Neighboring-Group Study in Solvolyses of Cyclopentyl and Cyclohexyl Tosylates

DONALD D. ROBERTS AND WILLIAM HENDRICKSON[1]

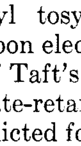
Department of Chemistry, Louisiana Polytechnic Institute, Ruston, Louisiana 71270

Received November 18, 1968

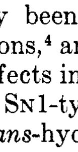
Solvolysis rates of cyclopentyl (**5**-H), cyclohexyl (**6**-H), *trans*-2-trifluoroacetoxycyclopentyl (**5**-OTf), *trans*-2-trifluoroacetoxycyclohexyl (**6**-OTf), *trans*-2-methoxycyclopentyl (**5**-OMe), *trans*-2-methoxycyclohexyl (**6**-OMe), *trans*-2-chlorocyclopentyl (**5**-Cl), and *trans*-2-chlorocyclohexyl (**6**-Cl) tosylates have been determined in acetic, formic, and trifluoroacetic acids. The neighboring trifluoroacetoxy substituent effect upon the rates of solvolysis is sensitive to reaction medium. In contrast, both the neighboring methoxy and chloro substituent effects upon the rates of solvolysis are insensitive to reaction medium. The implications of this solvolytic behavior is discussed in terms of solvent influence upon the opposing participation and inductive effects of the investigated neighboring groups.

The rates of solvolysis of a series of *trans*-2-hydroxycycloalkyl tosylates have recently been reported.[2,3] Based upon electrostatic considerations,[4] and the application of Taft's equation to polar effects in acetolyses,[5] a 10^{-2} rate-retarding influence upon SN1-type reactions was predicted for the neighboring *trans*-hydroxy substituent. Contrary to this expectation, it was found that the order of the expected rate retardation was greatly reduced in aqueous alcohol and acetic acid solvents, and was approached only in formic acid. The solvent dependency of this neighboring-group effect on the reaction rate was rationalized in terms of solvent influence upon the opposing participation and inductive effects of the *trans*-2-hydroxy substituent.

Prompted by these results, we were encouraged to extend this neighboring-group study to other substituents and also to increase the range of solvent ionizing strength.[6] Accordingly, this Article reports the kinetic investigations of the solvolytic reactions of cyclopentyl (**5**-H), *trans*-2-trifluoroacetoxycyclopentyl (**5**-OTf), *trans*-2-methoxycyclopentyl (**5**-OMe), *trans*-2-chlorocyclopentyl (**5**-Cl), cyclohexyl (**6**-H), *trans*-2-trifluoroacetoxycyclohexyl (**6**-OTf), *trans*-2-methoxycyclohexyl (**6**-OMe), and *trans*-2-chlorocyclohexyl (**6**-Cl) tosylates in trifluoroacetic acid. Since the sensitivity of the rates of limiting-type[6] solvolyses to neighboring-group effects is significantly enhanced in trifluoroacetic acid,[7,8] a kinetic investigation of the trifluoroacetolyses of the above compounds is of particular interest in the study of solvent influence upon such effects.



5-H, R = H
5-OTf, R = O_2CCF_3
5-OMe, R = OMe
5-Cl, R = Cl



6-H, R = H
6-OTf, R = O_2CCF_3
6-OMe, R = OMe
6-Cl, R = Cl

The first-order rate constants for the trifluoroacetolysis of **5**-H through **5**-Cl and **6**-H through **6**-Cl are given in Table I. In addition, the rate constants for the formolysis and acetolysis of selected substrates are reported.[9] The solvolysis rates of the reactions in trifluoroacetic and formic acid were measured spectrophotometrically using the method developed by Peterson, *et al.*[10] while the acetolysis reactions were followed titrimetrically.[2] The solvolysis reactions of **6**-OTf in trifluoroacetic acid gave clean first-order plots over only 15% reaction. Absorption curves for longer times showed steadily increasing absorbance indicating the formation of interfering side product(s). The rate constant listed for the trifluoroacetolysis of **6**-OTf is an average of six runs and is considered to be a maximal value. All of the other reactions exhibited first-order behavior through at least 75% conversion. The slower acetolysis reactions were followed to 20–30% conversion.

