

# Marked Difference in Solvation Effects and Mechanism between Solvolyses of Substituted Acetylchloride with Alkyl Groups and with Aromatic Rings in Aqueous Fluorinated Alcohol and in 2,2,2-Trifluoroethanol-Ethanol Solvent Systems

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Solvolyses rate constants of trimethylacetyl chloride (**2**), isobutyryl chloride (**3**), diphenylacetyl chloride (**4**) and *p*-methoxyphenylacetyl chloride (**5**) in 2,2,2-trifluoroethanol (TFE)-water, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP)-water and TFE-ethanol solvent systems at 10 °C are determined by a conductimetric method. Kinetic solvent isotope effects (KSIE) are reported from additional kinetic data for methanolyses of various substituted acetylchlorides in methanol. According to the results of those reactions analyzed in terms of rate-rate profiles, extended Grunwald-Winstein type correlations, application of a third order reaction model based a general base catalyzed (GBC) and KSIE values, regardless of the kind of neighboring groups (CH<sub>3</sub>- or Ph-groups) of reaction center, for aqueous fluorinated alcohol systems, solvolyses of **2**, **3**, **4**, and **5** were exposed to the reaction with the same mechanism (a loose S<sub>N</sub>2 type mechanism by electrophilic solvation) controlled by a similarity of solvation of the transition state (TS). Whereas, for TFE-ethanol solvent systems, the reactivity depended on whether substituted acetyl chloride have aromatic rings (Ph-) or alkyl groups (CH<sub>3</sub>-); the solvations by the predominant stoichiometric effect (third order reaction mechanism by GBC and/or by push-pull type) for Ph- groups (**4** and **5**) and the same solvation effects as those shown in TFE-water solvent systems for CH<sub>3</sub>- groups (**2** and **3**) were exhibited. Such phenomena can be interpreted as having relevance to the inductive effect (σ<sub>I</sub>) of substituted groups; the plot of log (KSIE) vs. σ<sub>I</sub> parameter give an acceptable the linear correlation with r = 0.970 (slope = 0.44 ± 0.06, n = 5).

**Key words** : Solvolysis, Aqueous fluorinated alcohol

## Introduction

The correlation of solvolysis rates and solvent composition has been evaluated by a Grunwald-Winstein equation<sup>1,2</sup> with single solvent parameter. For a long time, this has played a central role as a tool for the criteria of reaction mechanism.

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

In equation (1), *k* and *k*<sub>0</sub> are the rates of solvolyses in a given solvent and in 80% aqueous ethanol, respectively; *m* is the sensitivity to changes in ionizing power (Y: based on solvolyses of *tert*-butyl chloride<sup>1</sup> (**1**), Y<sub>Cl</sub>: those of 1-adamantyl chloride<sup>2</sup> as a standard substrate with *m* = 1.00), and *c* is a residual term.

Dispersed Grunwald-Winstein correlation<sup>3-6</sup> in the solvolyses has been handled by extended Grunwald-Winstein equation to involve a solvent nucleophilicity parameter, N<sub>T</sub> (Kevill's N<sub>T</sub> scale; the solvolyses of *S*-methyl dibenzothiophenium ion)<sup>7</sup>; *l* is the sensitivity to these parameter.

$$\log(k/k_0) = mY_{Cl} + lN_T + c \quad (2)$$

Dispersion of phenomena in solvolyses of trimethyl acetyl chloride (**2**)<sup>8</sup> in various aqueous organic solvent systems, led by the substitution of the three methyl groups (CH<sub>3</sub>-) into the acetyl chloride which was reported as an S<sub>N</sub>2 mechanism<sup>9</sup> with high nucleophilic attack- but non-carbonyl addition type, was attributed to a dual reaction channel (S<sub>N</sub>1-S<sub>N</sub>2 mechanism)

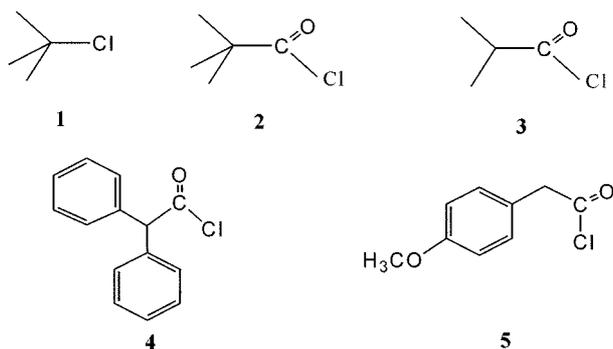
according to the results evaluated by equation (1).

And substituent effects in the reactions of aliphatic acyl chloride with methanol and phenol in acetonitrile were reported as the dominance of third order reactions based on a general base catalyst by Kevill.<sup>10</sup>

According to more recent the results studied by Ryu<sup>11</sup> *et al.*, fairly good the rate-rate profile correlations of the rate of solvolyses for substituted acetyl chloride including S- atom in more than 33 organic solvent mixtures were interpreted as a unit mechanism proceeding through a general base catalyzed reaction, regardless of the different neighboring groups (CH<sub>3</sub>S-, PhS- and 2-C<sub>5</sub>H<sub>4</sub>S-) of reaction center.

We have attempted to further investigate how to create the difference in solvation effects and mechanisms between solvolysis of acetyl chloride with alkyl groups, [trimethyl acetyl chloride (**2**) and isobutyryl chloride (**3**)], and with aromatic groups, [diphenyl acetyl chloride (**4**) and *p*-methoxy phenyl acetyl chloride (**5**)], in less nucleophilic solvents (a favorable solvent for the electrophilic solvation effect) such as 2,2,2-trifluoroethanol (TFE) and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) with water and in TFE-ethanol binary mixtures.

