

Solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides

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The rates of solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides [I] in a variety of solvents were measured by an electroconductometric method. LArSR relationships (Yukawa-Tsuno eq.) were found to give a linear plot, $\log(k/k_0) = -1.84[\sigma^+ + 0.918(\sigma^+ - \sigma^*)]$, in 80% aqueous ethanol. Small $|\rho|$ and r values in comparison with 1-aryl-1-(trifluoromethyl)ethyl tosylate ($\rho = -6.09$, $r = 1.59$) suggested that the carbocationic charge in the transition state was dispersed by a strong p - π donor, p -methoxy group. Linear mY plots with $m \approx 0.90$ for all of the substituents in aqueous acetone and $m = 0.60$ - 0.82 for those of aqueous ethanol indicate that this solvolysis proceeds *via* an S_N1 mechanism with nucleophilic solvent assistance. Thiourea effects and isokinetic temperatures for the rate of solvolysis also can prove the above mechanism.

Introduction

Since 1980, the interaction of an electron-withdrawing α -substituent with carbonium ion center developed in ionic reactions has been studied with important subject.¹⁻³ Solvolysis of systems containing α -trifluoromethyl and α -aryl group has been extensively studied by Liu,¹ Tsuno² and Tidwell.³ Liu^{1a} reported the solvolysis of 1-aryl-1-(trifluoromethyl)ethyl tosylates in which the $\sigma^+ \rho$ treatment gave two lines, one for activating substituents with a ρ value of -8.82 and the other for deactivating substituents with a ρ value of -6.40 . From these results, the author concluded that the carbonium ion intermediate of this compound has a high electron demand and the break in the $\sigma^+ \rho$ plot suggests a change of mechanism.

Nevertheless, Liu *et al.*^{1b} later noted that the solvolysis rates of 1-aryl-1-(trifluoromethyl)ethyl tosylates gave a straight line in the Hammett-Brown plots. The rate-retarding effect of the α -trifluoromethyl group is so large that the reaction constant had a highly negative value, -7.46 . It reveals that the reaction center has a very high electron demand.

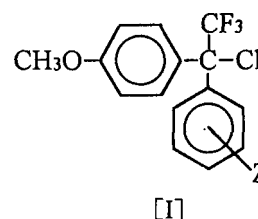
On the other hand, the application of the Yukawa-Tsuno equation of this reaction can also be correlated with a high r value of 1.59 and value of -6.09 . The authors suggested that the carbonium ion intermediate have very high electron demand and nucleophilic solvent assistance in the transition state.

In a recent study, The solvolyses of 1-aryl-1-phenyl-2,2,2-trifluoroethyl bromides, 1-aryl-1-(4-phenoxyphenyl)-2,2,2-trifluoroethyl bromides, and 1-aryl-1-(4-phenoxyphenyl)-2,2,2-trifluoroethyl chlorides were carried by Liu and his coworkers^{1c} in a variety of solvents. The treatment of the rate data with both Yukawa-Tsuno and Hammett-Brown equations resulted in good to excellent linear relationships and the inverse orders of reactivities, $k_{(p-CF_3)}/k_{(m-CF_3)} > 1$, were obtained for all three substances in different solvents.

Recently, Tsuno and his coworkers^{2b} reported the rates of solvolysis of 1-aryl-1-(trifluoromethyl)ethyl tosylates in 80 % aqueous ethanol for a series of substituents. The Ham-

mett-Brown treatment fails to give a simple linear plot, but all the p - π -donors deviate upward from the m -correlation line. On the other hand, Yukawa-Tsuno LArSR Eq. gives a linear correlation over the whole range of substituents, $\log(k/k_0) = -6.29[\sigma^+ + 1.39(\sigma^+ - \sigma^*)]$, with excellent precision. Strong destabilization of the carbocation intermediate by α -CF₃ appears to be reflected only in the extremely high r value.

In the present paper, we prepared 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides containing a strongly activating 4-methoxyphenyl group as shown in [I], and we now wish to report the results of the solvolysis and thiourea effect of this compound.



From those kinetic results, we attempt to compare with mechanistic shift of this compound and other deactivating compounds. And also we describe a useful probe for a solvolysis mechanism using the neutral nucleophile thiourea for which confusing salt effects are absent and solvent effects are small.

Result and Discussion

General Approach and Hammett plot. The first-order rate constants of the solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides were measured by electroconductometric method in aqueous ethanols and acetones. As shown in Tables 1 and 2, the electron-donating substituents facilitates the reaction, indicating the positive charge development at the reaction center containing an α -CF₃ group.

