

6-Deoxy-6-*p*-tolylsulphonyl- β -D-glucopyranosides

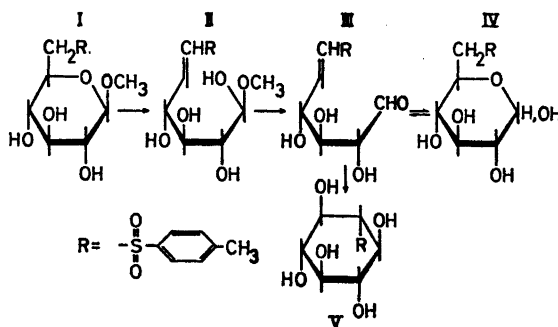
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The methyl 6-deoxy-6-*p*-tolylsulphonyl- α - and - β -D-glucopyranosides have been synthesised and their reactions in alkaline solution studied. The alkaline lability of this type of glycoside and the potential use of similar derivatives in structural polysaccharide chemistry are discussed.

Degradation methods which split a particular type of linkage while not affecting other linkages are needed in polysaccharide chemistry. One possible method would be to replace tosyl groups in primary positions with more strongly electron attracting groups, such as sulphone groups. This would render the glycosidic linkage alkali-labile.

A sequence of reactions, illustrated below for methyl 6-deoxy-6-*p*-tolylsulphonyl- β -D-glucopyranoside (I), would be expected to take place in aqueous alkaline solution.



1. β -Elimination should yield the unsaturated hemiacetal (II).
2. The unsaturated hemiacetal should rapidly hydrolyse to give the unsaturated sugar (III), which should be in equilibrium with the corresponding D-glucose (IV) and L-idose derivatives.

3. A mixture of cyclitols, *e.g.* (V), should be formed from the sugars by intramolecular aldol condensation, analogous to the known reaction of 6-deoxy-6-nitro-hexoses with alkali.¹

The structure elucidation of polysaccharides having a low percentage of primary hydroxyl groups, for example essentially 1 → 6-linked hexosans and polysaccharides containing predominantly pentopyranose and/or uronic acid residues might be facilitated by degradation employing this scheme.

The present paper reports the synthesis and alkaline degradation of the methyl 6-deoxy-6-*p*-tolylsulphonyl- α - and β -D-glucopyranosides. During the course of this work, studies on the alkaline degradation of 6-deoxy-6-nitro-glycosides have been reported.² The degradation followed the scheme outlined above (R = NO₂).

In preliminary experiments, methyl 6-*O*-tosyl- α - or β -D-glucopyranoside triacetate was treated with sodium-*p*-tolylsulphinat in dimethylformamide. The yields of the expected sulphones were low; however, yields improved considerably when the corresponding 6-deoxy-6-iodo-derivatives were treated with the same reagent. The acetyl derivatives could be deacetylated to the free glycosides and then converted by acid hydrolysis into the reducing sugar, 6-deoxy-6-*p*-tolylsulphonyl-D-glucose.]

The reactions of the methyl glycosides and the free sugar in 0.4 M aqueous sodium hydroxide at 40° were followed polarimetrically (Fig. 1) and by thin layer chromatography. For all substances the optical rotation approached zero. The reactions were approximately first order, the rate constants being; α -glycoside 11×10^{-5} , β -glycoside 5×10^{-5} , free sugar $16 \times 10^{-5} \text{ sec}^{-1}$. No formation of free sugar was observed from the glycoside. Chromatography of the

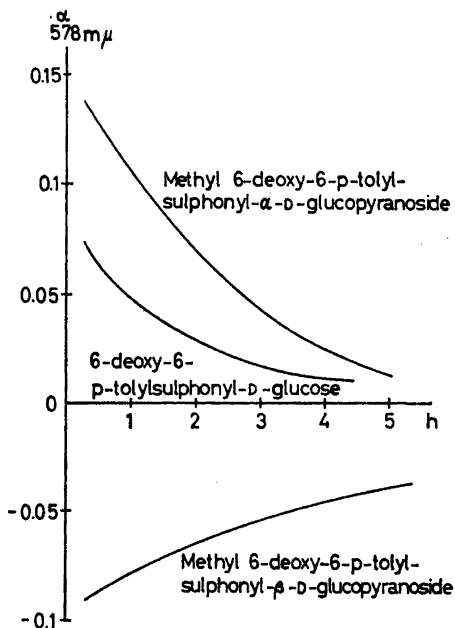


Fig. 1. Alkaline degradation of 6-deoxy-6-*p*-tolylsulphonyl-D-glucose and its methyl pyranosides.

final products from the three substances showed two spots in about the same relative proportions. These most probably represent isomeric deoxy-*p*-tolylsulphonyl-inositols, but the products, which did not crystallise, were not further investigated.

