The Solvolysis of Methyl 2,3-Di-*O*-methyl-6-*O*-methylsulphonyl-β-D-galactopyranoside: a Methoxy-group Participation

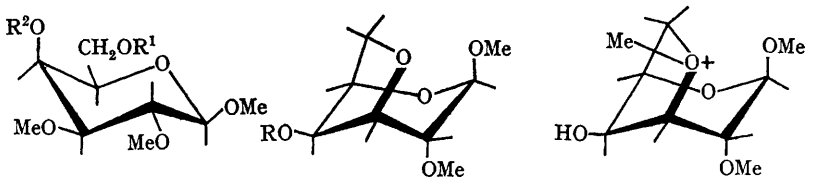
By J. S. BRIMACOMBE* and O. A. CHING

(*Chemistry Department, The University, Birmingham* 15)

EXAMPLES of methoxy-group participation in nucleophilic displacements of carbohydrate sulphonates and halides are comparatively rare and, in all reported cases,[1] the participating methoxy-group is substituted at C-1. The cyclic oxonium-ion intermediates are opened preferentially at C-1 with consequent migration of the methoxy-group. We report an example of neighbouring group participation by a methoxy-group which is substituted at C-3 of a pyranoid ring.

Solvolysis of methyl 2,3-di-*O*-methyl-6-*O*-methyl sulphonyl-β-D-galactopyranoside† (I), m.p. 84—86°, $[\alpha]_D$ −11° (*c* 2, $CHCl_3$), in boiling 50% aqueous methanol in the presence of sodium acetate for 96 hr., afforded three products which were separated by chromatography over silica gel and identified as methyl 3,6-anhydro-2-*O*-methyl-β-D-galactopyranoside (II, 32%), m.p. 46—47°, $[\alpha]_D$ −85° (*c* 0·5, $CHCl_3$), methyl 2,3,6-tri-*O*-methyl-β-D-galactopyranoside (III, 18%), $[\alpha]_D$ −22° (*c* 0·6, $CHCl_3$), and methyl 2,3-di-*O*-methyl-β-D-galactopyranoside (IV, > 26%), $[\alpha]_D$ *ca.* 0° (*c* 2·5, MeOH). Compounds (III) and (IV) were readily identified by comparison with authentic samples[2,3] and they were further characterised as the crystalline 4-*O*-methylsulphonate (V), m.p. and mixed m.p. 141—142°, and 6-*O*-methylsulphonate (I), m.p. and mixed m.p. 84—86°. The anhydro-sugar (II) was identified by elemental analyses and n.m.r. spectroscopy, which demonstrated the presence of two methoxy-groups, and also by its conversion into methyl 3,6-anhydro-2,4-di-*O*-methyl-β-D-galactopyranoside[4] (VI) on methylation. This assignment was supported by mass spectrometry of the derived methyl ether (VI) and the trideuteriomethylated analogue (VII). Prominent fragmentations[5] of permethylated 3,6-anhydropyranosides (e.g., VI) on electron impact are those leading to ions of *m/e* 101 ($MeO\overset{+}{C}H–CH=CHOMe$) and 71

† All new compounds gave satisfactory elemental analyses, and n.m.r. and i.r. spectra.



(I) R^1 = Ms, R^2 = H
(III) R^1 = Me, R^2 = H
(IV) R^1 = R^2 = H
(V) R^1 = Me, R^2 = Ms

(II) R = H
(VI) R = Me
(VII) R = CD_3

(VIII)

($MeO\overset{+}{C}H$–CH=CH_2), which contain carbon atoms 2—4 and 4—6 of the parent sugar, respectively. The mass spectrum of the deuteriated compound (VII) contained peaks at *m/e* 176 (*M* − 31), 104 ($MeO\overset{+}{C}H$–CH=$CHOCD_3$), and 74 ($CD_3O\overset{+}{C}H$–CH=CH_2) which identify the 4-hydroxy-group as the site of trideuteriomethylation and, hence, structure (II) for the parent anhydro-sugar.

Anhydro-sugar (II) is evidently produced from the bicyclic, tertiary oxonium ion (VIII), which is presumably formed by a methoxy-assisted solvolysis[6] of the sulphonate (I), while compounds (III) and (IV) may have arisen from a solvent-assisted reaction or from C-6–O bond cleavage of oxonium ion (VIII) by solvent attack.[6] Rearranged products possibly arising from C-3–O bond cleavage of oxonium ion (VIII) were not detected; an examination of molecular models revealed that the approach of nucleophiles to C-3 is sterically hindered so that solvent attack at this position is unlikely.

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