Results and Discussion

Although the degree of SN1 character for the acetolysis of secondary tosylates may be open to discussion,[7] the evidence supporting a limiting-type solvolysis for secondary tosylates in formic and trifluoroacetic acids is strong.[7,8,10] Previously, it was observed[3] that the values of k_5/k_6, the ratio of solvolysis of **5**-H to that of **6**-H, varied in a series of solvents from 27 (in ethanol) to 8.4 (in formic acid). This decrease in the relative rate (k_5/k_6) with decreasing nucleophilic strength[6] of the solvent was interpreted by a parallel decrease in the nucleophilic contribution of the solvent to the transition state. Consistent with this interpretation is the observation that the values of k_5/k_6 are quite similar in weakly nucleophilic, strongly ionizing[8] formic (8.4) and trifluoroacetic (7.2) acids.

Examination of the k^X/k^H ratios listed in Table II reveals that the neighboring trifluoroacetoxy substituent demonstrates a significant response to the medium change; the rate-retarding inductive effect is 20–30 times greater in trifluoroacetic acid than in acetic acid. Enhancement of the trifluoroacetoxy inductive effect in trifluoroacetolyses relative to acetolyses is in accord with the increased solvent hydrogen-bonding ability of trifluoroacetic acid. This explanation has been ad-

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[1] Undergraduate research assistant.

[2] D. D. Roberts and J. G. Traynham, *J. Org. Chem.*, **32**, 3177 (1967).

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[7] P. E. Peterson, R. J. Ropp, D. M. Chevli, E. L. Curran, D. E. Dillard, and R. J. Kamat, *J. Amer. Chem. Soc.*, **89**, 5902 (1967).

[8] J. E. Nordlander and W. G. Deadman, *ibid.*, **90**, 1590 (1968).

[9] Originally, the trifluoroacetolysis of *trans*-2-hydroxycyclopentyl (**5**-OH) and *trans*-2-hydroxycyclohexyl (**6**-OH) tosylates were included; however, it was found that 70% of **5**-OH was converted into **5**-OTf before 10% of the *p*-toluenesulfonic acid was liberated and that *ca.* 100% of **6**-OH was converted into **6**-OTf before 2% of the acid was liberated.

[10] P. E. Peterson, R. F. Kelley, Jr., R. Belloli, and K. A. Sipp, *ibid.*, **87**, 5169 (1965).

Table I
First-Order Solvolysis Rates

Tosylate[a]	Solvent	Temp, °C	k_1,[b] sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
Cyclopentyl	CF_3CO_2H	0	2.0×10^{-4}	15.6	−18
		10	5.6×10^{-4}		
		15	9.2×10^{-4}		
		20	15.3×10^{-4}		
trans-2-Trifluoro-acetoxycyclopentyl	CF_3CO_2H	50	6.5×10^{-6}		
		70	3.3×10^{-5}		
	HCO_2H	70	1.6×10^{-5}		
	CH_3CO_2H	70	1.8×10^{-6}		
trans-2-Methoxycyclopentyl	CF_3CO_2H	40	3.26×10^{-5}	22.6	−7
		50	10.0×10^{-5}		
		70	84.9×10^{-5}		
	HCO_2H	45	1.9×10^{-5}		
	CH_3CO_2H	45	8.6×10^{-8}		
trans-2-Chlorocyclopentyl	CF_3CO_2H	40	3.38×10^{-5}	15.4	−30
		45	5.0×10^{-5}		
		70	32.0×10^{-5}		
	CH_3CO_2H	70	2.8×10^{-7}		
Cyclohexyl	CF_3CO_2H	25	2.7×10^{-4}	18.5	−13
		30	4.3×10^{-4}		
		40	13.1×10^{-4}		
		45	21.0×10^{-4}		
		50	30.6×10^{-4}		
trans-2-Trifluoro-acetoxycyclohexyl	CF_3CO_2H	45	4.0×10^{-7}		
	HCO_2H	70	28.0×10^{-7}		
	CH_3CO_2H	70	7.2×10^{-8}		
trans-2-Methoxycyclohexyl	CF_3CO_2H	30	4.1×10^{-6}	23.2	−6
		50	58.2×10^{-6}		
		70	434×10^{-6}		
	HCO_2H	45	1.3×10^{-5}		
	CH_3CO_2H	45	2.6×10^{-8}		
trans-2-Chlorocyclohexyl	CF_3CO_2H	40	2.63×10^{-6}	17.9	−28
		50	4.63×10^{-6}		
		70	35.6×10^{-6}		
	CH_3CO_2H	70	1.0×10^{-8}		

