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CYCLOPROPANE AS A NEIGHBORING GROUP IN TRIFLUOROETHANOLYSIS OF 2-CYCLOPROPYLETHYL TOSYLATE

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The propensity of cyclopropane to stabilize remote incipient carbocationic centers has been demonstrated in the solvolyses of geometrically constrained substrates[1]. In contrast, cyclopropane-cation interaction ($k_{\Delta}^{c\text{-}C_3H_5}$) is weak compared to nucleophilic solvent assistance in the parent 2-cyclopropylethyl system[2,3]. Ethanolysis and acetolysis of 2-cyclopropylethyl brosylate and the sterically related isoamyl brosylate[3] were found to be mechanistically similar, both reacting via predominant nucleophilic solvent assistance (k_s). Only in formic acid was evidence for interaction observed in the formation of rearranged product, cyclopentyl formate.[2-4]

To gain further information on the ability of cyclopropane to function as a remote neighboring group in conformationally mobile systems, solvolyses of 2-cyclopropylethyl tosylate (1) and isoamyl tosylate (2)[4,5] have been studied in urea-buffered, anhydrous 2,2,2-trifluoroethanol (TFE), a medium of exceptional ability in promoting anchimeric assistance[6]. Rate constants, obtained using a spectrophotometric method[7], and activation parameters are listed in Table 1; solvolysis products are shown in the scheme below and Table 2.

Table 1: Trifluoroethanolysis First Order Rate Constants[a]

T(°C)	1-OTs $kX10^5(sec^{-1})$	2-OTs $kX10^5(sec^{-1})$
110.02	1.30 ± 0.18	0.425 ± 0.012
120.01	2.88 ± 0.17	1.04 ± 0.13
130.01	5.51 ± 0.15	1.96 ± 0.11
75.00[b]	0.0694	0.0204

[a]Rate constants are averages of 2-3 runs; [ROTs] = 0.9083 - 1.146 mM; [urea] = 1.000 - 1.319 mM; for 1-OTs, $\Delta H^{\neq}$ = 21.52 ± 1.10 kcal/mole, $\Delta S^{\neq}$ = -25.20 ± 2.80 eu; for 2-OTs, $\Delta H^{\neq}$ = 22.73 ± 2.59 kcal/mole, $\Delta S^{\neq}$ = -24.16 ± 6.60 eu. [b]extrapolated.

Trifluoroethanolysis of the analogous 1,1-dideuterated derivative (1-OTs-1-d_2)[5] gave 1-OTFE-2-d_2 and 4-OTFE-2-d_2 with the deuterium exclusively at the 1-position of 1-OTFE and in the methyl group of 4-OTFE, whereas the deuterium label in 3-OTFE was apparently scrambled[8]. (See reaction scheme.) Deuterium distribution in the two olefinic ethers 5-OTFE-d_2 and 6-OTFE-d_2 was not ascertained. Structural assignments were made on the basis of chemical and spectroscopic

evidence. Deuterium content and distribution were determined by nmr spectroscopy using acetophenone as an internal area standard. Products 1-OTFE and 3-OTFE were shown to be stable under solvolysis conditions.

Table 2: Trifluoroethanolysis Products of 1-OTs at 130° (Mole Percent Product)

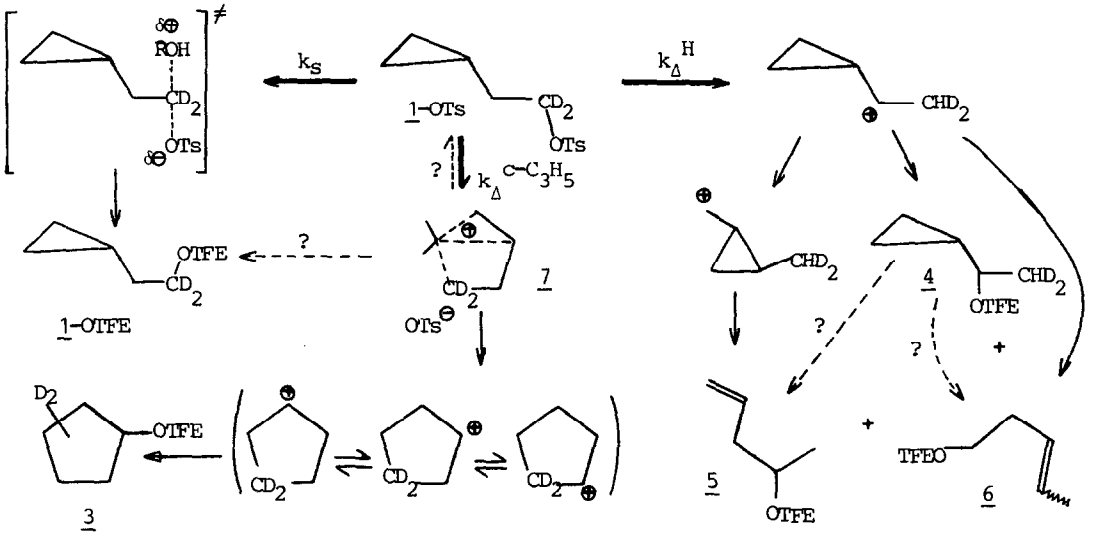
Equiv. Urea	$t_{1/2}$	1-OTFE	3-OTFE	4-OTFE	5-OTFE	6-OTFE
3.31	2.0	41	25	32	2.2	---
3.36	6.9	46	27	25	2.1	4.9
1.42	6.9	46	29	14	6.6	4.9
1.20	6.9	48	31	7.2	7.5	6.7

As shown in Table 2, product distribution for 1-OTs is dependent on base concentration rather than reaction time. Thus, a small fraction of the olefinic ethers may be formed from 4-OTFE at lower base concentrations. The corresponding formate, 4-OCHO, decomposes in formic acid (a more acidic medium than TFE) to 5-OCHO[2]. The two olefinic ethers may be formed from methylcyclopropylcarbinyl cations as shown in the scheme below. The activation enthalpy for 1-OTs is comparable to that of 2-phenylethyl tosylate[10] and slightly lower than that for the steric analogue 2-OTs, indicating some degree of participation. The large negative entropy of activation is commonly observed in TFE[6].