Aqueous ethanols are much stronger nucleophilic solvent than aqueous acetones. As a consequence, solvolysis reac-

Table 1. Rate Constants for Solvolysis of 1-(4-Methoxyphenyl)-aryl-2,2,2-trifluoroethyl Chlorides in Aqueous Acetone at Various Temperature

Substituents	Aq. Acetone (Vol.%)	$10^4 k, \text{sec}^{-1}$					
		25 °C	35 °C	45 °C	55 °C	65 °C	75 °C
4-MeO-3-Cl	80	0.528	1.49	3.47	7.90		
4-CH ₃	90	0.0170	0.0410	1.17*	0.571		
	80	0.179	0.541	1.60*	4.37		
	70	1.00	2.84	7.10*	17.0		
	60	4.22	11.1	24.1*	51.3		
	50	14.6	42.1	78.0*	151		
3-CH ₃	90	0.0110*		0.0670	0.247	0.369	
	80	0.0810	0.300	0.864*	2.42		
	70	0.437	1.47	4.05*	10.8		
	60	1.75	5.72	13.5*	31.9		
	50	7.34	20.9	45.9*	100		
H	90	0.00700*		0.0580	0.216	0.392	
	80	0.0660		0.575*	2.12		6.04
	70	0.354	2.77	9.10*		28.0	
	60	1.57		9.62*	26.0		79.0
	50	6.63		42.0	91.8		
4-CF ₃	80	0.0850*		0.294	0.421	0.837	
	70	0.0620	0.204	0.673*	2.03		
	60	0.261		2.16*	7.50		22.2
	50	1.07		7.23*	20.6		66.2
	40	2.69*	8.27	24.4	64.4		
3-CF ₃	80	0.0130*	0.0330	0.110*	0.419		1.43
	70	0.0830*	0.204	0.607*	1.97		6.74
	60	0.260		2.12*	7.34		21.5
	50	1.04		7.12*	23.1		56.5
	40	3.38	10.3	25.7*	62.2		

*: Extrapolated values from the data at other temperatures.

Table 2. Rate Constants for Solvolysis of 1-(4-Methoxyphenyl)-aryl-2,2,2-trifluoroethyl Chlorides in Aqueous Ethanol

Substituents	Aq. Ethanol (Vol.%)	$10^4 k, \text{sec}^{-1}$					
		25 °C	35 °C	45 °C	55 °C	65 °C	75 °C
4-MeO-3-Cl	80	3.93	6.75	18.1*	40.8		
4-CH ₃	90	0.600	1.84	4.61*	11.3		
	80	2.35	7.12	14.9*	31.9		
3-CH ₃	70	5.51	15.1	33.1*	71.8		
	90	0.256	0.896	2.25*	6.43		
	80	0.960	3.55	8.80*	22.2		
H	70	3.24*	8.79	24.0*	55.6		
	90	0.187		1.59*	4.54	22.2	
	80	0.764		6.05*	16.8	77.4	
4-CF ₃	70				44.1		
	90	0.0380*		0.295	0.769	1.68	4.19
	80	0.119		1.19*	3.49		21.6
3-CF ₃	70	0.345*	1.17	3.59	10.6		
	90	0.0460*		0.301*	0.721	1.54	3.46
	80	0.0890		0.857*	2.90		12.2
70	0.302*	0.827	2.58*	8.45		36.3	

*: Extrapolated values from the data at other temperatures.

tions proceeding with nucleophilic solvent assistance in aqueous ethanols show larger rate constants than that of aqueous acetones, since the large hydrogen bonding effects

in aqueous ethanols stabilize the transition state in this solvolysis reaction.

The Hammett-Brown treatment of the solvolytic rate cons-

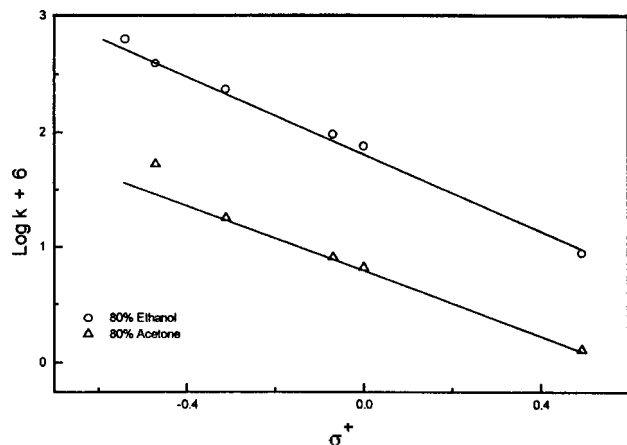


Figure 1. The Hammett-Brown treatment ($\rho = -1.74$, $R = 0.998$ in ethanol and $\rho = -1.60$, $R = 0.989$ in acetone) for the solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides in 80% ethanol and 80% acetone at 25 °C.