[a] Initial concentrations 0.30–0.050 and 0.125 *M* in sodium trifluoroacetate for the trifluoroacetolyses. [b] The standard deviation of these rate constants ranged from ±0.5 to ±4.0%.

Table II
Comparison of Reaction Rates of *trans*-2-X-Cycloalkyl and Cycloalkyl Tosylates in Various Solvents

Solvent	k^X/k^H		
	CF_3CO_2	CH_3O	Cl
Five-Membered-Ring Compounds			
AcOH	0.004[a]	0.004[b]	0.001[a]
HCO_2H	0.0003[a]	0.004[b]	
CF_3CO_2H	0.0003[a]	0.004[b]	0.002[b]
Six-Membered-Ring Compounds			
AcOH	0.003[a]	0.01[b]	0.002[a]
HCO_2H	0.0003[a]	0.02[b]	
CF_3CO_2H	0.0001[b]	0.01[b]	0.002[b]

[a] At 70°. [b] At 45°.

vanced by Peterson[11] to explain the large rate decreases in addition reactions of trifluoroacetic acid to 5-substituted 1-hexenes and by Taft[12] to explain the effects of solvent on the shielding parameter of *meta*-substituted fluorobenzenes with oxygen- and nitrogen-containing substituents.

In contrast to the solvent sensitive effect of the trifluoroacetoxy group in the solvolysis reactions of **5**-OTf and **6**-OTf, the effect of the methoxy neighboring group is insensitive to the solvent change in the solvolysis reactions of **5**-OMe and **6**-OMe. In fact, in all solvents investigated the magnitude of k^{OMe}/k^{H} is close to the predicted[4] value of 10^{-2} based purely on electrostatic considerations. Similarly, the effect of the chloro substituent is nearly insensitive to the medium change; the value of k^{Cl}/k^{H} is *ca.* 10^{-3} in both acetic and trifluoroacetic acids.

Although the substituent–solvent interaction for halo groups is small,[12] an enhanced rate retardation is to be expected for the trifluoroacetolysis of **5**-Cl or **6**-Cl owing to enhanced charge development in the transition state.[13] The fact that the substituent effect is invariant with the solvent change suggests that the predominantly rate-retarding inductive effect of the chloro group is partially compensated by neighboring-group assistance in trifluoroacetic acid and to a much lesser extent in formic acid. This suggestion is supported by the demonstrated ability of trifluoroacetic acid to promote both significant phenyl neighboring-group assistance in the solvolysis of 2-phenylethyl tosylate[8] and significant participation by the chloro group in the solvolysis of 5-chloro-2-hexyl tosylate.[7]

The apparent lack of solvent dependence of the methoxy neighboring-group effect is also understandable

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[11] P. E. Peterson and G. Allen, *J. Amer. Chem. Soc.*, **85**, 3608 (1963).

[12] R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davis, *ibid.*, **85**, 709 (1963).

