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STEREOCHEMISTRY OF NUCLEOPHILIC DISPLACEMENT REACTIONS OF A VICINAL PRIMARY AND SECONDARY SULFONIC DIESTER SYSTEM

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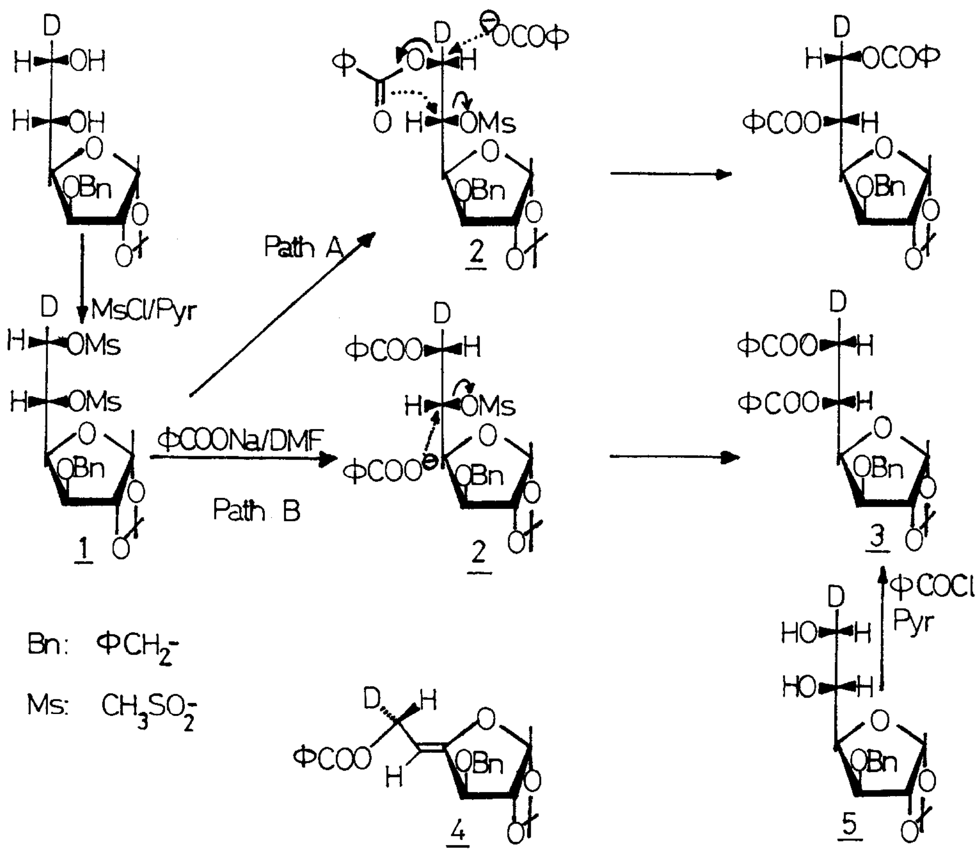
Although sulfonate esters have been widely used, especially in carbohydrate field,[1] for the stereochemically defined substitution reactions, neighboring group participations make those reactions complicated. So far, the mechanism of nucleophilic displacement reactions of a disulfonate ester such as 1 by carboxylates has been controversial whether an acyl migration takes place (Path A in the following scheme)[2] or a dual displacement (Path B) is involved.[3,4]

Recently, a synthesis of carbohydrates having a chiral hydroxymethyl group, *e.g.* (6R)- and (6S)-$[6\text{-}{}^{2}H_1]$-*D*-glucoses, was reported from this laboratory,[5] which may serve as useful tools to study these stereochemical problems, and the following experiments were undertaken to clarify the mechanism of the above displacement reactions. Thus, if Path A were the case, the configuration of the deuterated methylene carbon should be retained, whereas Path B would result in an inversion.