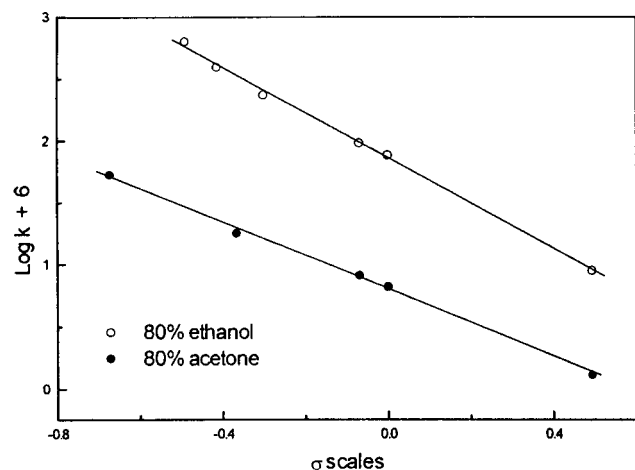


Figure 2. The Yukawa-Tsuno treatment ($\rho = -1.84$, $r = 0.918$, $R = 0.999$ in ethanol and $\rho = -1.36$, $r = 1.29$, $R = 0.999$ in acetone) for the solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides in 80% ethanol and acetone at 25 °C.

Table 3. Substituent parameters

Substituents	σ^o	σ^+	$\Delta\sigma_R^+$
4-methoxy	-0.100	-0.800	-0.700
4-methoxy-3-chloro	0.220	-0.470	-0.690
4-methyl	-0.124	-0.311	-0.187
3-methyl	-0.069	0	0
H	0	0	0
4-trifluoromethyl	0.505	0	0
3-trifluoromethyl	0.493	0	0

tant of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides in 80% aqueous ethanol and acetone displays a non-linear correlation as shown in Figure 1. But, the Yukawa-Tsuno LArSR Eq. gives a linear correlation $\log(k/k_o) = -1.84[\sigma^o + 0.918(\sigma^+ - \sigma^o)]$ in 80% aqueous ethanol with excellent preci-

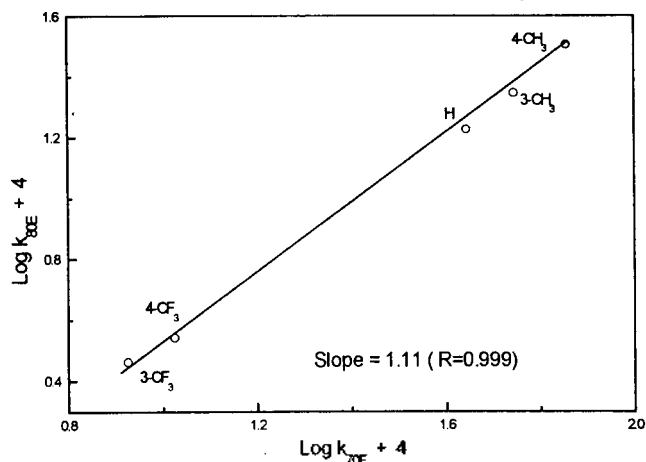


Figure 3. Log-log plot between the solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides in 80% and 70% ethanol at 55 °C.

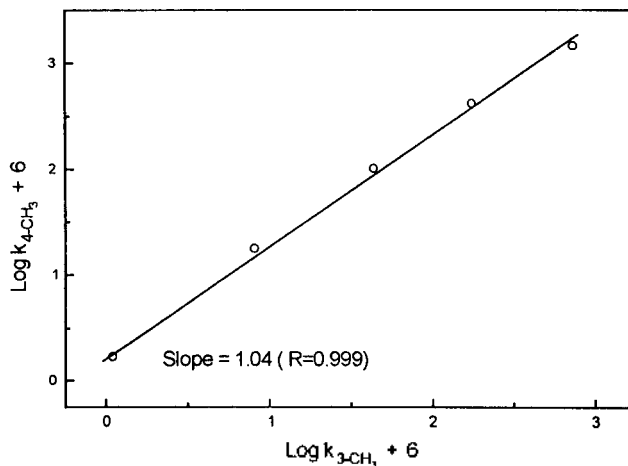


Figure 4. Log-log plot between the solvolysis of 1-(4-methoxyphenyl)-1-(4-methylphenyl)-2,2,2-trifluoroethyl chloride and 1-(4-methoxyphenyl)-1-(3-methylphenyl)-2,2,2-trifluoroethyl chloride in aq. acetones at 25 °C.

sion in Figure 2. Especially, small $|\rho|$ value (ρ^+ of H-B, ρ of Y-T Eq.) and r value for the solvolysis of compounds [I] in comparison with 1-aryl-1-(trifluoromethyl)ethyl tosylates^{1a} suggested that strongly destabilized carbocation intermediate by α -CF₃ group was stabilized by strong p - π -donor, p -methoxyphenyl group. The substituent parameters (σ^o , $\Delta\sigma_R^+$, and σ^+) employed in the present analysis are given in Table 3.

The logarithmic rate plot of 80E vs. 70E for the whole substituent range gives a linear correlation with slope of 1.12 without significant deviation as shown in Figure 3. The logarithmic rate comparison of the isomer of I_{3CH_3} with I_{4CH_3} shows also a linear correlation as shown in Figure 4. These are suggested that any mechanistic shift in solvolysis of this system was not observed for changes of ethanol % and substituents.

