*-benzylidene-3-*O*-toluene-*p*-sulphonyl-β-D-*arabino*-hexopyranosid-2-ulose[6] (5) (900 mg) in pyridine (10 ml) and water (2ml) was added hydroxylamine hydrochloride (1 g), and the mixture was stirrred at 60° for 6 h; the formation of a pyridinium salt was indicated by the presence of a new component which did not migrate in t.l.c. (ether). A solution of sodium nitrite (2 g) in water (30 ml) and 1,4-dioxan (30 ml) was added, and the reaction mixture was heated at 90° for 3 h. A crude product (305 mg) was isolated which, on crystallization from ethanol, afforded pure methyl 4,6-*O*-benzylidene-β-D-*erythro*-hexopyranosido[2,3; 3′,4′]furoxan (6), yield 254 mg (40%), m.p. 148—149°, $[\alpha]_D^{25}$ −217° (*c* 1·4, chloroform); $\lambda_{max}$ (ethanol) 212 ($\epsilon$ 7600) and 267 nm (7300) (furoxan[4]); $\nu_{max}$ (chloroform) 1645 (C=N), 1500–1440 (O–N→O), 1370 cm$^{-1}$ (N–O); *m/e* 306 $(M(\dot{+}$, 290 $(M - 16)^{+}$. The formulation of the furoxan derivative as a 5′-*N*-oxide (6) should also be regarded as tentative.

Full details of the syntheses described, and of other examples, will be published later. Biological evaluation of the carbohydrate furoxan derivatives is in progress.

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