Grunwald-Winstein correlations [equation (1) and (2)], the rate-rate profiles, the application of a third order reaction model and a regression analysis between kinetic solvent isotope effects (KSIE = *k*<sub>MeOH</sub>/*k*<sub>MeOD</sub>) and the inductive parameters (σ<sub>I</sub>) etc. were used as analytical tools for the achievement of our purpose in work.



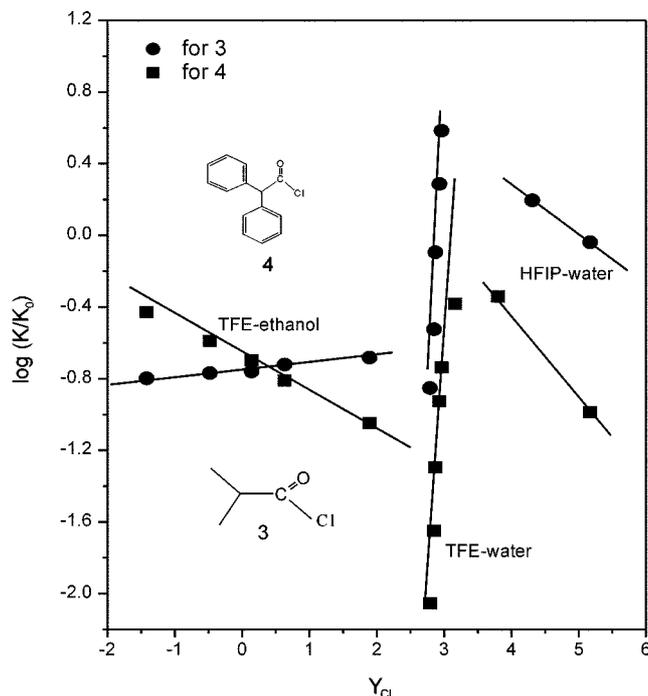
Scheme 1

### Results and Discussion

Solvolyses rate constants, determined by the conductimetric method for these compounds in solvent mixtures chosen at 10 °C, are represented in Table 1 and in order to inquire into the differences in solvation effects between alkyl groups and aromatic ring on solvolytic reaction, these results typically were analyzed for **3** and **4** by using equation (1) and were plotted as shown in Figure 1.

As shown in Figure 1, it makes us feel the necessity to divide this into three parts: TFE-water, HFIP-water and TFE-ethanol solvent systems, respectively, to further analyze the dependence of the ionizing power ( $Y_{Cl}$ ) on these reactions.

In the case of TFE-water system, both **3** and **4** show an unusually drastic increase in the rate constants [large positive slope ( $m$ )] according to the increase of  $Y_{Cl}$  and, in particular, a large residual constant ( $c$ ) was obtained. Such phenomena may probably suggest the stabilization of the



**Figure 1.** Grunwald-winstein plot for solvolyses of **3** and **4** compounds in various fluorinated solvent mixtures at 10 °C ( $m = 8.58$ ,  $c = -24.82$  for **3** and  $m = 4.37$ ,  $c = -13.95$  for **4** in TFE-water)

transition state (TS) from other specific solvent effects except for the solvent polarity ( $Y_{Cl}$ ).

Whereas, according to the addition of a molecule of water to HFIP solvent system, the reduced rate constants are also exhibited in Figure 1 (Table 1). Considering the greater

**Table 1.** First order rate constants ( $k \times 10^3/s^{-1}$ ) for solvolyses of various substituted acetyl chlorides in aqueous fluorinated alcohol and 2,2,2-trifluoroethanol (T)-ethanol (E) solvent mixtures at 10 °C<sup>a</sup>

Solvent <sup>b</sup>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	$Y_{Cl}$	$N_T$
100TFE	—	32.8 ± 0.8	0.370 ± 0.01	5.70 ± 0.04	2.79	-3.93
97 TFE <sup>c</sup>	20.7 ± 0.2	69.8 ± 0.8	0.94 ± 0.001	12.6 ± 0.4	2.85	-3.30
90 TFE	48.3 ± 0.2	188 ± 4	2.13 ± 0.06	36.2 ± 0.4	2.87	-2.55
80 TFE	115 ± 2	451 ± 1	4.97 ± 0.03	83.7 ± 0.4	2.93	-2.19
70 TFE	215 ± 2	895 ± 11	7.67 ± 0.10	154 ± 4	2.96	-1.98
50 TFE	661 ± 28	—	17.4 ± 0.2	391 ± 13	3.16	-1.73
97HFIP <sup>d</sup>	119 ± 4	213 ± 2	4.33 ± 0.01	20.9 ± 1.1	5.17	-5.26
90 HFIP	142 ± 1	366 ± 4	—	—	4.31	-3.84
50 HFIP	—	—	19.1 ± 0.2	208 ± 1	3.80	-2.49
80T-20E <sup>e</sup>	13.5 ± 0.2	48.4 ± 0.5	3.75 ± 0.07	19.5 ± 0.6	1.89	-1.76
60T-40E <sup>e</sup>	12.2 ± 0.3	44.3 ± 0.7	6.5 ± 0.05	26.7 ± 0.1	0.63	-0.94
50T-50E <sup>e</sup>	11.6 ± 0.4	40.6 ± 0.4	8.42 ± 0.04	30.6 ± 1.6	0.14	-0.64
40T-60E <sup>e</sup>	11.2 ± 0.2	39.7 ± 0.5	10.8 ± 0.2	35.1 ± 0.1	-0.48	-0.34
20T-80E <sup>e</sup>	11.1 ± 0.1	37.1 ± 0.5	15.6 ± 0.02	42.0 ± 0.1	-1.42	-0.08
100E <sup>e,f</sup>	—	34.2 ± 0.9	15.7 ± 0.05	42.3 ± 0.1	-2.52	0.37
80E <sup>e,g</sup>	36.8 ± 0.1	233 ± 1	41.9 ± 0.6	176 ± 4	0.00	0.00