(6S)-$[6\text{-}{}^{2}H_1]$-3-*O*-benzyl-1,2-*O*-isopropylidene-5,6-*O*-dimesyl-β-*L*-idofuranose 1, prepared by a conventional mesylation of the corresponding glycol,[5] showing the coupling constant of 2.5 Hz between H-5 observed at 4.98 ppm and *pro R* H-6 at 4.34 ppm, which is well accorded with that (2.5 Hz) of a $[6\text{-}{}^{2}H_1]$-3,5,6-*O*-triacetyl-1,2-*O*-isopropylidene-α-*D*-glucofuranose having an *erythro* configuration for the C-5 and C-6 portion,[6] was treated with C_6H_5COONa in DMF for 6 hrs at reflux to give a mixture of a monobenzoate 2 and a dibenzoate 3 in a ratio of 4:5, together with a trace of an elimination product 4. The preferential displacement taken place as expected at the primary site (C-6) with the Walden inversion was supported by the formation of 2, $[\alpha]_D^{26}$ +24.4° (*c* 1.0, $CHCl_3$), $\delta^{TMS}_{CDCl_3}$ 1.33 (3H, s), 1.49 (3H, s), 3.11 (3H, s), 3.99 (1H d, J=3 Hz, H-3), 4.36 (1H d, J=6 Hz, H_S-6), 4.44 (1H dd, J=3 and 9 Hz, H-4), 4.49 (1H d, J=11.5 Hz), 4.66 (1H d, J=4.0 Hz, H-2), 4.68 (1H d, J=11.5 Hz), 5.18 (1H dd, J=6 and 9 Hz, H-5), 5.98 (1H d, J=4.0 Hz, H-1), 7.30 (5H, s), 7.20-7.60 (3H, m) and 8.00-8.20 (2H, m), since the $J_{5,6S}$ value is consistent with that (6.5 Hz) of a *threo* configuration.[6] In contrast, the dibenzoate 3, $[\alpha]_D^{26}$ -49.4° (*c* 2.0, $CHCl_3$), $\delta^{TMS}_{CDCl_3}$ 1.34 (3H, s), 1.54 (3H, s), 4.07 (1H d, J=3.0 Hz, H-3), 4.43 (1H d, J=12.5 Hz), 4.56 (1H d, J=12.5 Hz), 4.63 (1H dd, J=3.0 and 8.5 Hz, H-4), 4.65 (1H d, J= 4.0 Hz, H-2), 4.96 (1H d, J=2.0 Hz, H_S-6), 5.76 (1H dd, J=2.0 and 8.5 Hz, H-5), 5.97 (1H d, J= 4.0 Hz, H-1) and 7.02-8.08 (15H, m), has the $J_{5,6S}$ (2.0 Hz) of an *erythro* configuration, suggesting that an inversion occurred at the secondary sulfonate site (C-5) of 2. Furthermore, this was confirmed by the pmr spectrum of (6R)-$[6\text{-}{}^{2}H_1]$-5,6-*O*-dibenzoyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-*D*-glucofuranose, prepared independently by a direct benzoylation of known (6R)-$[6\text{-}{}^{2}H_1]$-3-*O*-benzyl-1,2-*O*-isopropylidene-α-*D*-glucofuranose 5.[5] The spectrum was completely identical with that of 3.



In conclusion, since the configurational inversions were observed at each mesyloxylated carbons under these conditions, it appears that the reaction proceeds via the direct displacement (Path B) without participation of the initially introduced neighboring acyl group.

References and Notes

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The author described the mechanism of this type of reactions as direct displacements by referring the paper of Vargha,4) in which, 3,5-O-diacetyl-6-O-benzoyl-1,2-O-isopropylidene-L-idofuranose was reportedly formed by the reaction of 3-O-acetyl-6-O-benzoyl-1,2-O-isopropylidene-5-O-tosyl-D-glucofuranose with KOAc in acetic anhydride. However, the identification of the two acyl groups at C-5 and C-6 of the product was not furnished unambiguously so that the mechanistic discussions whether the acyl migration took place or not have been remained uncertain, though the described mechanism turned out to be confirmed by the present result.

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