

NUCLEOPHILIC DISPLACEMENT REACTIONS OF THE METHANESULFONATES OF
THE 1-O-BENZOYL-1,2-, -1,3-, and -1,4-GLYCOLS

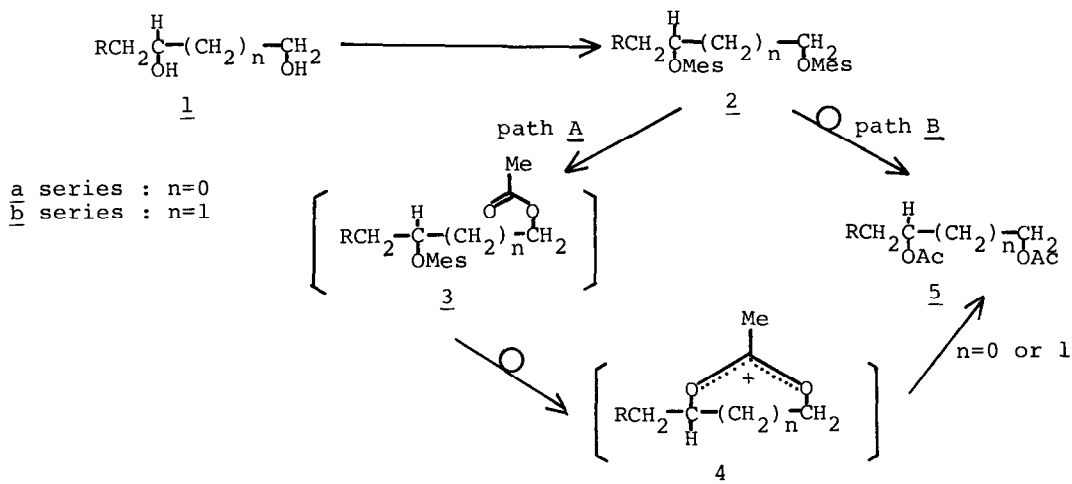
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Abstract: Nucleophilic displacement reactions of the methanesulfonates (8a-c) of the 1-O-benzoyl-1,2-, -1,3-, and -1,4-glycols (7a-c) with potassium acetate in boiling acetic anhydride have been examined. Both benzoyloxy-group participation pathway (path A) and S_N2 displacement pathway (path B) have been involved in the 1,2-(8a)- and 1,3-(8b)-substrates to give a mixture of the primary (10a,b) and the secondary (11a,b) acetates with complete inversion of chiralities. On the other hand, only S_N2 displacement pathway (path B) has been involved in the 1,4-substrate (8c) to give the secondary acetate (11c) with inversion of the chirality.

Recently, we reported an efficient chirality inversion reaction of some 1,2- and 1,3-glycol derivatives (1a,b) via the solvolytic treatment of their dimethanesulfonates (2a,b) with potassium acetate in boiling acetic anhydride¹⁻³ (Scheme 1). Although there were no evidences, we assumed that the inversion occurred by attack of the acetate ion at the primary center of an acetoxonium ion (4) formed by neighboring-group participation of the initially introduced acetoxy group at the primary carbon of a dimethanesulfonate (2) (path A) rather than by simple S_N2 displacement at the primary and the secondary centers with the acetate ion (path B) as a similar chirality inversion reaction by neighboring-group participation has been reported in carbohydrates containing a 1,2-glycol system^{4,5}. We report here our results on the solvolytic reactions of the methanesulfonates (8a-c) of the 1-O-benzoyl-1,2-, -1,3-, and -1,4-glycols (7a-c), prepared from the corresponding precursors (6a-c), with potassium acetate in boiling acetic anhydride.

Each of the methanesulfonates (8a-c) was prepared from the corresponding glycols, (R)-1,2-(6a)⁶, (S)-1,3-(6b)³, and (S)-1,4-(6c)⁷, respectively, via the primary benzoates (7a-c) by successive treatment with benzoyl chloride (1^{mol. equiv.}) and methanesulfonyl chloride under standard conditions.

Treatment of the 1,2-diester (8a) with potassium acetate (1.3^{mol. equiv.}) in boiling acetic anhydride gave an inseparable mixture of two isomeric products in 94 % yield of which ratio was