<sup>a</sup>Performed for this work within the solvent range of the specific composition of fluorinated solvents with solvent parameters ( $Y_{Cl}$  and  $N_T$ ) measured by previous workers as ref. 2 and 7, and determined conductimetrically at least in duplicate; typically injected 4  $\mu$ L of 1% (w/w) substrate in dry acetonitrile into the kinetic apparatus with a turbo-stirrer containing 2 mL of each solvent mixtures; errors shown are standard deviations. <sup>b</sup>Percentage of weight (w/w) % by TFE content. <sup>c</sup>Water contents for 97% (w/w) TFE were exactly measured as 97.37% by using a Karl Fisher Titrator. <sup>d</sup>Water content for 97% (w/w) HFIP were exactly measured as 97.42% by using Karl Fisher Titrator. <sup>e</sup>Percentage of volume by first named organic solvent composition (v/v%). <sup>f</sup>Pure ethanol. <sup>g</sup>80% (v/v) aqueous ethanol mixtures.

differences in the solvent nucleophilicity parameters ( $\Delta N_T$ ) relative to those in the solvent ionizing power parameters ( $\Delta Y_{Cl}$ ) [*i.e.*: 97% → 50% HFIP ( $\Delta Y_{Cl}$ : 1.37,  $\Delta N_T$ : 2.77) and/or 97% → 90% HFIP ( $\Delta Y_{Cl}$ : 0.86,  $\Delta N_T$ : 1.42)], it can be understood as possible evidence for the participation of appreciable solvent nucleophilic solvation step as well as those of electrophilic solvation at the rate determining.

Also, in the case of solvolysis rates of **3** with two methyl groups ( $CH_3$ -) in 90% HFIP and 100% TFE solvents, which have very similar nucleophilicities ( $N_T$ ) but different ionizing powers ( $Y_{Cl}$ ) as shown in Table 1, a small the ratio of rates in these solvent systems was obtained as  $k_{90HFIP}/k_{100TFE} = 11.2$ , compared with great differences in solvent ionizing power  $\{[Y_{Cl(90HFIP)} Y_{Cl(100TFE)}]_{N_T} = 1.52\}$ .

On the other hand, in nonaqueous solvent mixtures such as TFE-ethanol system, according to whether substrate was included by  $CH_3$ -(**3**) or Ph-group(**4**) adjacent to reaction center, quite different reactivity and the way of solvation of TS was indicated in Figure 1.

In ethanol solvent (a better nucleophilic solvent) and in 97(w/w)% TFE-water mixtures (a high electrophilic solvent system with less nucleophilicity), as shown in footnote b and f in Table 2, the rate ratio between the previous studied solvolyses rates of chlorodiphenylmethane (CDPM) and *p*-methoxybenzyl chloride (*p*-MBZC), known well as unimolecular reactions having an easy stabilization of the carbocation by the positive delocalization and the ratio of those rates of **4** and **5** as substituted acetyl chloride, given by the introduction of

**Table 2.** Solvolysis rate ratios between substrates chosen in ethanol and 97% TFE-water solvent system at 10 °C<sup>a</sup>

	$k_{CDPM}/k_{p-MBZC}$	$k_4/k_5$	$k_{CDPM}/k_4$
EtOH <sup>b</sup>	3.2 <sup>c</sup>	0.37(0.43) <sup>d</sup>	$4.73 \times 10^{-4e}$
97(w/w)% TFE <sup>f</sup>	6.6 <sup>c</sup>	0.07(0.12) <sup>d</sup>	367

<sup>a</sup>Rate constants of the corresponding number in subscript are in Table 1 and rate constants for chlorodiphenyl methane (represented as CDPM) and those for *p*-methoxy benzylchloride (represented as *p*-MBZC) are quoted from ref. 12. <sup>b</sup>Solvent parameters for pure ethanol revealed from ref. 7;  $Y_{Cl}$ : -2.52 and  $N_T$ : 0.37 °C at 25 °C. <sup>d</sup>Ratio of rate constants between solvolysis rate for **4** and the corresponding rate [ $k_{PAC} = (3.67 \pm 0.03) \times 10^{-2} s^{-1}$  for pure ethanol and  $(7.88 \pm 0.01) \times 10^{-3} s^{-1}$  for 97% TFE] for phenylacetyl chloride (PAC),  $k_4/k_{PAC}$  and an Arrhenius plot using the observed rate constants in pure ethanol at 0 °C, 5 °C and 10 °C,  $(2.04 \pm 0.10) \times 10^{-2} s^{-1}$ ,  $(2.72 \pm 0.03) \times 10^{-2} s^{-1}$  and  $(3.67 \pm 0.03) \times 10^{-2} s^{-1}$ , respectively, gives  $\Delta H^\ddagger = 8.5 kcal mol^{-1}$  and  $\Delta S^\ddagger = -35.7 cal k^{-1} mol^{-1}$  ( $r = 0.9998$ ). <sup>e</sup>The rate constant at 10 °C corresponding to CDPM,  $k_{CDPM} = 7.44 \times 10^{-6} s^{-1}$ , was calculated by an Arrhenius plot using kinetic data quoted at 25 °C and 50 °C from ref. 13, and  $\Delta H^\ddagger = 20.8 kcal mol^{-1}$  and  $\Delta S^\ddagger = -8.20 cal k^{-1} mol^{-1}$  were also obtained. <sup>f</sup>Solvent parameter for 97(w/w)% TFE-water revealed from ref. 7;  $Y_{Cl}$ : 2.85 and  $N_T$ : -3.30.

