Selective Transformation of *O*-Benzylidene Acetals into ω-Bromo-substituted Benzoate Esters

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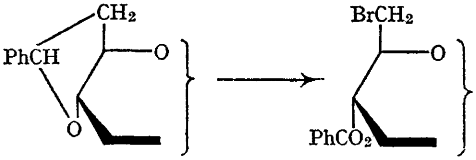
FREQUENTLY during a sequence of synthetic transformations it is desirable to block a glycol system by a benzylidene acetal group and then subsequently to de-block and convert one of the hydroxyl groups into a bromide or tosylate. To achieve selective formation of only a single bromide or tosylate is often difficult. We have now found that such a transformation can be conveniently conducted in one step by oxidizing cyclic benzylidene acetals with *N*-bromosuccinimide (NBS) under free-radical conditions[1] to form ω-bromo-substituted benzoate esters (Equation 1). Our method complements similar observations[2,3] recently reported.

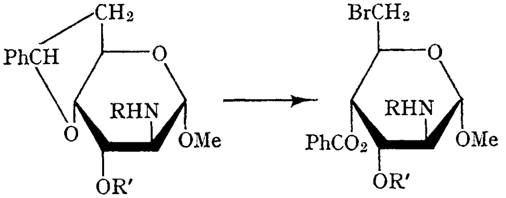
In a typical experiment methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside[4] was smoothly converted by NBS (1 mole equiv.) in refluxing benzene containing benzoyl peroxide (0·01 mole equiv.) into methyl 2,3,4-tri-*O*-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside, m.p. 125—126° (lit. m.p. 122°[5]), in 76% yield. In a similar



(1)

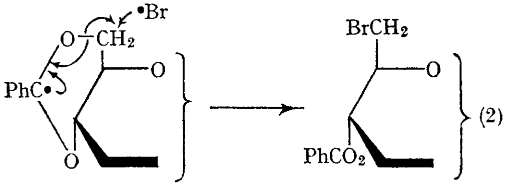
manner methyl 2-benzenesulphonamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside,[6] (I; m.p. 173—175°) was converted into methyl 2-benzenesulphonamido-4-*O*-benzoyl-6-bromo-2,6-dideoxy-α-D-altropyranoside[6] (III; m.p. 165—166°) in 70%

yield, and methyl 4,6-*O*-benzylidene-2-deoxy-2-(tolyl-*p*-sulphonamido)-3-*O*-(tolyl-*p*-sulphonyl)-α-D-altropyranoside[7] (II) gave methyl 4-*O*-benzoyl-6-bromo-2,6-dideoxy-2-(tolyl-*p*-sulphonamido)-3-*O*-(tolyl-*p*-sulphonyl)-α-D-altropyranoside[6] (IV; m.p. 124—127°) in 88% yield.

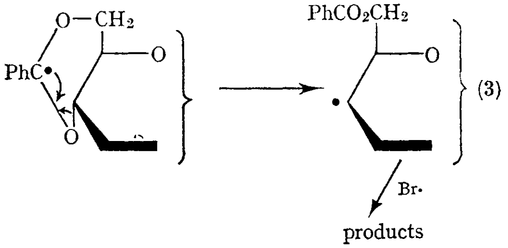


(I) R = $PhSO_2$, R' = H
(II) R = R' = p-$MeC_6H_4SO_2$
(III) R = $PhSO_2$, R' = H
(IV) R = R' = p-$MeC_6H_4SO_2$

Two aspects of these results are particularly noteworthy. First, reaction of NBS with these sugar derivatives occurs predominantly at the benzylidene acetal even though several other reactive groupings, *e.g.*, *p*-tolyl, amide, hydroxyl, and the acetal at the anomeric carbon atom[8] were present. Second, the 4,6-*O*-benzylidene acetal reacts to furnish preponderantly, if not exclusively, the primary, C-6, bromide rather than the secondary, C-4, bromide. This course of reaction is in agreement with a related study[2] and suggests that the reaction proceeds by a "radical-displacement" type of reaction at the least hindered carbon (Equation 2) rather than ring opening of the initial 1,3-dioxan radical to the more stable secondary radical[9] (Equation 3).



(2)



(3)

The direction and selectivity of these oxidations should thus prove particularly useful in the transformation of highly substituted carbohydrates into 6-bromo-6-deoxy-sugars and in removing the *O*-benzylidene group under non-acidic conditions.[3]

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[1] Oxidation of acyclic benzylidene acetals has been studied. See L. Horner and E. H. Winkelmann, in "Newer Methods of Preparative Organic Chemistry", Vol. III, ed. W. Foerst, Academic Press, New York, 1964, p. 151.

[2] J. D. Prugh and W. C. McCarthy, *Tetrahedron Letters*, 1966, 1351.

[3] S. Hanessian, *Carbohydrate Res.*, 1966, **2**, 86.

[4] P. A. Levene and G. M. Meyer, *J. Biol. Chem.*, 1928, **76**, 513.

[5] B. Helferich, W. Klein, and W. Schafer, *Annalen*, 1926, **447**, 19.

[6] All new compounds gave satisfactory elemental analyses and spectral data.

[7] B. R. Baker and T. L. Hullar, *J. Org. Chem.*, 1965, **30**, 4049.

[8] Oxidation of methyl 2,3,4,6-tetra-*O*-methyl-αβ-D-glucopyranoside with NBS in carbon tetrachloride containing benzoyl peroxide gave a syrupy product with infrared absorption at 1720 cm.$^{-1}$ (δ-lactonic or acyclic ester carbonyl) and was homogeneous by t.l.c. The product could not be adequately purified, however.

[9] *Cf.*, E. S. Huyser and Z. Garcia, *J. Org. Chem.*, 1962, **27**, 2716.