The Replacement of Sulphonyloxy-groups at C-4 in Pyranosides

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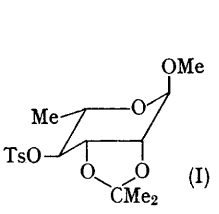
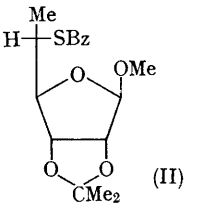
THE discovery[1] that rearrangement to a furanose system occurs when methyl 2,3-*O*-isopropylidene-4-*O*-tosyl-α-D-rhamnopyranoside [or the L-enantiomer (I)][2] reacts with azide ion led to the comment[2] that the reaction of the toluene-*p*-sulphonate (I) with potassium thiolbenzoate, assumed by Owen and Ragg[3] to proceed normally, might also have occurred with rearrangement. This suggestion has recently been confirmed[4] by synthesis of the thiolbenzoate (II) which was shown to be identical with the product derived from the toluene-*p*-sulphonate (I). This fact, coupled with the ring contraction found to occur during the solvolysis of some nitrobenzene-*p*-sulphonates of pyranosides,[5] casts doubt on the structures of two other substitution products described by Owen and Ragg,[3] namely methyl 4,6-bisacetylthio-4,6-dideoxy-2,3-di-*O*-methyl-β-D-glucoside (III) and methyl 4-acetylthio-4,6-dideoxy-2,3-di-*O*-methyl-β-D-glucoside (IV), obtained by reaction of potassium thiolacetate with the 4,6-di-*O*-methanesulphonate and the 4-*O*-methanesulphonate, respectively, of the appropriate compounds having the D-galactose configuration. The doubt was strengthened by the observation that the dithiol derived from the supposed bisthiolacetate (III) gave a positive result in a colour test claimed[6] to be specific for vicinal dithiols. Nevertheless, new evidence now confirms the original structures.

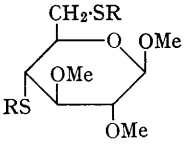
The dithiol (V), prepared[3] by base-catalysed solvolytic deacetylation of the bisthiolacetate, was desulphurised in boiling ethanol with freshly prepared Raney nickel to form methyl 4,6-dideoxy-2,3-di-*O*-methyl-β-D-*xylo*-hexoside (VI), (70%), b.p. 80°/0·4 mm., n_D^{22} 1·4320, $[\alpha]_D^{23}$ −30·0° (CCl_4), with satisfactory elemental analysis. The n.m.r. spectrum (CCl_4) showed a doublet centred at τ 6·08 (J = 7·5 c./sec.) for the anomeric proton, the three methoxyl resonances as sharp singlets, τ 6·57, 6·60, 6·66, and the C-6 methyl group as a sharp doublet centred at τ 8·82 (J = 6·0 c./sec.). Apart from the number of methoxyl resonances,



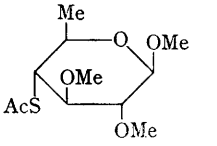
(I)



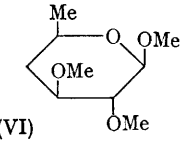
(II)



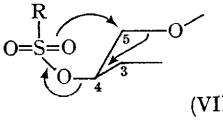
(III) R=Ac
(V) R=H



(IV)



(VI)



(VII)

the spectrum was very similar to that recorded[7] for methyl β-D-chalkopyranoside (VI; OH in place of OMe at C-2), and the character of the C-6 methyl signal, clearly not part of an ethyl group, eliminates the possibility that the desulphurised product is a 5,6-dideoxyfuranoside. Consequently

the original nucleophilic displacement reaction could not have resulted in rearrangement to a 5,6-bisthiolacetate. Furthermore, the mass spectra of the two thiolacetates (III) and (IV), kindly examined by Dr. E. S. Waight, contained no peaks corresponding to the loss of the side-chain from a furanoside structure, whereas the mass spectrum of the thiolbenzoate (II), run as a control, showed a weak peak for the molecular ion (*m/e* 338) and a strong peak (*m/e* 173) characteristic[8] of this type of fragmentation. From these confirmations of the structures of the thiolacetates, it follows that the formulations of those compounds derived from them, containing the thiofuranose ring,[3,9] are also substantiated.

It has been pointed out[2] that the rhamnose derivative (I), in the conformation shown, exhibits a *trans*-antiparallel relationship between the C-4 sulphonate bond and the C-5 ring oxygen bond, which would favour an intramolecular displacement with inversion at C-4, but no mechanism has been suggested to account for the retention of configuration at C-5. This stereochemical result rules out an attack by the nucleophile at this site concerted with the ring-contraction, but a two-stage process offers a possible explanation. The first stage (*cf.*, VII) involves a migration of the sulphonyloxy-group, from C-4 to C-5, concerted with ring contraction; this isomerisation, which is analogous to the *diaxial–diequatorial* equilibration of the sulphonate esters of steroid bromohydrins,[10] causes inversion at C-4 and at C-5.† The second stage is then a normal S_N2 displacement at C-5 by the nucleophile, leading to overall retention of configuration at that position.

The absence of rearrangement in the reactions of the methanesulphonyl precursors of the thiolacetates (III) and (IV) may be due to the fact that, with the galactose configuration, the *trans*-antiparallel arrangement necessary for the first stage would require a very unfavourable conformation. On the other hand, rearrangement might be expected in the reactions of the 2,3-diacetate and the 2,3-dibenzoate of methyl 4,6-di-*O*-methanesulphonyl-α-D-glucopyranoside, though none has been reported.[11]

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† The migration (which could also be expressed as involving an ion-pair with internal return) is of a different type to that in which a toluene-*p*-sulphonyl group is transferred, with retention of configuration, in the manner of a normal acyl migration. (J. S. Brimacombe and L. C. N. Tucker, *Chem. Comm.*, 1966, 903.)

[1] C. L. Stevens, R. P. Glinski, K. G. Taylor, P. Blumbergs, and F. Sirokman, *J. Amer. Chem. Soc.*, 1966, **88**, 2073.
[2] S. Hanessian, *Chem. Comm.*, 1966, 796.
[3] L. N. Owen and P. L. Ragg, *J. Chem. Soc.*, 1966, 1291.
[4] C. L. Stevens, R. P. Glinski, G. E. Gutowski, and J. P. Dickerson, *Tetrahedron Letters*, 1967, 649.
[5] P. W. Austin, J. G. Buchanan, and R. M. Saunders, *J. Chem. Soc.*, 1967, 372.
[6] D. H. Rosenblatt and G. N. Jean, *Analyt. Chem.*, 1955, **27**, 951.
[7] P. W. K. Woo, H. W. Dion, and L. F. Johnson, *J. Amer. Chem. Soc.*, 1962, **84**, 1066.
[8] K. Biemann, D. C. DeJongh, and H. K. Schnoes, *J. Amer. Chem. Soc.*, 1963, **85**, 1763.
[9] J. M. Cox and L. N. Owen, *J. Chem. Soc.* (*B*), 1967, in the press.
[10] J. F. King and R. G. Pews, *Canad. J. Chem.*, 1965, **43**, 845.
[11] *Cf.* J. Hill, L. Hough, and A. C. Richardson, *Proc. Chem. Soc.*, 1963, 346.