**Table 3.** Results for the correlation of logarithm of the rate constants for **2** in TFE-water mixtures at 10 °C with those corresponding rates for various acetyl chlorides<sup>a</sup>

Compound	Slope	Intercept	$r^b$
<b>3</b>	$1.08 \pm 0.02$	$-0.24 \pm 0.01$	0.9996
<b>4</b>	$0.84 \pm 0.04$	$-1.40 \pm 0.02$	0.997
<b>5</b>	$0.99 \pm 0.05$	$-0.84 \pm 0.03$	0.997

<sup>a</sup>See Table 1. <sup>b</sup>Correlation coefficient.

a C=O group to the substrates mentioned the above, are presented in Table 2.

In contrast with the case of  $k_{CDPM}/k_{p-MBZC}$ , the studied  $k_4/k_5$  ( $k_4/k_{PAC}$ ) were found to be <1 (particularly, those for 97% TFE-water), indicating the different reactivity and the results of  $k_{CDPM}/k_4$  strongly supported these facts.

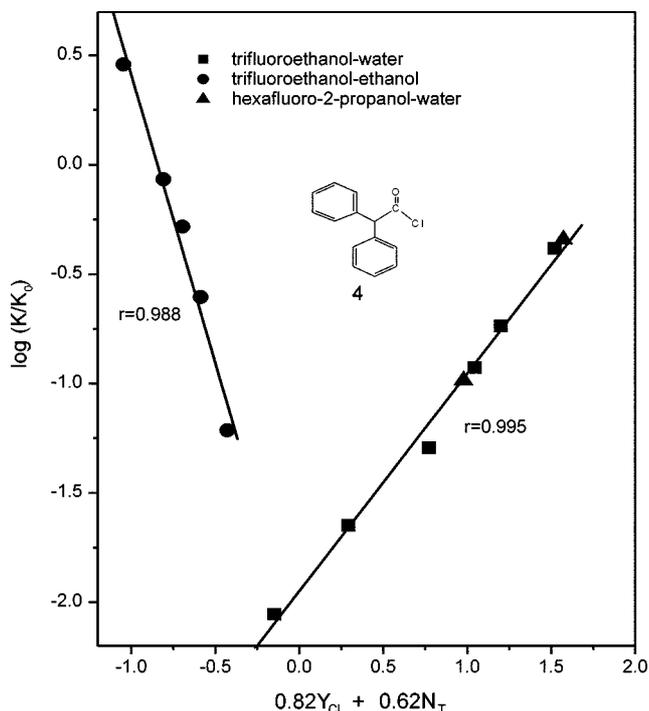
**In TFE-water solvent system.** An evaluation of rate-rate profiles for solvolysis rates of **3**, **4** and **5** on the basis of the corresponding rates of **2** give a very fairly correlation with the slope of close to one unit (slope = 0.84~1.08 and  $r \geq 0.997$ ) as shown in Table 3, indicating the solvolytic reactions are very similar mechanically to each other and a very the different values of the intercept obtained in these correlations (Table 3) can be interpreted as the results occurring due to different bulky solvations between Ph- and  $CH_3$ - groups and the number of corresponding groups as well, when these values are compared with each other.

**Extended Grunwald-Winstein parameter correlation.** These phenomena presented so far in aqueous fluorinated solvent systems, in which the solvent nucleophilicity ( $N_T$ ) can be expected to play a central role in the rate determining step, were analyzed in terms of equation (2). These results obtained from the multiple regression analysis displayed a good correlation with  $m = 0.75\sim 0.97$  and  $l = 0.62\sim 0.76$  ( $r \geq 0.978$ ) as described in Table 4. Even if these values were more or less different, the contribution to these reactions from the nucleophilicity ( $N_T$ ) and ionizing power ( $Y_{Cl}$ ) exposed almost the similar magnitude (the fraction of the contribution to those reaction from  $Y_{Cl}$ : 0.50~0.57) in this work. If considered the results for  $S_N1$  solvolysis (nucleophilic assisted) of **1**,<sup>7b</sup> phenylchlorothionoformate<sup>4a</sup> and N,N-diphenylcarbamoyl chloride<sup>14</sup> with the identical set of the fractions of the contribution from  $Y_{Cl}$ , led to 0.69, 0.73 and 0.72, respectively, and 0.55 (0.43) for N,N-dimethylcarbamoyl chloride<sup>15</sup> (cyclopropenyl tosylate<sup>16</sup>) reported as an  $S_N2$  mechanism with a loose TS ( $S_N2$  mechanism with early TS structure), our results could be rationalized in terms of being a similar mechanism with the same structure of the TS, controlled by the contribution from nucleophilic participation by a molecule of solvent as well as by solvent polarity (ionization) (*i.e.* ion pair intermediate in  $S_N2$  solvolysis), regardless of  $CH_3$ - or Ph- groups in the substituted acetyl chloride. These analyses provide support for the main reason why a good correlation with very similar slopes for the rate-

**Table 4.** Comparison of correlation analyses<sup>a</sup> for solvolytic reactivities in fluorinated solvent mixtures at 10 °C using extended Grunwald-Winstein equation (2)

Compound	$\log(k/k_0) = mY_{Cl} + lN_T$		$n^b$	$r^c$	$\left(\frac{A}{A+B}\right)^d$
	m (A)	l (B)			
<b>2</b>	$0.97 \pm 0.08$	$0.74 \pm 0.11$	7	0.978	0.57
<b>3</b>	$0.81 \pm 0.10$	$0.72 \pm 0.08$	6	0.982	0.53
<b>4<sup>e</sup></b>	$0.82 \pm 0.04$	$0.62 \pm 0.03$	8	0.996	0.57
<b>5</b>	$0.75 \pm 0.07$	$0.76 \pm 0.05$	7	0.992	0.50

<sup>a</sup>Values of solvent parameters for  $Y_{Cl}$  and  $N_T$  are quoted from ref. 2 and ref. 7. <sup>b</sup>Number of solvent. <sup>c</sup>Correlation coefficient. <sup>d</sup>Fraction of the contribution to ionization power. <sup>e</sup>Correlation included pure TFE solvent.



