Reactions of Carbohydrate α-Keto Toluene-*p*-sulphonates. Reaction of Methyl 4,6-*O*-Benzylidene-2-*O*-toluene-*p*-sulphonyl-α-D-*ribo*-hexopyranosid-3-ulose with Triethylamine–Methanol

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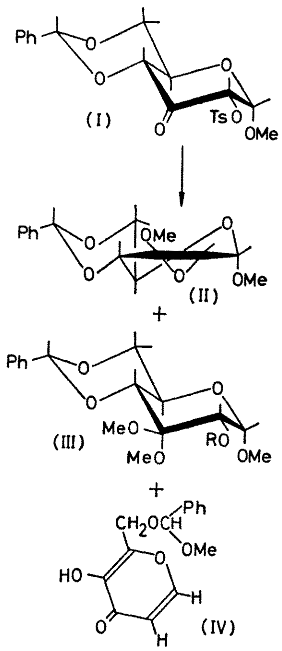
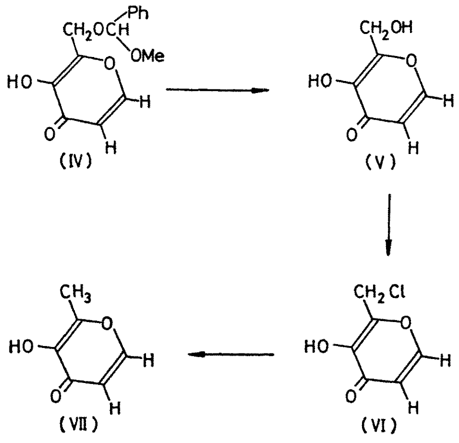
Summary. Reaction of methyl 4,6-*O*-benzylidene-2-*O*-toluene-*p*-sulphonyl-α-D-*ribo*-hexopyranosid-3-ulose (I) with triethylamine–methanol yields methyl 2,3-anhydro-4,6-*O*-benzylidene-3-methoxy-α-D-allopyranoside (II), methyl 4,6-*O*-benzylidene-α-D-*ribo*-hexopyranosid-3-ulose dimethyl acetal (III; R=H), and a derivative of 3-hydroxy-2-(hydroxymethyl)-4*H*-pyran-4-one (IV).

THE importance of sulphonic esters of carbohydrates as substrates for the preparation of a wide variety of sugars by nucleophilic displacement reactions has been firmly established.[1] The reactivity of a sulphonate group depends critically upon the position of the group and upon the stereochemistry and conformation of the carbohydrate molecule.[1,2] If a sulphonate is situated at C–2 of a pyranoside, then nucleophilic displacement with charged nucleophiles does not normally occur. Attempts have been made[3] to achieve nucleophilic displacements of a 2-sulphonate by using a more activated sulphonate as a leaving group as in methyl 4,6-*O*-benzylidene-2-*O*-toluene-*p*-sulphonyl-α-*ribo*-hexopyranosid-3-ulose (I); it is known that a carbonyl group adjacent to the reaction centre assists bimolecular substitution. Here we report the unusual compounds obtained from the reaction of the α-keto toluene-*p*-sulphonate[3,4] (I) with triethylamine–methanol.