[13] This argument is based on a generally accepted postulate of carbonium ion theory, *i.e.*, the faster an SN1-type reaction, the more ionic its transition state. For a recent discussion, see H. M. R. Hoffmann, *J. Chem. Soc.*, 6762 (1965).

in terms of a predominantly rate-retarding inductive effect partially compensated by methoxy participation in the ionization process; however, supperimposed on these effects is the possible presence of steric inhibition of solvation. Examination of the models of the carbonium ionlike transition state for the solvolysis of **5**-OMe and **6**-OMe suggests that steric interactions between the methoxy substituent and the ring hydrogens are minimized when the methoxy group is twisted out of the ring as illustrated in Figure 1. In the representation for **6**-OMe, the methoxy substituent is pictured in the stereoelectronically more favorable axial position.[14] In these particular conformations, hydrogen bonding of the methoxy group by the solvent molecules would introduce sufficient steric crowding to minimize the difference in hydrogen-bonding ability among the three solvents.

Experimental Section

Melting and boiling points were not corrected for stem exposure. The former were taken on a Mel-Temp apparatus. Spectra were determined on a Perkin-Elmer Model 21 spectrophotometer. An F & M Model 700 gas chromatograph equipped with a hydrogen-flame detector and a 6-ft column of 10% Carbowax 20M on Celite was used for analytical vpc work. All microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

Cyclopentyl tosylate (**5**-H) was prepared in 55% yield by the previously published procedure,[3] mp 29.0–29.5° (lit.[15] mp 29.1°).

***trans*-2-Methoxycyclopentanol.**—A mixture of 21.0 g (0.25 mol) of cyclopentene oxide, 100 ml of anhydrous methanol, and 2 drops of concentrated sulfuric acid was held under reflux for 8 hr. The acid was then neutralized with barium carbonate and the mixture filtered. Distillation of the filtrate gave 11.5 g (40% yield) of product: bp 80° (10 mm); $n^{25}\text{D}$ 1.4515 [lit.[16] bp 96° (27 mm); $n^{25.2}\text{D}$ 1.4513]. Gc analysis indicated minimum purity of 99%.

***trans*-2-Methoxycyclopentyl tosylate** (**5**–OMe) was prepared in 60% yield by standard procedure.[3] The crude ester was purified three times by precipitation from petroleum ether (bp 30–60°) at Dry Ice–acetone temperature. The final traces of solvent were removed by flash distillation under reduced pressure (*ca.* 0.1 mm) to yield an oil of greater than 97% purity by infinity absorbance: ir (neat), 1335 (ν_{SO_2} asymmetric), 1165 (ν_{SO_2} symmetric), and 1090 cm^{-1} (ether COC).

***trans*-2-Chlorocyclopentanol** was prepared in 80% yield by passing dry HCl into a solution of 150 g of cyclopentene oxide in 150 ml of carbon tetrachloride until the solution was saturated. The solution was then washed with water, sodium bicarbonate solution, and water, dried over magnesium sulfate, and distilled to give the product: bp 81–82° (15 mm); $n^{25}\text{D}$ 1.4775 [lit.[17] bp 81–82° (15 mm); $n^{35}\text{D}$ 1.4770].

***trans*-2-Chlorocyclopentyl tosylate** (**5**-Cl) was prepared in 72% yield by standard procedure.[3] Four recrystallizations from petroleum ether (bp 30–60°)-benzene gave the analytical sample of the ester, mp 38–39°.

Anal. Calcd for $C_{12}H_{15}ClO_3S$: C, 52.46; H, 5.50; Cl, 12.90. Found: C, 52.65; H, 5.54; Cl, 13.09.

***trans*-2-Trifluoroacetorycyclopentyl Tosylate** (**5**-OTf).—To a cold solution of *trans*-2-hydroxycyclopentyl tosylate[3] (2 g, 7.5 mmol) in 10 ml of dry pyridine was cautiously added 1.32 g (10 mmol) of trifluoroacetyl chloride.