**Figure 2.** Plots of  $\log(K/K_0)$  for solvolyses of diphenylacetyl chloride (**4**) at 10 °C against  $(0.82 Y_{Cl} + 0.62 N_T)$ . The five values for solvolyses in TFE-ethanol are not included in the correlation.

**Table 5.** Results for correlation of logarithm of the rate constants for **4** in TFE-ethanol mixtures at 10 °C with those corresponding rates for various acetylchlorides<sup>a</sup>

Compound	Slope	Intercept	$r^b$
<b>2</b>	$-0.15 \pm 0.02$	$-0.60 \pm 0.01$	-0.977
<b>3</b>	$-0.19 \pm 0.02$	$-0.88 \pm 0.01$	-0.991
<b>5</b>	$0.54 \pm 0.01$	$-0.39 \pm 0.01$	0.99993

<sup>a</sup>See Table 1. <sup>b</sup>Correlation coefficient.

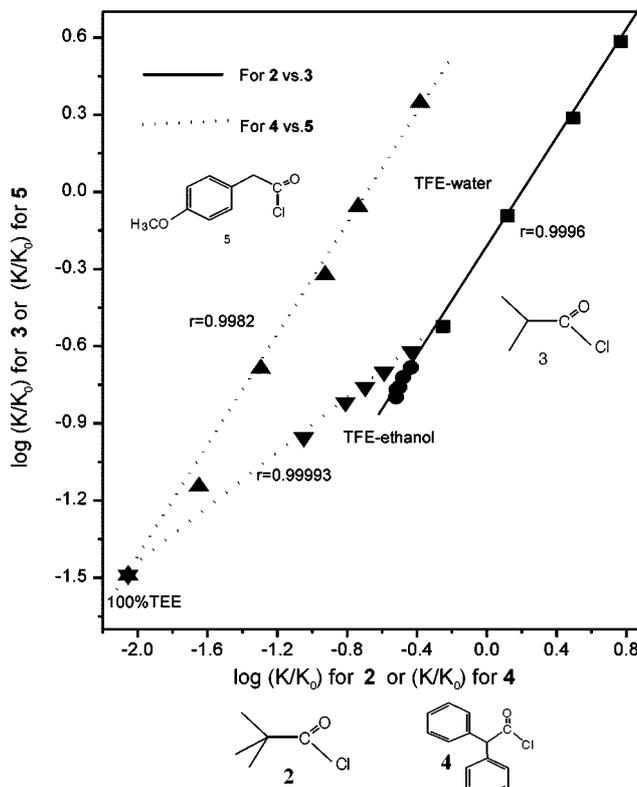
rate profile in TFE-water system were observed as shown in Table 3. The result well correlated by  $\log(k/k_0) = (0.82 \pm 0.04) Y_{Cl} + (0.62 \pm 0.03) N_T$  for solvolyses of **4** is demonstrated in Figure 2 but in TFE-ethanol solvent system containing ethanol which is known as the solvent with the highest probability of addition-elimination ( $S_{AN}$ ), the contrast slope (negative) in this correlation is also shown in Figure 2.

**For TFE-ethanol solvent system.** Quite different reactivities depending on whether the substituted acetyl chloride was replaced by Ph- or  $CH_3$ - groups are shown in Figures 1, 3 and Table 5, and are evaluated by the rate-rate correlation between those substrates.

In Table 5, the plot of the rate-rate between **4** and **5** had an excellent linear correlation ( $r = 0.99993$ ) with a positive slope of 0.54, implying a similarity in the way of stabilizing the TS but with about a 1/2 reduction of reactivity according to number of Ph- group.

In contrast with this, for **2** and **3** substrates involving  $CH_3$ - groups, these had a negative slope with the similar value (-0.15 and -0.19), implying a similar mechanism.

When compared with the correlation coefficients ( $r$ ) in



**Figure 3.** Rate-rate profile between solvolyses of compounds studied in TFE-water and TFE-ethanol mixtures at 10 °C.

Tables 3 and 5, we can probably deduce that the solvations of  $CH_3$ - groups are much better in electrophilic solvent systems ( $r = 0.9996$  for **3** in TFE-water solvent mixtures) and Ph- groups show more effective solvations by nucleophilic solvent systems ( $r = 0.99993$  for **5** in TFE-ethanol solvent mixtures). These values obtained by using the multiple regression analyses [equation (2)] in Table 4 also show the results connected with the above interpretation; that is, such phenomena indicate mechanistic differences between solvolyses of acetyl chloride substituted by  $CH_3$ - groups and those substituted by Ph-groups.

Figure 3 presents the results analyzed by the rate-rate profiles, considering the exclusion of the different solvation effects<sup>3,17</sup> (phenomena of dispersion) between Ph- and  $CH_3$ - groups adjacent to the reaction site.

The above Figure displays the dispersion into two separate lines with the slope =  $1.11 \pm 0.03$  ( $r = 0.998$ ) for TFE-water and  $0.54 \pm 0.01$  ( $r = 0.99993$ ) for TFE-ethanol solvent systems, respectively, in the rate-rate correlation of the rate constants for **5** in TFE-water and TFE-ethanol solvent systems vs. the corresponding rate constants for **4**.

