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ON THE EVIDENCE FOR INTRAMOLECULAR LIGAND EXCHANGE IN PENTACOORDINATE CARBONATE(IV) ANION: IMPLICATIONS FOR THE MECHANISM OF BIMOLECULAR NUCLEOPHILIC SUBSTITUTION AT SATURATED CARBON.

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The spectacular finding[1] that cis-3-ethoxycyclobutyl brosylate (1) undergoes S_N2 displacement by iodide and bromide ion with retention of configuration, as predicted[2] on theoretical grounds, understandably attracted the attention of the chemical community,[3] for this observation served to cast an entirely new light on the classical S_N2 mechanism: according to the experimental[1] and theoretical[2] evidence, the reaction proceeds through an intermediate pentacoordinate carbonate(IV) anion of trigonal bipyramidal geometry, which is capable of undergoing intramolecular ligand exchange, i.e. Berry pseudorotation or turnstile rotation.

We now report that halide displacement reactions on cis- and trans-1 in fact proceed cleanly with *inversion* of configuration.

Cis-1,[4] prepared from cis-3-ethoxycyclobutanol (2),[5] was converted in quantitative yield to trans-3-ethoxycyclobutyl acetate by treatment with potassium acetate in anhydrous dimethyl sulfoxide containing dicyclohexyl-18-crown-6.

Reaction of the acetate with methylmagnesium iodide gave trans-2, which was converted to trans-1.[4] Reaction of cis- and trans-1 with lithium bromide under the previously described conditions[1] yielded 3-ethoxycyclobutyl bromides (3),[6] which were analyzed by glc on a 10% Carbowax 20M column, using mesitylene as an internal standard. The results are graphically displayed in Figure 1.

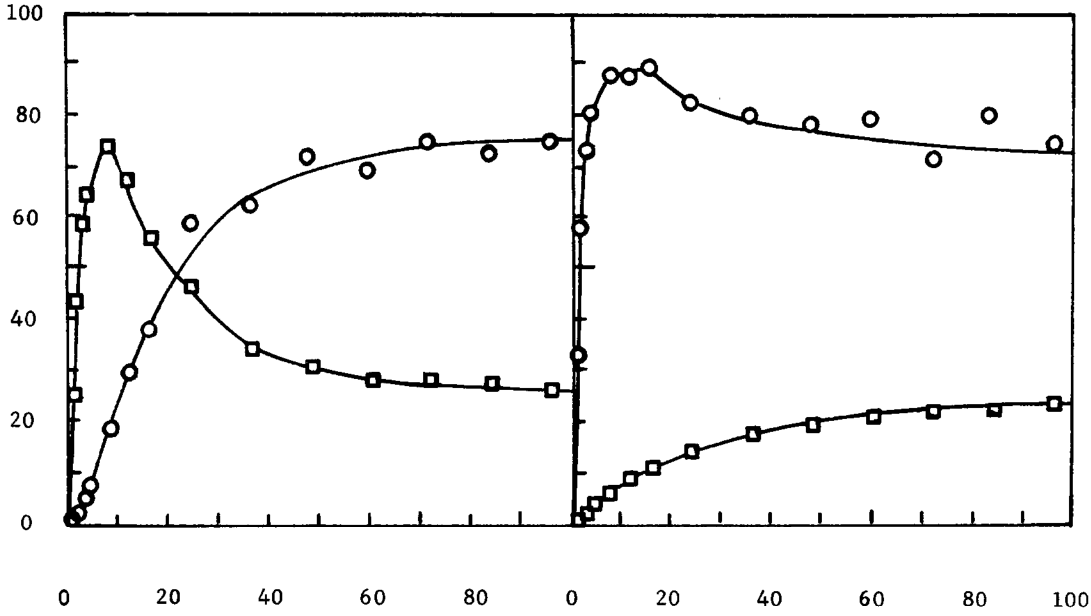

Figure 1. Percent conversion of 3-ethoxycyclobutyl brosylates (1) into bromides (3) (ordinate) as a function of reaction time, in hours (abscissa), starting with cis-1 (left) and trans-1 (right). Circles: cis-3. Squares: trans-3.

As seen by inspection of the Figure, initially stereospecific conversion of cis-1 into trans-3 and of trans-1 into cis-3 is followed by epimerization[9] to an equilibrium mixture of cis- and trans-3 in a ca. 3:1 ratio.[10] We hasten to emphasize that these stereochemical results, far from surprising, were in fact fully anticipated since it has long been known that S_N2 displacement reactions on related cyclobutane ring systems proceed with inversion of configuration,[5,11] and that cyclobutyl halides are epimerized by halide ion.[7a]

The present work obviously invalidates all evidence for the claim[1] that there exist carbon centered S_N2 reaction intermediates with lifetimes long enough for intramolecular ligand exchange. Furthermore, since retention was predicted[2] for S_N2 displacements at cyclobutyl carbon, the failure of that prediction necessarily vitiates the theoretical model[2] on which the prediction was based. In particular, it is now appropriate to question the claim,[2] based on CNDO/2 calculations, that electronegative substituents prefer the equatorial position in the putative trigonal bipyramidal carbon centered S_N2 intermediates. Further comments are reserved for our detailed paper on the subject.

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6. The configurational identities of *cis*- and *trans*-**1**, **2**, and **3** were determined by nmr, according to established precedent.[4,5,7] The configurational assignments[4] for **1** and **2** were confirmed by X-ray analysis on *cis*-**1**.[8]

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8. J.F. Blount, unpublished work.

9. In an independent experiment, reaction of *trans*-**3** with lithium bromide in refluxing acetone led to the same equilibrium mixture.

10. Similar results were obtained in reactions of **1** with sodium iodide in acetone.

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