After standing 20 hr at room temperature, the mixture was hydrolyzed by the addition of cold, dilute HCl. The precipitated oil was taken up in 40 ml of methylene chloride, washed once with cold, dilute HCl, once with water, once with cold sodium bicarbonate solution, once with water, dried over anhydrous Na_2SO_4, and the solvent removed by rotary evaporation to yield 2 g (76% yield) of an oil which solidified upon standing several hours. Two recrystallizations from petroleum ether (bp 30–60°)-ethyl acetate yielded the analytical sample, mp 44–45°.

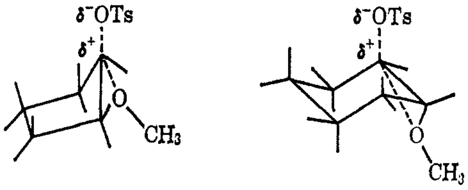

Figure 1.

Anal. Calcd for $C_{14}H_{15}F_3O_5S$: C, 47.72; H, 4.29; F, 16.18. Found: C, 47.96; H, 4.26; F, 16.11.

Cyclohexyl tosylate (**6**-H) was prepared in 75% yield by the previously published procedure,[3] mp 44.0–44.8° (lit.[18] mp 44.4–44.8°).

***trans*-2-Methoxycyclohexanol** was prepared in 50% yield by the method described for *trans*-2-methoxycyclopentanol: bp 72–73° (10 mm); $n^{25}\text{D}$ 1.4578 [lit.[19] bp 72.5–73.2° (10 mm); $n^{25}\text{D}$ 1.4586]. Treatment of a portion of the alcohol with 3,5-dinitrobenzoyl chloride in pyridine yielded *trans*-2-methoxycyclohexyl 3,5-dinitrobenzoate, mp 101–101.5° (lit.[19] mp 101°).

***trans*-2-Methoxycyclohexyl tosylate** (**6**-OME) was prepared in 62% yield by standard procedure.[3] The crude ester was purified three times by precipitation from petroleum ether (bp 30–60°) at Dry Ice–acetone temperature. The final traces of solvent were removed by flash distillation under reduced pressure (*ca.* 0.1 mm) to yield an oil of greater than 97% purity by infinity absorbance: ir (neat) 1335 (ν_{SO_2} asymmetric), 1163 (ν_{SO_2} symmetric), and 1090 cm^{-1} (ether COC).

***trans*-2-Chlorocyclohexanol** was prepared in 80% yield by the method described for *trans*-2-chlorocyclopentanol, bp 70–71° (7 mm) [lit.[20] bp 71° (7 mm)]. Gc analysis indicated minimum purity of 99%.

***trans*-2-Chlorocyclohexyl tosylate** (**6**-Cl) was prepared in 78% yield by standard procedure.[3] Four recrystallizations from petroleum ether (bp 30–60°)-benzene gave the analytical sample of the ester, mp 50–51°.

Anal. Calcd for $C_{13}H_{17}ClO_3S$: C, 54.07; H, 5.93; Cl, 12.28. Found: C, 53.82; H, 5.74; Cl, 12.49.

***trans*-2-Trifluoroacetorycyclohexyl tosylate** (**6**-OTf) was prepared in 80% yield by the method described for **5**-OTf: mp 83–84° [after three recrystallizations from petroleum ether (bp 30–60°)-ethyl acetate].

Anal. Calcd for $C_{15}H_{17}F_3O_5S$: C, 49.17; H, 4.68; F, 15.56. Found: C, 49.22; H, 4.56; F, 15.80.

Registry No.—**5**-H, 3558-06-3; **5**-OTf, 19990-19-3; **5**-OMe, 19990-12-6; **5**-Cl, 19990-13-7; **6**-H, 953-91-3; **6**-OTf, 19990-15-9; **6**-OMe, 19990-16-0; **6**-Cl, 19990-17-1.

Acknowledgment.—Grateful acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society. The authors also gratefully acknowledge the valuable comments of Dr. Paul E. Peterson of Saint Louis University who assisted in both the direction and interpretation of the work.

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