But, in the case of the rate-rate profile between **3** and **2**, a very nice linear correlation with the slope =  $1.06 \pm 0.01$  ( $r = 0.9996$ ), which was consistent with the slope value (1.11) of corresponding to Ph- groups in TFE-water solvent systems, for solvent systems containing TFE-ethanol and TFE-water solvent systems was obtained.

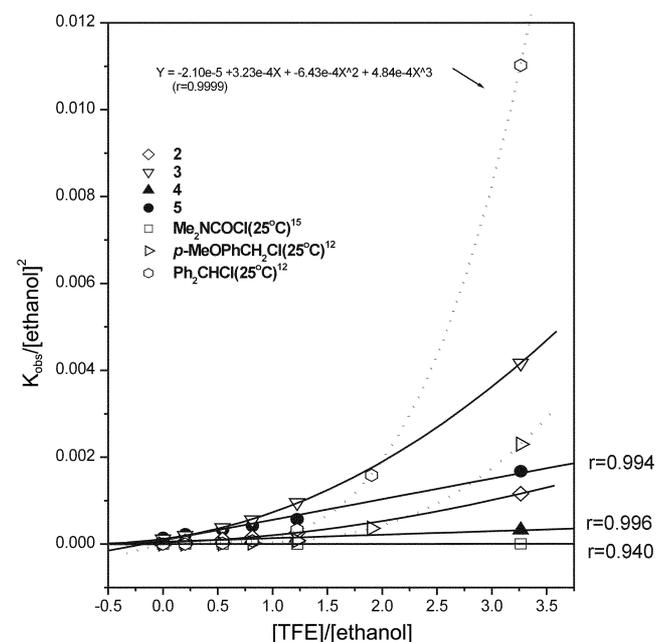
Phenomena of the same slope are rationalized in terms of the stabilization of the TS by a molecule of solvents in the

same way (the same TS-structure), and whereas, for TFE-ethanol solvent systems, the different slope value of 0.54 in separate correlation between **5** and **4** including Ph- groups was indicated as the different solvation of the TS from **3** and **2** including CH<sub>3</sub>- groups.

For solvolyses of **4** involving two Ph- groups in these solvent system, not only the Grunwald-Winstein plot (Figure 1) but also the extended Grunwald-Winstein plot (Figure 2) which considers the nucleophilicity term ( $N_T$ ), it is unusual because it shows a negative response to  $Y_{Cl}$  and to two solvent parameters ( $Y_{Cl}$  and  $N_T$ ) as well, and the rate-rate profile with positive slope in solvolysis of **5** (Table 5 and Figure 3 shown different slopes) is also unusual.

In Table 1, when the solvent composition were changed from 100% ethanol to 20T-80E, there is an increase in the rate constants for **3** but almost no change (meaning the possibility of the existence of the maximum rate constant in the specific solvent composition)<sup>18</sup> in the rate constants for **4** and **5**. Consequently, these for **4** and **5** are predicted to have relevance to a third order rate constant, based on a general base catalyst (GBC) by the two different molecules of solvents (ethanol and TFE), the  $k_{ET}$  ( $k_{TE}$ ) terms. Whereas, for **3**, the importance of the solvent electrophilic solvation was related.

**Third order reaction model.** We tried to further investigate further such phenomena in terms of a third order model<sup>19</sup> based on a general base catalyst by a molecule of solvent (occasionally, reported in solvolyses rates of aqueous alcohol solvent mixtures). For solvolyses in TFE-ethanol binary mixtures, there are four possible a third order rate constants: (i)  $k_{EE}$ ; one molecule of ethanol acting as a nucleophile and second molecule of ethanol acting as a general base. (ii)  $k_{ET}$ ; one molecule of ethanol acting as a nucleophile and second molecule of TFE acting as general base. (iii)  $k_{TE}$ ; the case of the contrast role to the  $k_{ET}$  term.



**Figure 4.** Plots of  $K_{obs}/[\text{ethanol}]^2$  vs. molar ratio of TFE and ethanol for solvolysis of various substrates in TFE-ethanol mixture at 10 °C.

**Table 6.** The results of analyses using the third order model equation (4) for solvolyses of **4** and **5** in TFE-ethanol solvent mixtures at 10 °C

Compound	$k/10^{-4}\text{s}^{-1}\text{L}^2\text{mol}^{-2}$		$r^a$	$(k_{ET}+k_{TE})/k_{EE}$
	Slope ( $k_{ET}+k_{TE}$ )	Intercept ( $k_{EE}$ )		
<b>4</b>	$0.803 \pm 0.004$	$0.557 \pm 0.006$ (0.541) <sup>b</sup>	0.996	1.44
<b>5</b>	$3.44 \pm 0.07$	$1.49 \pm 0.05$ (1.47) <sup>b</sup>	0.994	2.31

<sup>a</sup>Correlation coefficient. <sup>b</sup>Calculated from first order rate constant in pure ethanol by  $k_{EE} = k_{obs}/[\text{EtOH}]^2$ .

(iv)  $k_{TT}$ ; the role of a molecule of TFE solvent as a nucleophile and a general base but considering the character of TFE solvent (the greater acidity of TFE,  $\text{pK}_a = 12.39$  relative to ethanol,  $\text{pK}_a = 15.93$ ),<sup>20</sup> the  $k_{TT}$  term may be ignored.

Consequently, we could establish equation (3) having three possible third order reactions as shown below

$$k_{obs} = k_{EE}[\text{ethanol}]^2 + (k_{ET} + k_{TE}) [\text{ethanol}][\text{TFE}] \quad (3)$$

And these can be rearranged to make a useful for linear equation (4) as shown below

$$k_{obs}/[\text{ethanol}]^2 = k_{EE} + (k_{ET} + k_{TE}) [\text{TFE}]/[\text{ethanol}] \quad (4)$$

If the rate constants are not variables, or vary in the same way with solvent, then a plot of  $k_{obs}/[\text{ethanol}]^2$  vs  $[\text{TFE}]/[\text{ethanol}]$  should give a straight line of slope,  $(k_{ET} + k_{TE})$  and intercept,  $k_{EE}$  and  $k_{EE}$  can be calculated directly from the observed rate constants in pure ethanol as  $k_{EE} = k_{obs}/[\text{ethanol}]^2$ .