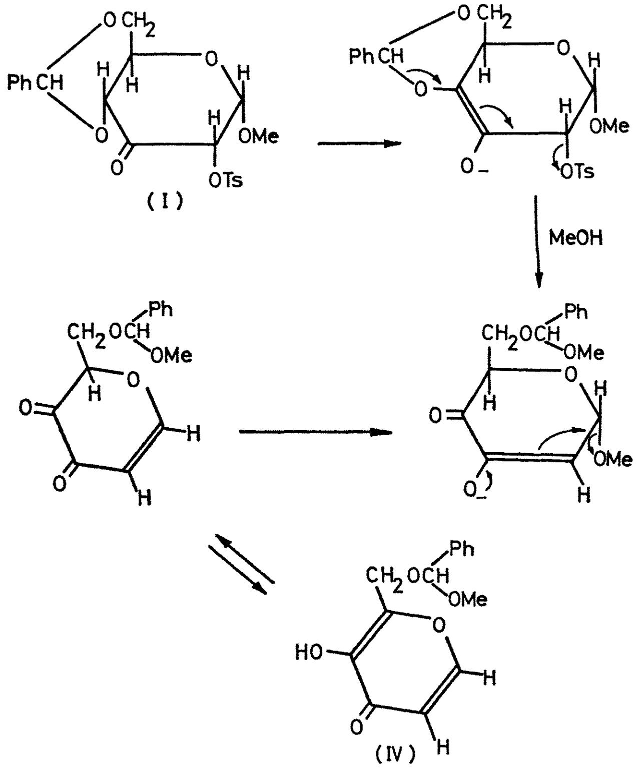
SCHEME 1

A solution of compound (I) (2·5 g) in triethylamine (1·6 ml) and methanol (65 ml) was heated at reflux temperature; after 50 min t.l.c.† revealed that all of the starting material (R_F 0·65) had been consumed, and showed the presence of two new components, having R_F values of 0·61 and *ca.* 0·29 (elongated spot), in addition to material which did not migrate. The faster-moving component crystallized from chloroform–ethanol gave pure methyl 2,3-anhydro-4,6-*O*-benzylidene-3-methoxy-α-D-allopyranoside (II), m.p. 187–190°, $[\alpha]_D$ + 108° (c 1·32); n.m.r. data: τ 2·4–2·7 (5H multiplet, Ph), 4·40 (1H singlet, benzylidene-methine H), 5·13 (1H doublet, $J_{1,2}$ 3 Hz, 1-H), 6·30 (1H doublet, 2-H), 6·55 and 6·60 (3H singlets, 1-OMe and 3-OMe); no OH or C=O absorptions in i.r. spectrum (Nujol mull). The D-*allo*-configuration was assigned to (II) on the basis of the magnitude of $J_{1,2}$; it has been shown[5] in several 2,3-anhydroglycopyranosides that, when the 2,3-epoxy-group and the anomeric alkoxy-group were *trans*, $J_{1,2}$ was *ca.* 0, whereas when the groups were in the *cis*-arrangement, $J_{1,2}$ was 2·5–4·5 Hz. The formulation of (II) as an α-methoxy-epoxide was substantiated by its conversion, on treatment with lithium aluminium hydride in tetrahydrofuran, into methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside,[6] m.p. 128–130°, $[\alpha]_D$ + 138° (c 1·16). A possible mechanism for the formation of (II) and (I) involves initial epimerization to give the axial toluene-*p*-sulphonate, followed by equatorial attack by methanol on the carbonyl carbon, and finally internal displacement of the toluene-*p*-sulphonyloxy-group by the carbonyl oxygen.



SCHEME 2

The slower-moving component was isolated by evaporation of the filtrate, remaining after separation of compound (II), to give a residue, which crystallized from chloroform–petroleum, yield 0·563 g (38%). Recrystallization afforded an analytically pure sample of the derivative of 3-hydroxy-2-(hydroxymethyl)-4*H*-pyran-4-one (IV), m.p. 115–117°; n.m.r. data $[(CD_3)_2SO]$: τ 1·90, 3·62 (1H doublets, $J_{5,6}$ 5·6 Hz, 5-H and 6-H), 2·60 (5H, Ph), 4·08 (1H singlet, acetal-methane H), 5·45 (2H singlet, CH_2), and 6·70 (3H singlet, OMe); ν_{max} (Nujol mull) 1658 and



SCHEME 3

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† T.l.c. was performed with Silica Gel G as the adsorbent and 2 : 1 (v/v) ethyl acetate–petroleum (b.p. 60—80°) as the developing solvent. Optical rotations were measured at 23 ± 2° in chloroform. N.m.r. data, obtained at 60 MHz, refer to $CDCl_3$ solutions, unless otherwise stated. All new compounds gave satisfactory elemental analyses.

1640 cm^{-1} (·C=C·CO·C=C·); positive ferric chloride test. The structure assigned to (IV) was confirmed by the chemical transformations shown in Scheme 2. Thus, acid-catalysed hydrolysis of (IV) gave 3-hydroxy-2-(hydroxymethyl)-4*H*-pyran-4-one (V), which was converted into maltol (VII) essentially by the procedure described by Stodola,[7] namely, by treatment of (V) with thionyl chloride to give the chloro-derivative (VI), followed by reduction of (VI) with zinc dust and acetic acid. A possible rationalization for the formation of the γ-pyrone (IV) from the α-keto toluene-*p*-sulphonate (I) on treatment with triethylamine–methanol is shown in Scheme 3.‡

In a separate experiment, a solution of compound (I) in triethylamine–methanol was heated at reflux temperature for a period longer than 50 min; a third new component (R_F 0·54) was formed, which was shown to be methyl 4,6-*O*-benzylidene-α-D-*ribo*-hexopyranosid-3-ulose dimethyl acetal (III; R=H), a maximum yield of which was obtained in 48 h, at which time the presence of the α-methoxy-epoxide (II) could no longer be detected by t.l.c. Compound (III; R=H) was isolated by column chromatography as a syrup, yield 21%, $[\alpha]_D + 112°$ (*c* 1·24); n.m.r. data: τ 7·20 (1H doublet, J 12 Hz, disappeared on deuteriation, OH), 5·35 (1H doublet, $J_{1,2}$ 4 Hz, 1-H), 6·38, 6·45, and 6·55 (3H singlets, 1-OMe and two 3-OMe's); ν_{max} (film) 3500 cm^{-1} (OH). The magnitude of the splitting observed for the 1-H signal in the n.m.r. spectrum is consistent with values reported[8] for an equatorial–axial arrangement of 1-H and 2-H, respectively, in methyl 4,6-*O*-benzylidene-α-D-hexopyranosides. Compound (III; R=H) afforded a crystalline toluene-*p*-sulphonate (III; R=Ts), m.p. 136–138° (decomp.), $[\alpha]_D + 3·51°$ (*c* 1·23).

Full details of these and other reactions of carbohydrate α-keto toluene-*p*-sulphonates will be published later.

We thank the National Research Council of Canada for financial support.

(*Received, June 17th,* 1971; *Com.* 993.)

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‡ A comparable elimination reaction has recently been reported (W. Meyer zu Reckendorf, *Chem. Ber.*, 1970, **103**, 2418).

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