The mechanism of unimolecular solvolysis reactions can be effectively predicted by the use of the Grunwald-Winstein

Table 4. m_{AW} and m_{EW} Values for 1-(4-Methoxyphenyl)-aryl-2,2,2-trifluoroethyl Chlorides in Aqueous Acetone and Ethanol Solvents at 25 °C

Substituents	m_{AW}		m_{EW}	
	Y_{t-BuCl}	Y_{1-AdCl}	Y_{t-BuCl}	Y_{1-AdCl}
4-CH ₃	0.91	0.76	0.72	0.57
3-CH ₃	0.87	0.77	0.82	0.65
H	0.91	0.79		
4-CF ₃	0.90	0.73	0.71	0.56
3-CF ₃	0.90	0.71	0.60	0.48

equation (1).⁴ In equation (1), k and k_0 are the rate constant of solvolysis in any solvent and 80% v/v ethanol/water, respectively. The m value is a measure of the sensitivity of the specific rate of solvolysis of the substrate under investigation to changes in the Y value, defined by $m=1$ for solvolysis of tert-butyl chloride at 25 °C.

$$\log(k/k_0) = mY \quad (1)$$

The Y scale based on the solvolysis of tert-butyl chloride has been shown to contain a component based on the nucleophilic characteristics of the solvent. It has been recommended that this component be eliminated by choosing as the standard substrate 1-adamantyl chloride or 2-adamantyl tosylate. Bentley *et al.*⁵ defined a scale of solvent ionizing power for chlorides (designated Y_{Cl}) by equation (2), with R_{Cl} referring to 1-adamantyl chloride ($m=1$),

$$\log(k/k_0)_{R_{Cl}} = mY_{Cl} \quad (2)$$

where k and k_0 are the same as in equation (1).

Solvolysis rates of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides were determined in a wide variety of solvents and the solvent effects were analyzed by the Grunwald-Winstein equation (1). The results of correlation analysis using Equations (1) and (2) are listed in Table 4.

The plots of logarithm of Y and Y_{Cl} vs. solvolytic rate constants of compound I_{4-CH_3} in aqueous acetone and aqueous ethanol were divided into two lines in which upper line represents the nucleophilic solvent assistance during the solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides. General trend, the m_{AW} values for aqueous acetone (the range of 0.71-0.91) are larger than those of aqueous ethanol in which m_{EW} values are in the range of 0.48-0.82. This suggests that nucleophilic solvent assistance is more significant for the reaction in aqueous ethanol. Consequently, the correlation coefficients are not so good in aqueous ethanol, especially electron withdrawing groups. For aqueous acetone series, the m_{AW} values by using Equation (1) and (2) are constant of ca. 0.9 and 0.71-0.79, and independent on the substituent change.

The large and constant m_{AW} values covering all substituents indicate that carbocationic intermediate was produced in the solvolysis of compound [I] as in the solvolysis of tert-butyl chloride and 1-adamantyl chloride. On the other hand, the m_{EW} values vary in the range of 0.60-0.82 and 0.48-0.65 based on Y and Y_{Cl} scale. These results support that the solvolysis mechanism of compound [I] proceeds *via*

Table 5. Effect of Thiourea Addition on Solvolysis Rate of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl Chlorides in 80% Acetone and 80% Ethanol at 55 °C

Solvents	Substituents	Thiourea, mol/L			k_N/k_{sol}
		0	0.04	0.1	
80% Acetone	4-CH ₃	4.36	4.52	7.52	7.55
	3-CH ₃	2.42	2.57	3.14	3.05
	H	2.12	2.23	2.81	3.41
	4-CF ₃	0.42	0.43	0.58	3.84
	3-CF ₃	0.42	0.43	0.67	6.28
80% Ethanol	4-CH ₃	31.9	37.8	45.8	4.33
	3-CH ₃	22.2	27.6	29.9	3.41
	H	16.8	21.0	23.1	3.61
	4-CF ₃	3.49	3.92	4.58	3.13
	3-CF ₃	2.90	3.45	3.91	3.42

a carbonium ion intermediate.; that is, The solvolysis reaction of compound [I] represents S_N1 mechanism, in which the character of carbonium ion in aqueous acetone is larger than aqueous ethanol.

Thiourea effect. McManus and his coworkers⁶ reported that kinetic effects of the neutral thiourea is a useful probe in elucidating a solvolysis mechanism since the neutral thiourea can eliminate the complexities arising from a kind of salt effect. The rates constants for the solvolysis of compound [I] in the presence or absence of thiourea were measured by an electroconductometric method in 80% ethanol and 80% acetone, respectively. The concentration of thiourea was in the range of 0.04 and 0.1 mol/L at the initial substrate concentration of ca. 10^{-4} mol/L. The observed rate constants (k_{obs}) in the presence of thiourea were a little larger than the one in the absence of thiourea as shown in Table 5.

