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SOLVOLYSIS OF 3-ETHOXYCYCLOBUTYL BROSYLATES; ABSENCE OF ANCHIMERIC PATHWAYS

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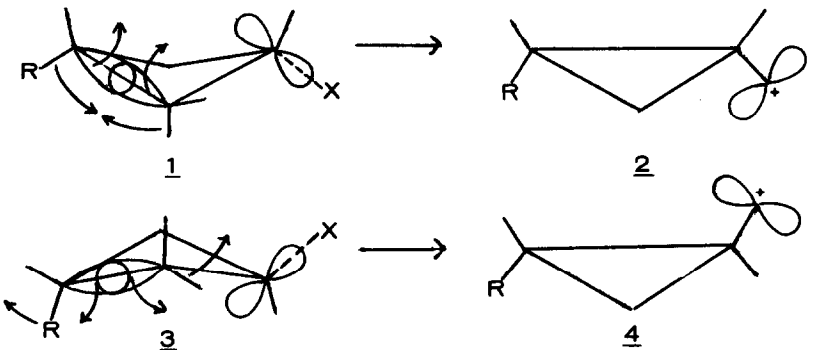
The cationic rearrangement of 3-substituted cyclobutyl derivatives proceeds initially through stereospecific, rate-determining participation of the C_2-C_3 bond orbitals in the formation of a cyclopropylcarbinyl cation[1-5] This ion is partitioned between further rearrangement and solvent capture to an extent dependent on its "openness", as is particularly evident from comparison of deamination and solvolysis results[1] The conformational effects of changes in substituent repulsive interactions ensuing from disrotatory orbital opening backside to the leaving group in both cyclobutyl and cyclopropylcarbinyl cases may be correlated with product distribution. The relative retardation of cis as compared to trans 3-substituted cyclobutyl solvolysis rates is attributable to such an effect. Thus, rate retardation stems from R-H interactions developed in process 1 - 2 (cis), while process 3 - 4 (trans) is free of such hindrance. As the 3-substituent is



varied from methyl[1] to isopropyl[4] to t-butyl[2] in the cis-3-alkylcyclobutyl arenesulfonates, solvolysis rate retardation becomes greater, It is thus evident that when anchimeric assistance to ionization through participation by the C_2- C_3 orbitals is opposed,

the rate of unassisted cyclobutyl ionization[6] is expectedly low. Similar results have emerged from the study of bicyclic cyclobutyl arenesulfonate solvolyses[7].

We have reported an analogous but apparently electronic interdiction of C_2-C_3 orbital participation in ionization, in the case of deamination of an isomeric mixture of 3-ethoxycyclobutylamine, in which predominantly unrearranged product was obtained[8]. Solvolysis of the isomeric 3-ethoxycyclobutyl brosylates has confirmed this observation. Rate retardation by the ethoxy group is several-fold larger than is anticipated on the basis of an ordinary -I inductive effect, for either isomer, and the products contain the unrearranged cyclobutyl ring.

Base-catalyzed condensation of 1-bromo-3-chloro-2-ethoxypropane[9] with malonic ester was followed by conversion of the resultant diethyl 3-ethoxycyclobutane-1,1-dicarboxylate to 3-ethoxycyclobutanol by a sequence described for the 3-isopropyl compounds[5]. The isomeric alcohols were readily separated by vpc. The protons geminal to the substituents in the trans isomer were at lower field (4.38 and 4.07 ppm) than those in the cis isomer (3.79 and 3.51 ppm)[10]. The assignment of configuration was confirmed by equilibration of the ethyl monoesters (NaOH/EtOH), which gave $K_{eq,78^o} = 1.5$ favoring the cis isomer[11]. Preparation of brosylates was routine. The solvolysis rates are listed in Table 1 with those for the parent compound.

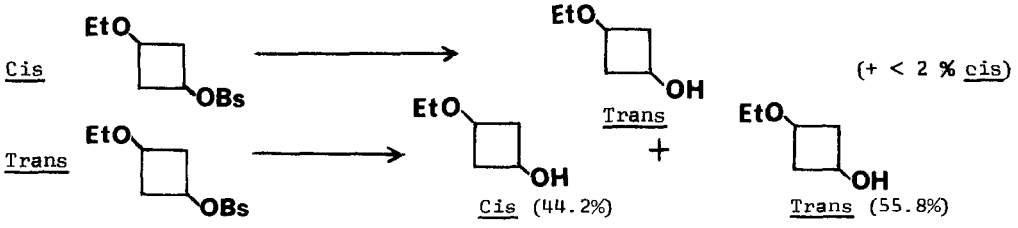
TABLE 1 Solvolysis Rates in 70% Aqueous Acetone (Conductimetric)

Brosylate	T	k (sec^{-1})	$k_{rel}(50.6^o)$
Cyclobutyl	41.1	5.850×10^{-4}	
	50.6	15.195	1.00
Cis-3-ethoxycyclobutyl	41.1	2.638×10^{-6}	
	50.6	5.280	0.0035
Trans-3-ethoxycyclobutyl	41.1	0.927×10^{-6}	
	50.6	1.980	0.0013

The trans/cis rate preference observed in the 3-alkyl cases is reversed in the 3-ethoxy cases. This suggests that the effect in the ethoxy compounds is predominantly electronic rather than steric. The small effective bulk of the ethoxy group is apparently insufficient to make conformational hindrance to process 1 - 2 more significant than the

more potent effect of its equatorial conformation. Both isomers solvolyze several hundred times more slowly than that to be expected from an ethoxy group three carbons removed from the leaving group in an aqueous solvolysis of an arenesulfonate, which is of the order of only 6-7 fold[12]. Compelling evidence that the inductive effect of the ethoxy group has effectively cancelled the anchimeric reactivity of the C_2-C_3 orbitals[13] is obtained from the product analysis. The differing degree of isomeric stereoselectivity suggests that the trans solvolysis proceeds through a more open carbonium ion than the cis.

Product Distribution, Solvolysis in 70% Buffered Acetone at Reflux



This is contrary to what would be expected on the basis of backside participation by the ethoxy group[8], as is the rate ratio. Such participation should produce an enhanced trans rate and retained stereochemistry[14]. However, both sets of observations may be accomodated by the conclusion that the ethoxy group will experience greater cross-ring interaction with the cationic center generated by the leaving group when both are in the equatorial conformation[15]. This interaction appears to further enhance the relative cis rate in the absence of steric retardation in the transition state, presumably due to better delocalization of cationic charge to the equatorial ethoxy group. Further, some type of cross-ring interaction of this type must be invoked to explain the almost complete inversion observed in the cis case. Thus, the enhanced trans rate observed in the solvolysis of isomeric 3-hydroxy-2,2,4,4,-tetramethylcyclobutyl tosylates[16] should be preferably explained in terms of the steric interaction created in the cis transition state by analogy with the cis 3-alkyl compounds, rather than by an enhanced -I effect of equatorial OH.[17]

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