As shown Figure 4, only these rates corresponding to **4** and **5** of the solvolytic reactions for the various substrate with CH<sub>3</sub>- and Ph- groups [included the substituted acetylchloride (**2**, **3**, **4** and **5**) used in this work] were evaluated as good linear correlations ( $r = 0.996$  for **4** and  $r = 0.994$  for **5**), so that the fact to obey third order reaction mechanism, recognized as stoichiometric solvation effects,<sup>18,21</sup> in the solvolysis rates of **4** and **5** were convinced by the these linearity plotted and these results are summarized in Table 6.

The  $k_{EE}$  value obtained from the intercept agrees satisfactorily with the values calculated from  $k_{obs}/[\text{ethanol}]^2$  in pure ethanol. These may be another evidence for the validity for the third order model, and the  $(k_{ET} + k_{TE})/k_{EE}$  third order rate ratio presented as a slope/intercept are observed as the different values between **4** and **5**.

2,2,2-trifluoroethoxide,  $\text{CF}_3\text{CH}_2\text{O}^-$  stabilizes the negative charge because of its having an electron withdrawing group (*i.e.* the equilibrium constant ( $K$ ) for the reaction with sodium hydroxide,  $\text{OH}^-$  dissolved in TFE: 2200).<sup>20</sup> Whereas, ethoxide,  $\text{CH}_3\text{CH}_2\text{O}^-$ , destabilizes the negative charge by having an electron donating group (*i.e.*  $K$  value of corresponding ethanol: 0.65)<sup>20</sup>; therefore, a molecule of TFE is a very poor solvent as a general base for a third order reaction mechanism ( $k_{ET} \approx 0$ ).

But considering excellent solvation of anion (leaving group,  $\text{Cl}^-$ ), third order reaction model ( $k_{ET}$ ) going through push-pull type (nucleophilic attack on the reaction site by the molecule of ethanol and electrophilic catalysis of the molecule of TFE) is thought to be more rationalized (*i.e.*,  $k_{ET} \neq 0$ ).

$k_{TE} \approx 0$  and  $k_{TT} \approx 0$ ), so that the  $(k_{ET} + k_{TE})$  term of the corresponding the slope can be modified as a only single  $k_{ET}$  term.

The analysis of the results now presented show the importance of the  $k_{ET}$  term, compared to the  $k_{EE}$  term on solvolyses of **5** involving a single Ph- group, for the nucleophilic solvation at the TS and in the case of **4** involving two Ph- groups, the similar magnitude of  $k_{EE}$  and  $k_{ET}$  values were presented even if these were more or less different values (Table 6).

$(k_{ET} + k_{TE})/k_{EE}$  values as a  $k_{ET}/k_{EE}$  third order rate ratio were reduced from 2.31 to 1.44 according to the change of one Ph- group (**5**) to two Ph- groups (**4**) in the substituted acetyl chloride. These results might be regarded as an improvement of the contribution to the stabilization of TS with nucleophilic solvation from  $k_{EE}$  according to number of Ph-group, and these results are consistent with those of the rate-rate profile with the slope of 0.54, which can be attributed to the differences in the contribution from the  $k_{EE}$  term, between **4** and **5**.

On the other hand, acid chloride with  $\text{CH}_3$ - groups showed a nonlinear correlation, meaning there was no nucleophilic stabilization of TS undergoing a GBC by a molecule of the solvent, as shown Figure 4. In particular, CDPM (*p*-MBZC), which is relatively more reactive in high ionizing power ( $Y_{Cl}$ ) (see Table 2), is shown as a significant deviation from the linearity; that is, it is a polynomial expression even if it has Ph- groups. This can be interpreted as the phenomena caused by differential solvation effect on the reaction center. The various deviations in the linear correlations according to the degree of the contribution to the TS from the solvent polarity ( $Y_{Cl}$ ) have been shown in Figure 4. Consequently, such phenomena can be rationalized as mechanistic differences between solvolyses of acetyl chloride with  $\text{CH}_3$ - groups and with Ph- groups.

**Kinetic solvent isotope effect (KSIE =  $k_{\text{MeOH}}/k_{\text{MeOD}}$ ).** KSIE in methanol for the solvolytic reaction has been used as the barometer of the nucleophilic solvation on the reaction center [KSIE values  $\geq 1.6$ <sup>22</sup> for solvolyses of acid chloride

**Table 7.** First order rate constants for solvolyses in methanol for kinetic solvent isotope effect (KSIE) and  $\sigma_I$  parameter for inductive effect

Compound	$k \times 10^3/\text{s}^{-1}$		KSIE <sup>a</sup>	$\sigma_I^b$ (substituent)
	MeOH	MeOD		
<b>2</b> (0 °C)	178	122	1.46	-0.01 (Bu <sup>t</sup> -)
<b>3</b> (10 °C)	167	122	1.37	0.01 ( <i>i</i> -pr-)
<b>4</b> (10 °C)	68.3	42.5	1.61	-
<b>5</b> (10 °C) <sup>c</sup>	172	105	1.64	-
MeCOCl (0 °C)	109	821	1.32 <sup>d</sup>	-0.01 (Me-)
PhCOCl (25 °C) <sup>e</sup>			1.55	0.12 (Ph-)
PhCH <sub>2</sub> COCl (10 °C)	144	103	1.40	0.03 (PhCH <sub>2</sub> -)
MeSCH <sub>2</sub> COCl (10 °C) <sup>f</sup>	164	110	1.49	0.12 (MeSCH <sub>2</sub> -)
PhSCH <sub>2</sub> COCl (10 °C) <sup>f</sup>	157	93.6	1.68	