Thiourea had a slight rate-retarding effect⁶ in the solvolysis of 1-adamantyl bromide. This rate retardation might be caused by a slight reduction in ionizing power of the medium. To the contrary, salts are known to cause rate accelerations by specific solvation and by increasing the ionic strength of the medium.^{7,8}

In this work, we found a linear kinetic response to thiourea concentration. Thus, the effect of thiourea on the observed rate can be described by Equation (3),⁶ where k_N is the second-order rate constant for the reaction of thiourea addition and $[Nu]$ is the molarity of added thiourea.

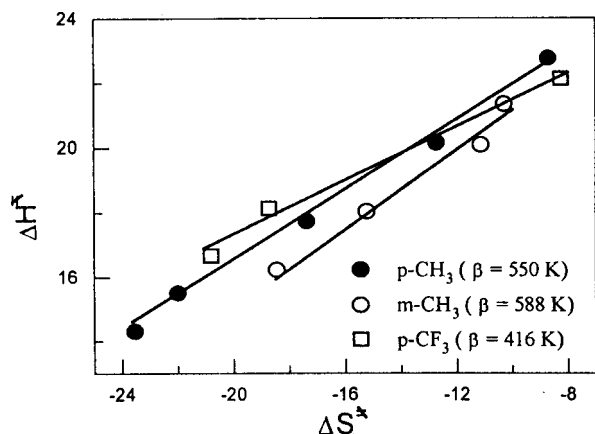
$$k_{obs} = k_{sol} + k_N[Nu] \quad (3)$$

From the plots of k_{obs} against concentration of thiourea, we can get the value of k_N/k_{sol} . This value is the susceptibility of substrates to nucleophilic attack by the added thiourea.

The k_N/k_{sol} values⁶ for the solvolysis of 1-adamantyl bromide, 2-octylmesylate, ethyl tosylate and methyl tosylate are -0.390, 18.3, 31.1 and 43.6, respectively. From the above results, we can see that the k_N/k_{sol} values is increasing with increasing S_N2 character. Consequently, the kinetic effects of added thiourea might be a useful probe for elucidating the reaction mechanism between S_N1 and S_N2 type reactions. In the 80E and 80A, the values of k_N/k_{sol} of the solvolysis

Table 6. The Activation Parameters for the Solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl Chlorides in Aqueous Ethanol and Acetone

Substituents	Ethanol			Acetone		
	Solv.	ΔH^\ddagger (kcal/mol)	ΔS^\ddagger (e.u.)	Solv.	ΔH^\ddagger (kcal/mol)	ΔS^\ddagger (e.u.)
4-CH ₃	90E	18.32	-16.41	90A	22.75	-8.69
	80E	16.08	-21.19	80A	20.14	-12.72
	70E	15.93	-20.02	70A	17.73	-17.37
				60A	15.50	-22.00
				50A	14.30	-23.55
3-CH ₃	90E	20.17	-11.91	80A	21.34	-10.29
	80E	19.53	-11.43	70A	20.08	-11.12
				60A	18.04	-15.22
				50A	16.23	-18.45
H	90E	19.23	-15.69	80A	18.51	-20.19
	80E	18.57	-15.08	70A	17.78	-19.27
				60A	15.81	-22.91
				50A	16.51	-17.72
4-CF ₃	80E	20.17	-13.43	70A	22.11	-8.24
				60A	18.13	-18.72
				50A	16.67	-20.80
3-CF ₃	80E	19.97	-14.66	60A	18.03	-19.06
	70E	19.64	-13.36	50A	16.30	-22.08
				40A	18.18	-13.45

**Figure 5.** Plots of ΔH^\ddagger vs. ΔS^\ddagger for the solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chloride in aqueous acetone.

of compound [I] are in the range of 3.05-7.55 as shown in Table 5.

Therefore, we can predict that the solvolysis of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl chlorides in aqueous ethanol and aqueous acetone favors the S_N1 reaction with nucleophilic solvent assistance.

Isokinetic relationship. It has often been found that a linear relationship¹¹ exists between the enthalpies and entropies of activation for a series of related reactions as shown in (4).

$$\Delta\Delta H^\ddagger = \beta\Delta\Delta S^\ddagger \quad (4)$$

The constant β has the dimensions of temperature and is

actual or virtual temperature at which rates of all members of the series are equal, the isokinetic temperature. A plot of ΔH^\ddagger vs. ΔS^\ddagger for the solvolysis reactions yielded good correlation line with an isokinetic temperature of 550 K, 558 K and 416 K for 4-CH₃, 3-CH₃, and 4-CF₃ compounds in aqueous acetone as shown in Table 6 and Figure 5.

