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OXIRANYLIDENE INTERMEDIATE IN THE REACTION OF TRANS-2-CHLORO-3-TERT-BUTYLOXIRANE WITH SODIUM PHENOXIDE.

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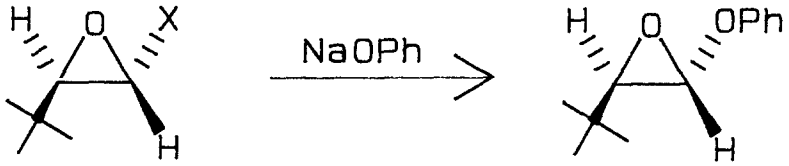
Abstract: The reaction of *trans*-2-chloro-3-(t-butyl)oxirane with sodium phenoxide in acetonitrile to give *trans*-2-phenoxy-3-(t-butyl)oxirane involves α-elimination to give an oxiranylidene which undergoes a stereoselective stepwise addition of phenol to give product.

Recently it was shown that reaction of *trans*-2-chloro- (1-Cl) or 2-bromo-3-(t-butyl)oxirane (1-Br) with phenoxides in acetonitrile results in replacement of halide by phenoxide with retention of configuration to give *trans*-2-phenoxy-3-(t-butyl)oxirane (2).[1] On the basis of kinetic studies,

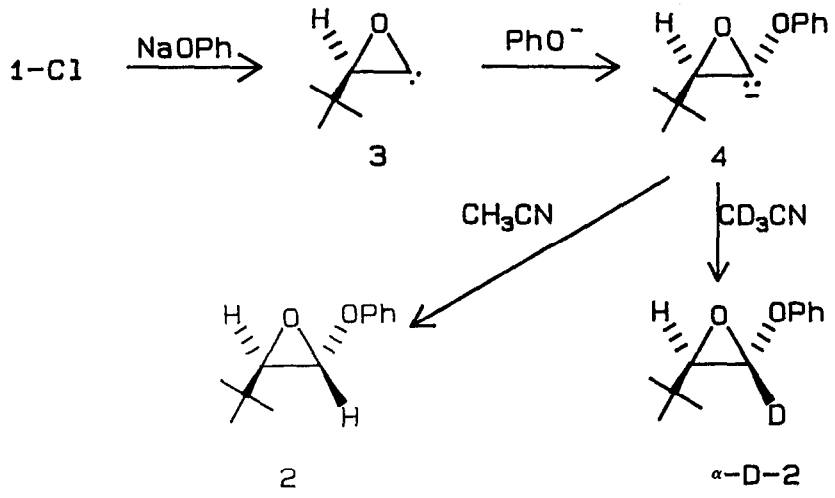


1 2

and other control experiments that ruled out various plausible intermediates, it was concluded that this transformation involves "... a bimolecular S_N2 type reaction."[1] This interpretation is not only at odds with the inevitable inversion of configuration for S_N2 displacements but also with the known chemistry of cyclopropyl derivatives, *i. e.*, nucleophilic substitution reactions are difficult[2] and often proceed by an elimination-addition sequence or other mechanism.[3] Moreover, unambiguous S_N2 reactions proceed with inversion of configuration of the cyclopropane carbon.[4] It should also be noted that the cis isomer of 1, which is substantially less

reactive than 1, reacts with inversion of configuration to give 2.[1]

We now report that the conversion of 1-Cl to 2[5] does not involve a bimolecular displacement but instead involves α-elimination of hydrogen chloride to give the cyclic carbene (3) which reacts with phenoxide ion to give the carbanion (4) which in turn is protonated (primarily by solvent) to give 2. The 3 ⟶ 2 conversion is completely stereoselective. By analogy with cyclopropyl carbanions[7], we presume that 4 is stereochemically stable and that the 3 ⟶ 4 transformation is stereoselective as indicated.



The evidence is as follows. 1) Reaction of α-D-1-Cl with sodium phenoxide in CH_3CN[5] gives 2 with 83% loss of deuterium. No exchange is observed in unreacted α-D-1-Cl which together with the earlier report[1] that 1-Br is 1700 times more reactive than 1-Cl suggests that the α-elimination is concerted. 2) Under the same conditions[5], reaction of 1-Cl in CD_3CN gives mainly α-D-2 (81% D). 3) Reaction of β-D-1-Cl under these conditions gives β-D-2 without loss or change of location of the deuterium. 4) Competetive experiments[8] showed that the rate constant ratio for β-D-1-Cl and α-D-1-Cl is $k_{\beta\text{-D}}/k_{\alpha\text{-D}} = 1.7 \pm 0.2$ (average of 4 experiments). Presumably a β-deuterium has no effect on reactivity and thus this ratio corresponds to the α-deuterium kinetic isotope effect (k_H/k_D). The observed ratio is too large for a secondary isotope effect and about the same as the primary isotope effect reported for conversion of halomethanes to carbenes ($1.8 \pm .2$).[9]

The results of the present experiments and the earlier kinetic studies[1]

suggest that phenoxide functions as a base in a rate-limiting α-elimination to give 3. Theoretical considerations indicate that 3 is a reasonable intermediate; the calculated barrier for isomerization to ketene is 105-131 kJ/mole.[10] Attempts to trap 3 with added methanol were unsuccessful. From this, and the incorporation of a proton or deuterium from the solvent (acetonitrile), we conclude that the conversion of 3 to 2 is stepwise rather than a 1-step insertion into the O-H bond of phenol.

The labelled compounds, α-D-1-Cl and β-D-1-Cl were prepared by modified established routes to the parent, 1-Cl. Reduction[11] of dichloropinacolone[12] by $NaBD_4$ gave an 80% yield of β-D-1-Cl (90% *trans* isomer).[13] Reaction of pivaldehyde with $LiCDCl_2$[14] in THF at -110 °C, followed by aqueous quench after ten minutes, gave 1-deuterio-1,1-dichloro-3,3-dimethyl-2-butanol. Treatment of the latter with NaOH in a two-phase system[11] gave α-D-1-Cl (91% trans)[13] in an overall yield of 80%. Pure trans isomers, α-D-1-Cl and β-D-1-Cl, were obtained by preparative GC (6 ft. Carbowax 20M, 105 °C). The ^{2}H-NMR spectra of α-D-1-Cl and β-D-1-Cl ($CHCl_3$, singlets at 4.91 and 2.90 ppm, respectively) and the absence of the corresponding signals in the ^{1}H-NMR spectra[15,16], showed these samples to be discretely labelled (> 98% D at indicated positions).

It is noteworthy that alkyllithium reagents also give substitution products with 1-Cl (stereochemistry not indicated).[17] The mechanism proposed for this substitution involves deprotonation of 1-Cl to give the α-lithiated chlorooxirane (carbenoid). However, carbene 3 seems equally likely.[18] Solvent is reported to determine whether 1-Cl gives substitution or ring-opened products.[17] This is also the case for reaction of 1-Cl with alkoxides. For example, reaction of 1-Cl with methanolic NaOMe gives the ring-opened hydroxyacetal in high yield.[19]

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