The free sugar (IV) reacts at a rate which is of the same order of magnitude as that of the glycosides but does not accumulate during the alkaline treatment of the latter. This, together with the observed first order kinetics of the overall reactions, indicates that β -elimination is the rate determining step. The hydrolysis of the hemiacetal (II) is expected to be rapid and the formation of the cyclitols (*e.g.* V) from the unsaturated sugar (III) should thus be considerably faster than its conversion into D-glucose (IV) or L-idose derivatives.

EXPERIMENTAL

Melting points are corrected. Thin layer chromatography was performed on silicic acid using as irrigant ethyl acetate-methanol, 5:1 (Solvent system A) and 1:1 (Solvent system B).

Methyl 2,3,4-tri-O-acetyl-6-deoxy-6-p-tolylsulphonyl- α -D-glucoside. A solution of methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo- α -D-glucopyranoside³ (4.0 g) and anhydrous sodium *p*-tolylsulphinate (5 g) in dimethylformamide (50 ml) was heated on a steam bath for 2 h. The solution was concentrated under reduced pressure at 60° and the residue partitioned between chloroform (100 ml) and water (100 ml). The chloroform phase was washed with aqueous sodium thiosulphate and water, dried over anhydrous sodium sulphate and concentrated. Three crystallisations of the residue from methanol-water (3:2) yielded the pure substance (3.1 g), m.p. 166.5–167°, $[\alpha]_{578}^{20} + 106^\circ$ (c 1.3, chloroform). (Found: C 52.5; H 5.65; O 35.0; S 6.81. C₂₀H₂₆O₁₀S requires: C 52.4; H 5.71; O 34.9; S 6.99).

Methyl 2,3,4-tri-O-acetyl-6-deoxy-6-p-tolylsulphonyl- β -D-glucoside was prepared analogously from methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo- β -D-glucoside³ (10 g) and sodium *p*-tolylsulphinate (16 g). Crystallisations from methanol yielded the pure substance (6.6 g), m.p. 194–194.5°, $[\alpha]_{578}^{20} - 14^\circ$ (c 3.8, chloroform). (Found: C 52.4; H 5.72; S 6.98. C₂₀H₂₆O₁₀S requires: C 52.4; H 5.71; S 6.99).

Methyl 6-deoxy-6-p-tolylsulphonyl- α -D-glucopyranoside was prepared from the corresponding triacetate (0.5 g), which was dissolved in a mixture of methanol (40 ml), 33 % aqueous trimethylamine (10 ml) and water (2.5 ml), kept overnight at room temperature and then concentrated. The substance, which was obtained in a quantitative yield, was chromatographically pure ($R_{\text{Glucose}} = 4.2$, solvent A) but did not crystallise. It showed $[\alpha]_{578}^{22} + 79^\circ$ (c 0.5, water).

Methyl 6-deoxy-6-p-tolylsulphonyl- β -D-glucopyranoside was prepared in the same manner from the corresponding triacetate (5.0 g). Crystallisation from water yielded the pure substance (3.3 g), m.p. 203–205°, $[\alpha]_{578}^{22} - 9^\circ$ (c 1.7, water), $R_{\text{Glucose}} = 5.0$, solvent A. (Found: C 50.7; H 6.00; O 33.9; S 9.55. C₁₄H₂₀O₇S requires: C 50.6; H 6.00; O 33.7; S 9.61).

6-Deoxy-6-p-tolylsulphonyl-D-glucose was prepared from both methylglycosides (150 mg) by hydrolysis in 5 M sulphuric acid (6 ml) at 100° for 5 h. The solution was then made up to 10.0 ml and the optical rotation determined. The value, $[\alpha]_{578}^{22}$, obtained in this manner was +44° for the product prepared from the α -glucoside and +46° for the product prepared from the β -glucoside. The solutions were titrated to pH 5 with aqueous barium hydroxide, centrifuged and concentrated. The free sugar which did not crystallise was chromatographically pure ($R_{\text{Glucose}} = 3.8$, solvent A) and gave a positive reaction with anisidine hydrochloride.

Alkaline degradation. The substance (20–120 mg) was dissolved in 0.40 M aqueous sodium hydroxide (10.0 ml) and transferred to a jacketed polarimeter tube maintained at 40° by circulating water. The optical rotations were determined with a Perkin Elmer Model 141 photoelectrical polarimeter.

In parallel experiments samples were withdrawn at intervals and investigated by thin layer chromatography. The gradual disappearance of the starting material and the appearance of two new spots (R_{Glucose} 0.4 and 0.9, solvent B) was observed. No formation of substances, giving positive reactions with anisidine hydrochloride was observed.

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