Since the above β values are below the experimental temperature, this solvolysis reaction is controlled by activation enthalpy. This results support that the solvolysis reaction of compound I represents S_N1 character.

Experimental section

General remarks. NMR spectra were recorded on a Bruker AM-300 Spectrometer with TMS as an internal standard. Mass spectral analysis was obtained with HP 5890 series II GC/5970 instrument. Purities of synthetic materials were investigated with a Varian 3300 gas chromatography. For the isolation and identification of synthetic materials were used silica gel and Art 5554 DC-Alufolien Kieselgel 60 F₂₅₄ from Merck.

Materials. Acetone and ethanol for the kinetic studies were used reagent grade of Merck and purified according to standard procedures.^{9a,b} Water for kinetics was obtained by distilling deionized water twice after oxidation by KMnO₄.^{9c} For diethylether, after drying with metal sodium, it was refluxed over benzophenone (10 g) for 30 hours until the color of the solution appears blue and distilled.

Reagents for the preparation of alcohols, which were obtained from commercial sources were used without purification; trifluoroacetic acid from Junsei, magnesium turning, *p*-bromoanisole, *p*-bromotoluene, bromobenzene, *p*-bromobenzotrifluoride, *m*-bromobenzotrifluoride from Aldrich.

Ethyl trifluoroacetate. 14.1 mL (0.241 mole) of ethanol was added into 16.7 mL (0.219 mole) of trifluoroacetic acid at 0 °C and 13.5 mL (0.241 mole) of 95%-H₂SO₄ was added to the above mixture in small portions carefully with swirling. The mixture was allowed to cool and heated the mixture to reflux for 1 hour. The crude ester was fractionated: bp 60-61 °C (lit.^{9d} bp 60-62 °C)

4-methoxy- α,α,α -trifluoroacetophenone. (CH₃OC₆H₄COCF₃) According to an ordinary method,^{9e} 4-methoxyphenylmagnesium bromide was prepared by slow addition of 18.7 g (0.100 mole) of 4-bromoanisole dissolved in 20 mL of anhydrous ether into 2.67 g (0.110 mole) of magnesium turning in 20 mL anhydrous ether. The Grignard reagent was added dropwise to a stirred solution of ethyl trifluoroacetate (14.207 g, 0.1 mole) in 20 mL anhydrous ether under nitrogen at the dry-ice-acetone temperature. The stirring of reaction mixture was continued for 2 hours at room temperature. The reaction mixture was treated with 10% NH₄Cl solution, and then extracted three times with ether. The extract was washed, neutralized with 10% NaHCO₃ solution, and dried with anhydrous MgSO₄. 4-methoxy- α,α,α -trifluoroacetophenone was isolated by distillation (Yield 23%).

: NMR (300 MHz, CDCl₃); δ 3.78 (3H, s, OCH₃), 6.70-7.0 (4H, m, Ar)

1-(4-methoxyphenyl)-1-(4-methylphenyl)-2,2,2-trifluoroethanol. Grignard reagent made from the reaction of 4-bromotoluene (7 g, 0.04 mole) with magnesium turning (1.2 g, 0.05 mole) was added dropwise into a stirred solution

Table 7. NMR and Mass Spectral Data of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethanols

Substituents	(¹ H) NMR, δ (ppm)	Mass, m/e
4-CH ₃	2.23 (s, 3H, CH ₃)	296 (M ⁻)
	3.53 (s, 1H, OH)	227 (M ⁺ -CF ₃)
	3.57 (s, 3H, OCH ₃)	
	6.70-7.46 (m, 8H, Ar)	
3-CH ₃	2.20 (s, 3H, CH ₃)	296 (M ⁺)
	3.52 (s, 3H, OCH ₃)	227 (M ⁺ -CF ₃)
	3.69 (s, 1H, OH)	
	6.69-7.52 (m, 8H, Ar)	
H	3.51 (s, 3H, OCH ₃)	282 (M ⁻)
	3.67 (s, 1H, OH)	213 (M ⁺ -CF ₃)
	6.65-7.72 (m, 9H, Ar)	
4-CF ₃	3.56 (s, 3H, OCH ₃)	350 (M ⁺)
	3.85 (s, 1H, OH)	281 (M ⁺ -CF ₃)
	6.71-7.69 (m, 8H, Ar)	
3-CF ₃	3.58 (s, 3H, OCH ₃)	350 (M ⁻)
	4.04 (s, 1H, OH)	281 (M ⁺ -CF ₃)
	6.74-7.99 (m, 8H, Ar)	

Table 8. NMR and Mass Spectral Data of 1-(4-methoxyphenyl)-1-aryl-2,2,2-trifluoroethyl Chlorides

