Preliminary communication

Facile acid hydrolysis of glycoside 2-sulphates

P. F. LLOYD and P. F. FORRESTER
Department of Chemistry, University College of North Wales, Bangor, Caerns. (Great Britain)
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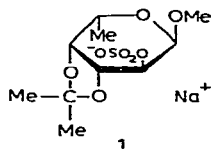
In aldohexopyranoside derivatives, glycosidic and sulphate hemiester linkages[1–5] are hydrolysed by hot, aqueous acids, the latter 10–100 times more rapidly. When both types of linkage occur in the same molecule as, for example, in the 3- and 6-sulphates of methyl α-D-galactopyranoside, the two substituent groupings mutually stabilise each other to a small extent, the effect of ester on glycoside being the greater[4]. From a consideration of the acid hydrolysis of 3-, 4-, and 6-sulphates of D-glucose and D-galactose and a range of sulphated polysaccharides, it was concluded[6] that the rate of hydrolysis of carbohydrate sulphates depended upon both location (*i.e.* whether a primary or secondary ester) and on the orientation of the ester group in the stable conformer. We now report that glycoside 2-sulphates display a much higher susceptibility to acid hydrolysis than do the 3-, 4-, and 6-esters.

Methyl α-L-fucopyranoside 2-(sodium sulphate) (2) {barium salt, m.p. ~ 89° (diffuse), $[\alpha]_D^{20}$ −71.5° (*c* 0.1, water), ν_{max} (Nujol) 844 cm^{-1}} was synthesised by a route which involved, in the penultimate stage, acid hydrolysis of the 3,4-*O*-isopropylidene derivative (1); this occurred under extremely mild conditions (pH 3.1, 60°, 5 h). The structure of 2 was confirmed by periodate-oxidation and spectroscopic studies. When 2 was heated with 1% aqueous acetic acid at 100° for 2 h, it underwent hydrolysis to give only methyl α-L-fucopyranoside (3, the product of desulphation) and L-fucose 2-sulphate {barium salt, indefinite m.p., $[\alpha]_D^{20}$ −49° (*c* 0.1, water), ν_{max} (Nujol) 852 cm^{-1}} (4, the product of deglycosidation) in yields, respectively, of 62 and 38%. Neither the starting material nor the product of total hydrolysis, *i.e.* L-fucose, could be detected in the reaction mixture. When compounds 3 and 4 were isolated and purified, it was found that they were not hydrolysed by dilute acetic acid, but required more-severe conditions (0.25M sulphuric acid at 100°) to give L-fucose.

It is known[7] that the rate constants for the acid-catalysed hydrolysis of 6-deoxyhexosides are appreciably higher than those for the corresponding hexosides, and it seemed possible that the facile hydrolysis of 2 was attributable in part to this factor. However, methyl α-L-rhamnopyranoside 4-(sodium sulphate)[8] (5) {barium salt, indefinite m.p., $[\alpha]_D^{20}$ −46° (*c* 0.1, water)} is also hydrolysed in a manner analogous to that of the hexoside 4-sulphates; after treatment with 0.25M sulphuric acid at 100° for 35 min (conditions established as optimal for the formation of L-rhamnose 4-sulphate), starting material, the desulphated product, the deglycosidated product, and also L-rhamnose were present.



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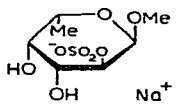

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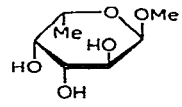

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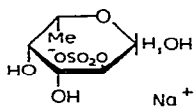

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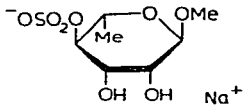

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Hexopyranoside 2-sulphates are also very acid-labile. Whereas methyl α-D-glucopyranoside 3-sulphate required treatment with 0.5M sulphuric acid at 100° for facile hydrolysis, methyl α-D-glucopyranoside 2-sulphate{ barium salt, diffuse m.p., $[\alpha]_D^{20}$ + 67.2° (*c* 0.1, water), ν_{max} (Nujol) 829 cm^{-1}} was hydrolysed completely by 5mM sulphuric acid in 5 h at 60°, paralleling the hydrolysis of the 6-deoxyglycoside 2-sulphate in that it yielded only the corresponding glycoside and glycose sulphate and no detectable free sugar. Preliminary studies of methyl α-D-galactopyranoside 2-sulphate have given similar results. There is also evidence that the enhanced acid-lability of acetal substituents (*e.g.* isopropylidene and benzylidene groups) in rings containing proximal sulphate groups is a general phenomenon.

These effects may be due, in part at least, to an electrostatic effect of the $-OSO_2O^-$ group which enhances the approach of cationic groups (*e.g.* H_3O^+) to the adjacent glycosidic centre. A similar type of effect, though opposite in character, is thought to be responsible for the abnormally high resistance to acid hydrolysis of 2-amino-2-deoxy-glycosides[9]. Steric factors may also be involved, as may a mechanism involving participation of the ester; kinetic studies and work on the anomeric β-D-glycoside sulphates are in progress.

The results reported herein are likely to be important in the interpretation of the acid hydrolysis of sulphated polysaccharides and may have applications in the specific degradation of polysaccharides and in synthesis.

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