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SECONDARY DEUTERIUM ISOTOPE EFFECTS IN TRIFLUOROACETOLYSIS OF ISOPROPYL p-TOLUENESULFONATE.

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Recent studies by Peterson (1) and Nordlander (2) have presented considerable evidence for the low nucleophilicity and high ionizing power of trifluoroacetic acid. More specifically, much of this evidence is interpreted as indicating that trifluoroacetolysis of secondary tosylates is more limiting than acetolysis and suggests that a study of deuterium isotope effects in solvolysis of a secondary tosylate would provide useful evidence concerning both the nucleophilicity of trifluoroacetic acid and the relative limiting character of "ordinary" solvolyses of secondary sulfonate esters.

We have measured the rates of trifluoroacetolysis of isopropyl-α-d and isopropyl-β-d_6 p-toluenesulfonates, obtaining the results summarized in Table I.**

The rates were measured using the uv method of Peterson (4), except for the determination of 5 to 7 infinity points and minor modifications. In each run both compounds indicated were run simultaneously, and the isotope effects were calculated in the same manner. In Run 3 the hydrogen rate constant was 9% lower than the average of the other three determinations. This run had to be interrupted by cooling because of a uv failure, but this interruption apparently did not affect the simultaneous d_6 run. Accordingly, we included this isotope effect and accepted the larger average experimental error; this error is still too small to affect our conclusions.

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** Substrates were prepared using standard procedures and gave satisfactory elemental analyses. Deuterium analysis by nmr and mass spectroscopy showed about 99% deuteration in the indicated positions. Trifluoroacetic acid (Aldrich Chemical Corporation) was twice-distilled from H_2SO_4 and stored under N_2.

TABLE I

Isotope Effects in Trifluoroacetolysis of Isopropyl Tosylate.

Compound	Run No. (10^5 k, sec^{-1})[a]			
	1	2	3	4
$(CH_3)_2CHOTs$	2.31[b,c] ± .02	2.29[c] ± .03	2.07[d,e] ± .03	2.21[d] ± .06
$(CH_3)_2CDOTs$	1.88 ± .02	1.88 ± .02	--	--
$(CD_3)_2CHOTs$	--	--	1.01[e] ± .01	1.01 ± .01

$(k_H/k_D)_\alpha$ = 1.22 ± .02 $(k_H/k_D)_\beta$ = 2.12 ± 0.1

$\Delta\Delta F^*$ = 117 ± 9 cal/mole $\Delta\Delta F^*/n$ = 74 ± 5 cal/mole

a. All runs were .05 M in ROTs and 0.125 M in $NaOOCCF_3$. Rate constants were obtained using a nonlinear least-squares program (LSKIN1)(3); error estimates for individual rates are the standard deviations given by the program.

b. cf. Peterson's value of 2.49 ± .25 × 10^{-5} sec^{-1} at 25° (4). (Error from Peterson's estimate, ref. 1.)

c. Runs at 24.93 ± .02°C.

d. Runs at 24.99 ± .02°C.

e. See text for further comment on this run.

The rate for the undeuterated compound has also been measured at 44.43 ± .02°C under otherwise identical conditions, giving k_H = 1.82 ± .06 × 10^{-4} sec^{-1}, ΔH^* = 18.5 ± 1 kcal/mole, and ΔS^* = -17 ± 4 e.u. The entropy of activation is more negative than that for acetolysis of isopropyl tosylate (-5.8 e.u.) (5), but could be accounted for by greater hydrogen bonding solvation of the leaving group, an effect demonstrated by Peterson in other systems (6).

α-Deuterium isotope effects have been widely interpreted as measures of the geometries of transition states (7). Mislow, Borčić, and Prelog (8) have reported an α-isotope effect of k_H/k_D = 1.12 or $\Delta\Delta F^*$ = 77 cal/mole for acetolysis of isopropyl brosylate at 70°, a value substantially lower than our trifluoroacetolysis result of 117 ± 9 cal/mole. This comparison strongly suggests that the acetolysis reaction is less limiting; i.e., it has more nucleophilic solvent participation.

β-Deuterium isotope effects appear to be useful measures of the magnitude of charge development in solvolysis transition states (7). A direct experimental measurement of the acetolysis of an isopropyl-β-d_6 sulfonate is not available. However, a reasonable estimate can be made of the β-isotope effect expected for this case. Acetolysis of 2-pentyl-1,1,1,3,3-$\underline{d}_5$ tosylate gives an isotope effect corresponding to an average $\Delta\Delta F^* = 65$ cal/mole at 65° (9). This result is already lower than our value of 74 cal/mole but Shiner (10) has found methylene hydrogens to contribute a larger isotope effect per hydrogen than methyl hydrogens. If we assume that the same ratio of effectiveness of methyl to methylene hydrogens applies to 2-pentyl tosylate acetolysis as to tert-amyl chloride solvolysis in 80% aqueous ethanol, we calculate the actual $\Delta\Delta F^*/n$ contribution of methyl deuteriums in the former case to be 49 cal/mole. This number is our estimate for the β-deuterium isotope effect for acetolysis of isopropyl tosylate. This estimate is substantially lower than our result for trifluoroacetolysis and supports the contention that the transition state for trifluoroacetolysis has greater carbonium ion character than for acetolysis.

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References

1. P. E. Peterson, R. J. Bopp, D. M. Chevli, E. L. Curran, D. E. Dillard, and R. J. Kamat, *J. Amer. Chem. Soc.*, **89**, 5902 (1967) and preceding papers.
2. J. E. Nordlander and W. G. Deadman, *J. Amer. Chem. Soc.*, **90**, 1590 (1968).
3. D. F. DeTar and C. E. DeTar, *Computer Programs for Chemistry*, Vol. 1, Benjamin, N.Y., in press.
4. P. E. Peterson, R. E. Kelley, Jr., R. Belloli, and K. A. Sipp, *J. Amer. Chem. Soc.*, **87**, 5169 (1965).
5. W. Pritzkow and K. H. Schoeppler, *Chem. Ber.*, **95**, 834 (1962).
6. P. E. Peterson, D. M. Chevli, and K. A. Sipp, *J. Org. Chem.*, **33**, 972 (1968).
7. E. A. Halevi, *Progr. Phys. Org. Chem.*, **1**, 109 (1963); E. R. Thornton, *Solvolysis Mechanisms*, Ronald Press Co., N.Y., 1964, p. 194 ff;

A. Streitwieser, Jr., Solvolytic Displacement Reactions, McGraw-Hill Book Co., N.Y., 1962, pp. 98-101, 172-175; L. Melander, Isotope Effects on Reaction Rates, Ronald Press Co., N.Y., 1960; V. J. Shiner, Jr., W. E. Buddenbaum, B. L. Murr, and G. Lamaty, J. Amer. Chem. Soc., **90**, 418 (1968).

8. K. Mislow, S. Borčić, and V. Prelog, Helv. Chim. Acta, **40**, 2477 (1957).
9. E. S. Lewis and C. E. Boozer, J. Amer. Chem. Soc., **76**, 791 (1954).
10. V. J. Shiner, Jr., J. Amer. Chem. Soc., **75**, 2925 (1953).