Substituents	(¹ H) NMR, δ (ppm)	Mass, m/e
4-CH ₃	2.45 (s, 3H, CH ₃)	316 (M+2)
	3.78 (s, 3H, OCH ₃)	314 (M ⁺)
	6.80-7.43 (m, 8H, Ar)	279 (M ⁺ -Cl)
3-CH ₃	2.43 (s, 3H, CH ₃)	316 (M+2)
	3.80 (s, 3H, OCH ₃)	314 (M ⁺)
	6.83-7.50 (m, 8H, Ar)	279 (M ⁺ -Cl)
H	3.81 (s, 3H, OCH ₃)	302 (M+2)
	6.84-7.52 (m, 9H, Ar)	300 (M ⁺)
		265 (M ⁺ -Cl)
4-CF ₃	3.82 (s, 3H, OCH ₃)	370 (M+2)
	6.87-7.68 (m, 8H, Ar)	368 (M ⁺)
		333 (M ⁺ -Cl)
3-CF ₃	3.81 (s, 3H, OCH ₃)	370 (M+2)
	6.85-7.82 (m, 8H, Ar)	368 (M ⁺)
		333 (M ⁺ -Cl)

of 4-methoxy- α,α,α -trifluoroacetophenone (8.35 g, 0.04 mole) in 15 mL of anhydrous ether under nitrogen at 0 °C and stirred for 2 hours at room temperature. The reaction mixture was hydrolyzed, extracted, and dried as in the above procedures. Extracted alcohol was identified with TLC and separated with silicagel column.

¹H NMR and Mass spectral data of all alcohols are listed in Table 7.

1-(4-methoxyphenyl)-1-(4-methylphenyl)-2,2,2-trif-

luoroethyl chloride. The chlorination of tertiary alcohols proceeded with thionyl chloride to give the chlorides (80-95% yield). The chloride compound was monitored by TLC and separated by column chromatography (benzene : hexane = 1 : 1).

¹H NMR and Mass spectral data are listed in Table 8.

Kinetics. Solvolysis rates were measured by an electroconductometric method.^{9a} Conductance measurement were made in a cell with platinum electrodes using approximately a 25 cm³ solution at an initial concentration of 10⁻⁴ mol/L of substrate. Conductivity readings were taken by using a conductivity meter (CM-60S equipped with time interval unit and printer, TOA Electric Ltd.). All solvolysis reaction were followed by taking at least 40 points for three half-lives and an infinity reading was taken after 10 half-lives. The first-order rate constants were determined by least squares computer program and gave excellent first-order behavior with correlation coefficient of greater than 0.999. Arrhenius plots of rate data obtained at 35, 55, 65 and 75 °C were used to estimate rate constant at 25 °C.

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References

- (a) Liu, K.-T.; Sheu, C.-F. *Tetrahedron Letters* **1980**, *21*, 4091. (b) Liu, K.-T.; Kuo, M.-Y.; Shu, C.-F. *J. Am. Chem. Soc.* **1982**, *104*, 211. (c) Liu, K.-T.; Kuo, M.-Y. *J. Chem. Soc., Chem. Commun.* **1987**, 640. (d) Liu, K.-T.; Sheu, C.-F. *J. Org. Chem.* **1991**, *56*, 3021. (e) Liu, K.-T.; Chang, S.-M.; Chen, H.-I.; Chiu, P.-F.; Wu, T.-R. *J. Org. Chem.* **1991**, *56*, 1315.
- (a) Fujiyama, R.; Kamimura, I.; Yoshida, M.; Suzuki, K.; Kiyooka, S.; Murata, A.; Goto, M.; Fujio, M.; Tsuno, Y. *Chem. Lett.* **1987**, 1043. (b) Murata, A.; Goto, M.; Fujiyama, R.; Mishima, M.; Fujio, M.; Tsuno, Y. *ibid.* **1990**, *63*, 1129. (c) Murata, A.; Sakaguchi, S.-I.; Fujiyama, R.; Mishima, M.; Fujio, M.; Tsuno, Y. *ibid.* **1990**, *63*, 1137.
- (a) Gassman, P. G.; Tidwell, T. T. *Acc. Chem. Res.* **1983**, *16*, 279. (b) Tidwell, T. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 20. (c) Allen, A. D.; Jansen, M. P.; Koshy, K. M.; Mangru, N. N.; Tidwell, T. T. *J. Am. Chem. Soc.* **1982**, *104*, 207.
- (a) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc.* **1948**, *70*, 846. (b) Fainberg, A. H.; Winstein, S. *ibid.* **1956**, *78*, 2770. (c) Winstein, S.; Grunwald, E.; Jones, H. W. *ibid.* **1951**, *73*, 2700.
- Bentley, T. W.; Carter, G. E. *ibid.* **1982**, *104*, 5741.
- McManus, S. P.; Neamati-Mazraeh, N.; Karaman, R. M.; Harris, J. M. *J. Org. Chem.* **1986**, *51*, 876.
- (a) Harris, J. M. *Prog. Phys. Org. Chem.* **1974**, *11*, 89. (b) Bentley, T. W.; Schleyer, P. V. R. *Adv. Phys. Org. Chem.* **1977**, *14*, 1. (c) Harris, J. M.; McManus, S. P. *J. Am. Chem. Soc.* **1974**, *96*, 4693.
- McLennay, D. J. *Tetrahedron Letters* **1975**, 4689.
- (a) Perrin, D. N.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon press: New York,