Scheme 1

determined to be 6 : 1 by ^1H -nmr spectrum. Comparing its ^1H -nmr spectrum with those of authentic 1-*O*-acetyl-2-*O*-benzoyl-(10a)- and 2-*O*-acetyl-1-*O*-benzoyl(11a)-1,2-glycols prepared from the original glycol (6a)⁸, the major component was assigned to be the former (10a) formed by neighboring-group participation pathway (path A) and the minor one to be the latter (11a) formed by $\text{S}_{\text{N}}2$ displacement pathway (path B). Treatment of the mixture with methanolic potassium carbonate allowed a facile deacylation to give the 1,2-glycol (6a) in 70 % yield which was identical with the original 1,2-glycol (6a) in all respects except the sign of optical rotations. Since optical rotations of (6a) was found to be very variable on concentration, both the materials were converted into the diacetate for the comparison. The diacetate from the original (*R*)-1,2-glycol (6a) possessed $[\alpha]_{\text{D}} + 16.69^\circ$ (c 4.50, CHCl_3), while the diacetate from the reaction product showed $[\alpha]_{\text{D}} - 16.54^\circ$ (c 3.06, CHCl_3) indicating a complete inversion in the solvolysis. This also indicated that the formation of (11a) was not resulted by attack of the acetate ion at the secondary center of the benzoxonium intermediate (9a), but by direct $\text{S}_{\text{N}}2$ displacement at the secondary center of the mesylate (8a).

On the same solvolytic treatment, the 1,3-diester(6b) gave an inseparable mixture of two components in 4 : 1 ratio, in 86 % yield, which were assigned to be the 3-*O*-acetyl-1-*O*-benzoyl(11b)- and 1-*O*-acetyl-3-*O*-benzoyl(10b)-1,3-glycols, respectively, by ^1H -nmr comparison with authentic materials obtained from the 1,3-glycol (6b)⁹. Hydrolysis of the mixture gave a single product (6b), $[\alpha]_{\text{D}} + 7.90^\circ$ (c 7.56, MeOH), in 85 % yield, which was identical in all respects except the sign of rotations with the original 1,3-glycol (6b), $[\alpha]_{\text{D}} - 7.56^\circ$ (c 3.65, MeOH)³, indicating complete inversion

References:

- 1) S. Takano, K. Seya, E. Goto, M. Hirama, and K. Ogasawara, Synthesis, 116 (1983).
- 2) S. Takano, E. Goto, and K. Ogasawara, Chemistry Lett., 1913 (1982).
- 3) S. Takano, C. Kasahara, and K. Ogasawara, Chemistry Lett., 175 (1983).
- 4) R. C. Chalk, D. H. Ball, M. A. Litner, and L. Long, Jun., J. Chem. Soc., Chem. Comm., 245 (1970)
- 5) Under certain conditions, the inversion was proven to occur only by S_N2 displacement pathway: see, K. Kakinuma, Tetrahedron Lett., 765 (1978).
- 6) S. Takano, E. Goto, M. Hirama, and K. Ogasawara, Heterocycles, 16, 381 (1981).
- 7) Prepared by lithium aluminum hydride reduction of the known γ -lactone derivative (see, M. Taniguchi, K. Koga, and S. Yamada, Tetrahedron, 30, 3547 (1974)). 6c: bp 145-150°C (0.06 torr.) (Kugelrohr), $[\alpha]_D - 5.26^\circ$ (c 4.94, MeOH).
- 8) 10a: bp 180-190°C (0.09 torr.) (Kugelrohr), $[\alpha]_D + 15.02^\circ$ (c 4.21, CHCl₃), δ (CDCl₃) 2.01 (3H, s), 4.40 (1H, d, J=6.5Hz), 4.41 (1H, d, J=4Hz), 5.3-5.6 (1H, m) (ppm). 11a: bp 185-190°C (0.04 torr.) (Kugelrohr), $[\alpha]_D + 7.71^\circ$ (c 5.11, CHCl₃), δ (CDCl₃) 2.08 (3H, s), 4.4-4.6 (2H, m), 5.2-5.5 (1H, m) (ppm).
- 9) 10b: bp 180-190°C (0.06 torr.) (Kugelrohr), $[\alpha]_D - 16.16^\circ$ (c 5.54, MeOH), δ (CDCl₃) 1.97 (3H, s), 3.67 (2H, d, J=5Hz), 4.17 (2H, t, J=6.4Hz), 5.25-5.55 (1H, m) (ppm). 11b: bp 180-190°C (0.07 torr.) (Kugelrohr), $[\alpha]_D - 20.54^\circ$ (c 6.16, MeOH), δ (CDCl₃) 2.04 (3H, s), 3.57 (2H, d, J=5Hz), 4.29 (1H, dt, J=12, 5.7Hz), 4.43 (1H, dt, J=12, 5.7Hz), 5.1-5.35 (1H, m) (ppm). 10c: bp 204-211°C (0.08 torr.) (Kugelrohr), $[\alpha]_D - 3.20^\circ$ (c 3.18, MeOH), δ (CDCl₃) 2.02 (3H, s), 3.63 (2H, d, J=5Hz), 4.08 (2H, br.t, J=6Hz), 5.1-5.5 (1H, m) (ppm).
- 10) 11c: bp 202-206°C (0.09 torr.) (Kugelrohr), $[\alpha]_D - 5.94^\circ$ (c 4.11, MeOH), δ (CDCl₃) 2.07 (3H, s), 3.53 (2H, d, J=5Hz), 4.1-4.5 (2H, m), 4.9-5.3 (1H, m) (ppm).

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