Ring Contraction in the Hydrolysis of Methyl 4-*O*-Nitrobenzene-*p*-sulphonyl-α-D-glucopyranoside

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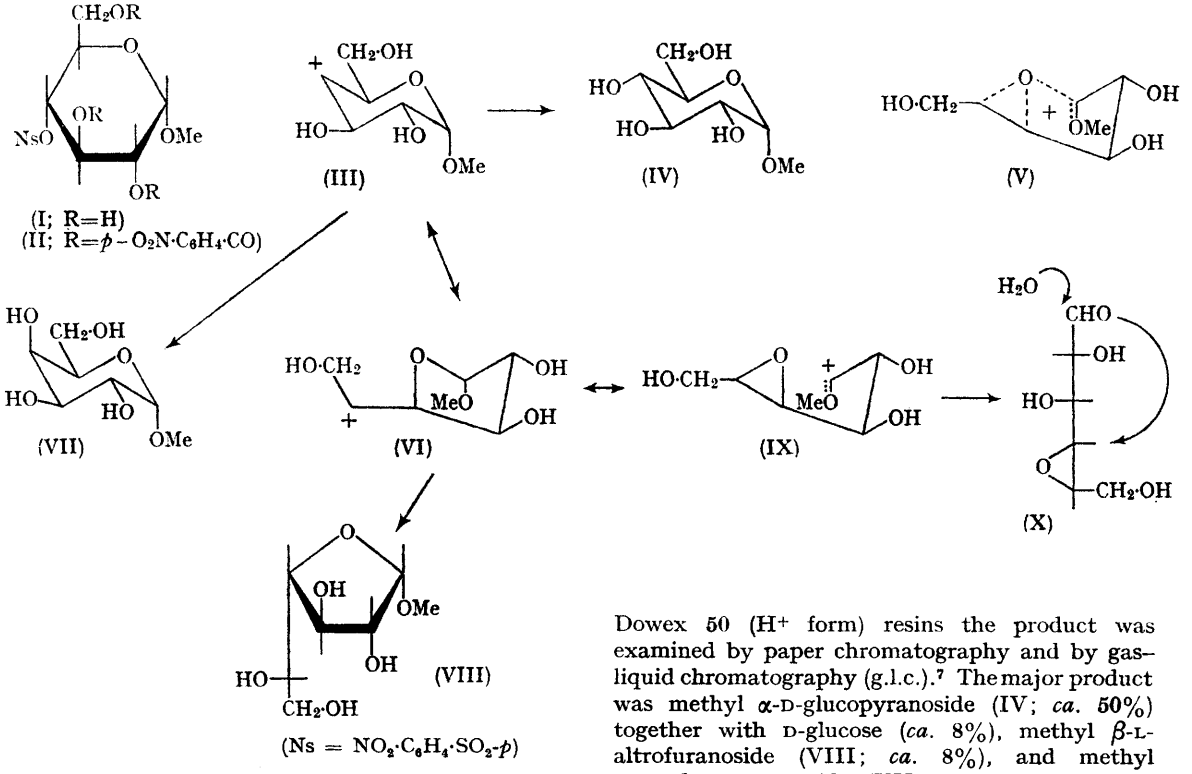
We have described the hydrolysis of the 3-nitrobenzene-*p*-sulphonates of methyl α-D-gluco- and -manno-pyranoside, in which the major product had undergone ring contraction.[1] The hydrolysis of methyl 4-*O*-nitrobenzene-*p*-sulphonyl-α-D-glucopyranoside (I) has now been examined in the expectation that a similar ring contraction would result in formation of a furanoside. Recent publications[2–4] prompt us to report our findings at this stage.



The nitrobenzenesulphonate (I) was prepared by an orthodox route. The benzylidene group of methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-nitrobenzoyl-α-D-glucopyranoside[5] was removed by acidic hydrolysis and the resulting diol treated, in pyridine, with *p*-nitrobenzoyl chloride (1·1 mol.), followed by nitrobenzene-*p*-sulphonyl chloride (3 mol.). The nitrobenzene-*p*-sulphonate (II), m.p. 183·5—185° (decomp.), $[\alpha]_D$ + 111·5° ($CHCl_3$) was debenzoylated catalytically with sodium methoxide in methanol to give the sulphonate (I), m.p. 152—153·5° (decomp.), $[\alpha]_D$ + 84·5° (CH_3OH); some conversion of (I) into the 3,4-anhydrogalactoside[6] was unavoidable.

The sulphonate (I) was heated in water at 100° in the presence of acetate buffer at pH 4—5 for 5 hr.[1] After removal of nitrobenzenesulphonate and sodium ions using Dowex 1 (HCO_3^- form) and Dowex 50 (H^+ form) resins the product was examined by paper chromatography and by gas–liquid chromatography (g.l.c.).[7] The major product was methyl α-D-glucopyranoside (IV; *ca.* 50%) together with D-glucose (*ca.* 8%), methyl β-L-altrofuranoside (VIII; *ca.* 8%), and methyl α-D-galactopyranoside (VII; *ca.* 8%); traces of other products were present. On a preparative scale the mixture was fractionated by chromatography on Dowex 1 (OH^- form) resin.[8] The pyranosides (IV) and (VII) were isolated in crystalline form and the hitherto unknown methyl β-L-altrofuranoside (VIII), m.p. 94—97°, $[\alpha]_D$ + 89·8° (H_2O), crystallised after further purification by paper chromatography. For comparison

purposes D-altrose was treated with methanolic hydrogen chloride and the resulting glycosides separated by chromatography on Dowex 1 (OH^- form) resin.[8] Methyl β-D-altrofuranoside, m.p. 98—98·5°, $[\alpha]_D$ −89·8° (H_2O) and methyl α-D-altrofuranoside, m.p. 99·5—101°, $[\alpha]_D$ + 104° (H_2O) crystallised. The β-anomer was indistinguishable from the solvolysis product when each was examined by mass spectrometry, infrared spectroscopy, g.l.c., and paper chromatography, and the two were clearly enantiomeric.

The pyranoside products (IV) and (VII) may be accounted for by initial formation of the solvated carbonium ion (III) which collapses to give predominantly the equatorial glucoside (IV) together with some of the axial galactoside (VII). Methyl α-D-glucopyranoside has also been identified as the major product in nitrous acid deamination of methyl 4-amino-4-deoxy-α-D-glucopyranoside,[9] confirming the similarity between nitrobenzenesulphonate solvolysis and amine diazotisation already noted in the 2- and 3-substituted glucosides.[1]

Rearrangement of the carbonium ion (III) may lead to (VI) and (IX), expressed in the resonance structure (V). The L-altrofuranoside (VIII) may arise by hydration of the carbonium ion (VI). Alternatively, attack on the ion (V) at C-5 with inversion would yield exclusively the L-*altro*-isomer. None of the C-5 epimer of (VIII), the α-D-galactofuranoside, could be detected in the reaction mixture. This second interpretation would not, however, account for the stereochemistry of the furanoside products reported by Stevens[2,4] and Hanessian.[3]

The glucose formed in the solvolysis does not appear to arise by acidic hydrolysis of the glucoside (IV) since no free altrose was detected, despite the greater acid-lability of the altrofuranoside (VIII). Hydrolysis of the ion (IX) may yield 4,5-anhydro-D-galactose (X) which would undergo intramolecular ring opening of the vicinal epoxide to give glucose.[10] (We thank Dr. N. A. Hughes for fruitful discussions on this point.)

(*Received, March 10th*, 1967; *Com.* 233.)

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