The trifluoroethanolysis rate ratio at 75°, k_1/k_2 = 3.4 (3.1 at 110°), although small, is significantly enhanced over those for ethanolysis (0.92), acetolysis (0.97), and formolysis (1.1)[3] (T = 75°). This rate enhancement, although small compared to the rate increments observed in certain rigid polycyclic systems[1], is nonetheless connotative of anchimeric assistance. More convincing evidence for this assertion was furnished by product studies. The relative yields of cyclopentyl products increase from 0%[2,3] in the highly nucleophilic acetic acid to 13-20%[3,4] and 25-31% in the more limiting solvents formic acid and TFE, respectively. Since any cyclopentyl products must arise via cyclopropyl participation ($k_{\Delta}^{c\text{-}C_3H_5}$) the cyclopentyl yield reflects the increasing ability of cyclopropane to assist with decreasing solvent nucleophilicity and increasing solvent ionizing power since the increase in cyclopentyl products is accompanied by a decrease in the 2-cyclopropylethyl product (i.e. 100% in acetic acid[2,3], 70-82% in formic acid[3,4], and 41-48% in TFE). A similar increment in hydrogen participation (k_{Δ}^{H}) is indicated by formation of hydrogen migration products (i.e. 0% in acetic acid[2,3], 5.1-11% in formic acid[3,4], and 27-34% in TFE).

A mechanistic rationale depicting these discrete processes is presented below. Three competing mechanistic paths are proposed. Formation of the major product 1-OTFE may occur predominantly by a k_s mechanism typical of simple primary substrates. This is supported by the lack

of rearrangement (a formal 1,2-cyclopropyl shift, observed to be dominant in cyclopropyl substituted neopentyl systems[11]) that otherwise would scramble deuterium from C-1 to C-2. Secondly, interaction of cyclopropane with the developing electron deficient center may give a bridged intermediate 7, best represented as an intramolecularly corner-alkylated cyclopropane,



analogous to corner protonation of cyclopropane as postulated by others[12]. This may be attacked by solvent to give some fraction of 1-OTFE[13] or it may undergo rearrangement to the more stable cyclopentyl carbenium ion. The latter is sufficiently long lived to scramble the deuterium label before being trapped by TFE. Rapid 1,2-hydride shifts in the cyclopentyl cation are known from low temperature nmr work by Olah[14]. Thirdly, an irreversible 1,2-hydride shift via k_{Δ}^{H} may give a methylcyclopropylcarbinyl cation, the chemistry of which has been described[2,15].

The effectiveness of cyclopropane to anchimerically assist in the trifluoroethanolysis of 1-OTs is more clearly seen upon dissection of the observed rate constant ($k_{obs.}$) into its components, provided that attack by solvent or any internal nucleophile (hydrogen, cyclopropane) is concerted with ionization. The general equation $k_{obs} = k_s + k_{\Delta}$[16] may be expanded as $k_{obs} = k_s + k_{\Delta}^{c\text{-}C_3H_5} + k_{\Delta}^{H}$ (symbols defined above).

Noting that the magnitude of k_s should be approximately the same in both 1-OTs and 2-OTs (which has $k_s = 2X10^{-5}sec^{-1}$) the following values for 1-OTs may be derived at 130°: ($X10^5$ sec) $k_s = 2.28$, $k_{\Delta}^{c\text{-}C_3H_5} = 1.37$ and $k_{\Delta}^{H} = 1.86$. In this medium $k_{\Delta}^{c\text{-}C_3H_5}$ is a competitive mechanism contrary to previous conclusions drawn for solvolyses in other media[2,3]. Furthermore, k_{Δ}^{H} is also highly competitive (unlike in 2-OTs, which has no cyclopropylcarbinyl driving force) elevating the overall k_{Δ} for 1-OTs to 3.23 as compared to 2.28 for k_s.

References and Notes

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8. Attempted cleavage of 3-OTFE-d_2 with sodium naphthalide radical anion[9] failed to give the corresponding alcohol which could be analyzed for deuterium distribution. However, nmr analysis of the ether indicated that deuterium is most likely scrambled. Analytical integration (internal area standard) shows that the ratio of protons at the 1-position to all ether ring protons is 1:8 in 3-OTFE-d_2 and that both peaks are reduced in intensity by 2/9. Supporting evidence comes from repetition of the related formolysis of 1-OTs-1-d_2 under kinetically controlled conditions[3].The cyclopentyl product 3-O_2CH-d_2 was shown to have deuterium scrambled randomly to all five possible positions by analytical integration of a Eu(fod)$_3$ shifted spectrum of the corresponding alcohol. As TFE and HCO_2H have similar ionizing powers and TFE is considerably less nucleophilic, scrambling over all five positions in 3-OTFE-d_2 is not unanticipated.

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