

Ring Contraction Accompanying Nucleophilic Substitution in 1,3-Dioxan Derivatives†

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Summary The reaction of *cis*-2-phenyl-1,3-dioxan-5-ol with triphenyl phosphine and carbon tetrabromide gives a mixture of diastereomeric 2-phenyl-4-bromomethyl-1,3-dioxolans, whereas only *trans*-2-phenyl-5-bromo-1,3-dioxan is obtained from the reaction of *cis*-2-phenyl-1,3-dioxan-5-yl *p*-toluenesulphonate with lithium bromide.

cis-2-PHENYL-1,3-DIOXAN-5-OL (I) and related derivatives are normally stable under neutral and alkaline conditions, and these protected intermediates are used¹ extensively for the synthesis of structurally pure glycerides free from isomer impurities. However, we report now that even under neutral conditions, rearrangement to 1,3-dioxalans (II) can occur.

The reaction of *cis*-2-phenyl-1,3-dioxan-5-yl *p*-toluenesulphonate² (III) with lithium bromide in anhydrous acetonitrile gave (IV)‡ m.p. 83–86°C. The 220 MHz n.m.r. and mass spectral data indicate the expected 1,3-dioxan structure for the product.

The reaction of (I) with PPh₃ and CBr₄³ in anhydrous benzene under reflux gave a mixture of three components (g.l.c.). The minor component (*ca.* 5%) was (IV) (g.l.c. and m.s.). Mass and 220 MHz n.m.r. spectra showed that the two major components had structure (V).

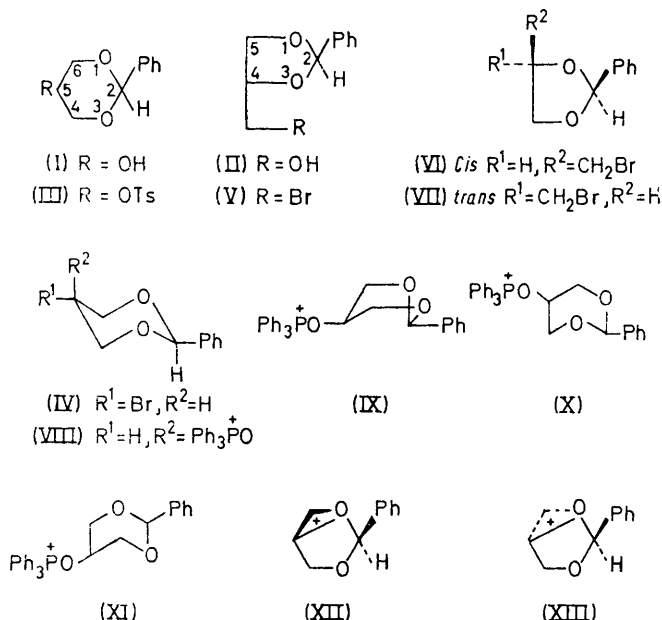
In the 220 MHz n.m.r. spectrum of (IV), the PhCH signal appears as a sharp singlet at τ 4.50. In contrast, the PhCH signal appears as two sharp singlets of almost equal intensity at τ 4.11 and 4.27 for the mixture (V). Comparison with the 100 MHz spectrum established that these two peaks are singlets arising from two different molecular species present in the product. Structure (V) can exist in two diastereomeric forms (and their enantiomers), hence singlets at τ 4.11 and 4.27 could arise from the *cis* (VI) and the *trans* (VII) diastereomers respectively (*cf.* ref. 4).

The recognition that two molecular species are contributing to the greater part of the 220 MHz n.m.r. spectrum permits analyses of the other peaks which comprise three

† Presented by R. Aneja to the 8th International Symposium on the Chemistry of Natural Products, I.U.P.A.C., New Delhi, Feb. 6–12, 1972.

‡ Correct elemental analyses were obtained for the bromodeoxy derivatives examined.

complex multiplets centred at τ 5.64 (9 lines) and τ 6.0 (10 lines) and τ 6.63 (14 lines). By a judicious choice of the line separations from the observed spectrum, a theoretical spectrum was calculated⁵ for each of the two diastereomers (VI) and (VII) by iterative calculation and refining to the best fit. Superposition of the two calculated spectra gave a composite result identical with the observed spectrum.



The reaction of (I) with PPh_3 and CCl_4 gave analogous chlorodeoxy products.

If the reaction follows the pathway suggested earlier,³ then plausible differences in the conformational structures of (III) and the presumed reaction intermediate (*cf.* ref. 4) in the reaction with PPh_3 and CBr_4 appear to offer an explanation for the different results. Compound (I) is known⁶ to exist entirely in the chair conformation with an equatorial phenyl and a *cis* axial hydroxyl on C-2 and C-5 respectively. Presumably, at the temperature of the reaction, (III) also exists in a boat conformation and this sterically precludes intramolecular attack at C-5 by the ring oxygen atoms and hence the reaction proceeds intermolecularly by normal rear-side attack at C-5 (S_N2 type). On the other hand, the intermediate (VIII), should exist predominantly in the boat (IX) or skew boat [(X) and (XI)] conformations, since here both bulky substituents occupy equatorial positions. In the boat conformation(s), the ring oxygen atoms are well placed for intramolecular attack on C-5 to displace PPh_3O and give the two diastereomeric bicyclo-dioxalanium intermediates (XII) and (XIII). Reaction of bromide ion at C-5 in both leads to (IV), while (VI) and (VII) arise from (XII) and (XIII) respectively by reaction at C-6. Of course, reaction by participation of the other ring oxygen is equally plausible, but leads to the same products, *i.e.* (VI) and (VII).

Mass spectra were obtained by Dr. T. Bryce and the calculation for n.m.r. coupling constants were carried out by Mr. J. A. Knaggs. The authors gratefully acknowledge their help.

(Received, 24th April 1972; Com. 701.)

¹ See T. Malkin and T. H. Bevan, *Progr. Chem. Fats and Lipids*, 1957, 97; D. J. Hanahan, *Lipid Chemistry*, Wiley, New York, 1960, pp. 178–207; P. E. Verkade, *Bull. Soc. chim. France*, 1963, 10, 1993.

² N. Baggett, M. A. Bukhari, A. B. Foster, J. Lehmann, and J. B. Webber, *J. Chem. Soc.*, 1963, 4157.

³ A. J. Burn and J. I. G. Cadogan, *J. Chem. Soc.*, 1963, 5788; I. M. Downie, J. B. Holmes, and J. B. Lee, *Chem. Ind.*, 1966, 900; J. B. Lee and I. M. Downie, *Tetrahedron*, 1967, 23, 359.

⁴ T. D. Inch and N. Williams, *J. Chem. Soc.*, (C), 1970, 263; B. Serdarevich, *J. Amer. Oil Chemist's Soc.*, 1967, 44, 381.

⁵ Programme LAOCN3 by Bothner-By and Castellano was employed.

⁶ N. Baggett, J. S. Brimacombe, A. B. Foster, M. Stacey, and D. H. Whiffen, *J. Chem. Soc.*, 1960, 2574.