1988. (b) Yoh, S.-D.; Tsuno, Y.; Fujio, M.; Sawada, M.; Yukawa, Y. *J. Chem. Soc., Perkin Trans.* 1989, 2, 7. (c) Yoh, S.-D.; Cheong, D.-Y.; Tsuno, Y. *J. Phy. Org. Chem.* 1993, 6, 23. (d) *Beilstein 2(2)*, 186, and *Catalog Hand Book of Fine Chemicals*, Aldrich, 1994-1995, 689. (e) Dishart,

K. T.; Levine, R. *J. Am. Chem. Soc.* 1956, 78, 2268.
10. Yoh, S.-D.; Kim, D.-J. *J. Korean Chem. Soc.* 1981, 25(6), 376.
11. Leffler, J. E. *J. Org. Chem.* 1955, 20, 1202.

The Effect of Solvent on Reactions of *p*-Nitrophenyl Acetate with Alicyclic Secondary Amines and with Anionic Nucleophiles in MeCN-H₂O Mixtures of Varying Compositions

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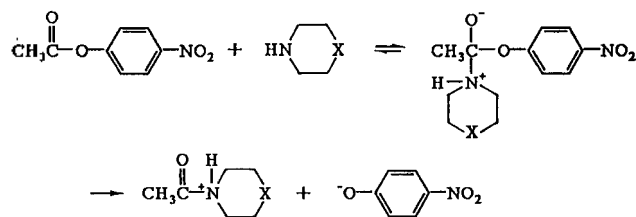
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Second-order rate constants have been measured spectrophotometrically for the reaction of *p*-nitrophenyl acetate (PNPA) with morpholine, piperazine and piperidine in MeCN-H₂O mixtures of varying compositions. The rate of the present aminolysis decreases upon additions of MeCN into H₂O up to near 30-40 mole % MeCN and remains nearly constant upon further additions of MeCN. The reaction of PNPA with anionic nucleophiles, such as HO⁻, *p*-chlorophenoxide and butane-2,3-dione monoximate, has also exhibited two distinguishable reactivity zones. However, the reactivity trend for the anionic nucleophiles is quite different from the one obtained for the amine system, e.g. an initial rate decrease in the H₂O-rich region followed by an increasing rate trend upon further additions of MeCN in the MeCN-rich region. The rate behaviors shown by the amine system in the MeCN-rich and by the anionic system in the H₂O-rich region are unexpected based on the Hughes-Ingold rules. The present unusual rate trends have been attributed to changes in the solvent structure and *pK_a* of the nucleophiles upon the addition of MeCN into H₂O. The effect of solvent appears to be more significant for the TS than the GS, and the TS structure is considered to become tighter in the higher MeCN concentration.

Introduction

The effect of solvent on organic reactions have been extensively studied.¹⁻⁵ Current research is mostly focused on the investigation of solvent effect on reaction rates and mechanisms in binary mixtures of H₂O with dipolar aprotic solvents, such as dimethyl sulfoxide (DMSO)⁴ and acetonitrile (MeCN).⁵ Significant rate accelerations have often been reported upon additions of aprotic dipolar solvents into H₂O for the reactions involving anionic nucleophiles.⁶ However, on the contrary, rate retardations have also been observed for reactions of neutral species developing a charge in the transition state (TS) upon solvent changes from H₂O to aqueous diolar aprotic solvent mixtures.⁷ Such solvent effects on reaction rates could be nicely explained by the Hughes-Ingold rules in a qualitative manner,⁸ since gradual increase of the mole % of such organic solvents is considered to change H-bonding structure of H₂O and the microenvironment of the reactant and TS.

We have performed a systematic study for the reaction of *p*-nitrophenyl acetate (PNPA) with alicyclic amines and with anionic nucleophiles, as shown in Scheme 1 for the aminolyses. Aminolyses of esters have been extensively studied due to importance of acyl transfer reactions in biological processes, such as the acylation of chymotrypsin and other serine proteases by amides or the analogous acylation of



X = CH₂ ; piperidine

X = NH ; piperazine

X = O ; morpholine

Scheme 1.

papain and other cystein proteases.⁹ However, systematic studies of solvent effect on aminolyses have been lacking. Since dissection of solvent effect into the ground state (GS) and TS contributions would be expected to give us useful information about solvent effect, we have measured enthalpies of solution (ΔH_{sol}) of the nucleophilic amines as well as activation parameters (ΔH^* and $T\Delta S^*$) for the aminolyses. In the present paper, we wish to report unexpected rate trends based on the Hughes-Ingold rules and plausible explanations for the unusual rate trends upon the present solvent change.