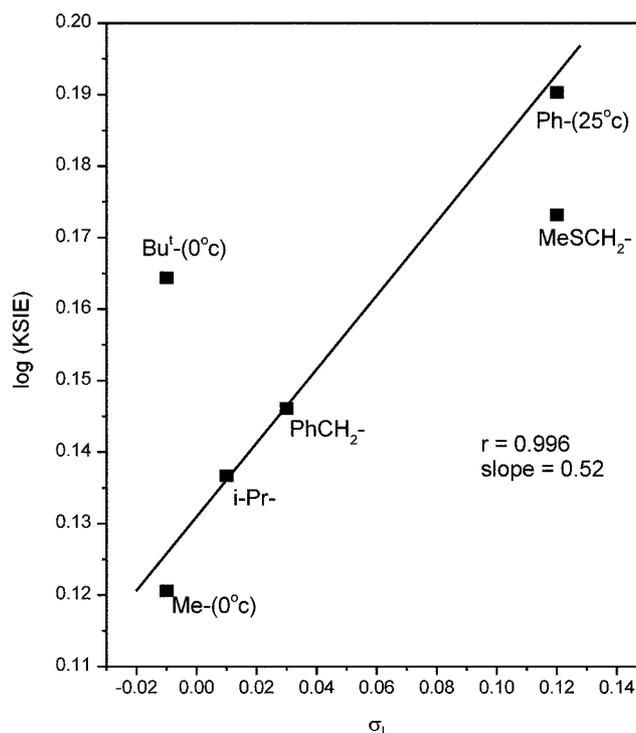
<sup>a</sup>KSIE =  $k_{\text{MeOH}}/k_{\text{MeOD}}$ . <sup>b</sup>Data from ref. 23. <sup>c</sup>Calculated from the kinetic data at low temperatures. <sup>d</sup>Ref. 9 reported a value of  $1.29 \pm 0.03$ . <sup>e</sup>Data from ref. 24. <sup>f</sup>Data from ref. 11.

were reported as a general base catalyzed reaction ( $S_{AN}$  mechanism)].

The solvolytic reaction for acetyl chloride (**4** and **5**), substituted by Ph-groups by showing that KSIE values are  $>1.6$  (Table 7), can be confirmed as a third order reaction mechanism as previously stated in TFE-ethanol system. **5** with *p*-OCH<sub>3</sub> substituent and unsubstituted phenylacetyl chloride (PhCH<sub>2</sub>COCl) have very similar rate constants at 10 °C for methanol-*d* but the different rate constant at the same temperature ( $1.72 \times 10^{-1} \text{s}^{-1}$  for **5** and  $1.44 \times 10^{-1} \text{s}^{-1}$  for PhCH<sub>2</sub>COCl) obtained in methanol. This is responsible for more effective stabilization of the TS by molecules of methanol in methanolysis rate of **5** relative to unsubstituted PhCH<sub>2</sub>COCl.

According to whether the substrates involved either the Ph- or  $\text{CH}_3$ - group, the difference in KSIE values were about 0.2 (the greater value of the Ph- group).

**A regression analysis between KSIE values and the inductive parameter ( $\sigma_I$ )<sup>23</sup>.** As a result, in order to search for a reasonable cause for the difference in nucleophilic solvation between  $\text{CH}_3$ - and Ph- groups from a KSIE effect (independence of temperature) and an inductive effect point of view, we have carefully approached these to solve them by means of the correlation between KSIE value and the  $\sigma_I$  parameter (Table 7), which is the electron withdrawing parameter (inductive parameter). This result demonstrated an acceptable linear correlation with  $r = 0.970$  (positive slope =  $0.44 \pm 0.06$ ,  $n = 5$ ) in the plot of  $\log(\text{KSIE})$  vs.  $\sigma_I$  parameter.  $(\text{CH}_3)_3\text{C}$ - group, which is expected to have dominance by the bulky effect (sterically-hindered compound),



**Figure 5.** Plot of  $\log(\text{KSIE})$  in methanol vs inductive parameter ( $\sigma_I$ ) for substituted acetyl chloride at 10 °C [(removed two point (Bu<sup>t</sup>- and MeSCH<sub>2</sub>-groups) in correlation)]

was excepted from this correlation, and if also CH<sub>3</sub>SCH<sub>2</sub>-group including S-atom (with electron lone pair which can influence the reaction site) is removed, it provides a much better linear correlation with  $r = 0.996$  (slope =  $0.52 \pm 0.03$ ,  $n = 4$ ) as shown in Figure 5.

Consequently, the nucleophilic solvation in the solvolytic reaction for substituted acetylchloride in TFE-ethanol systems had something to do with a mainly the inductive effect, and the cause for the difference in the nucleophilic solvation between CH<sub>3</sub> and Ph- groups can also be due to the inductive effect.

### Experimental Section

**Materials.** Solvents for kinetics in this paper were dried and distilled by standard methods except for 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP, AR: 99%) and methanol-*d* ( $>99.5 \pm >$  %) which used Aldrich reagents without distillation, and aqueous fluorinated solvent mixtures were prepared by mixing appropriate weights at ambient temperatures. Accurate water contents of 97%(w/w) TFE-water and 97%(w/w) HFIP-water mixture were determined by a Karl Fisher titration, which is a Model: ORION AF instrument using Karl Fisher reagent (Hydranal composit 5 K, precision: 0.3% at 1 mg H<sub>2</sub>O). In the case of TFE-ethanol and other solvent mixtures, these solvent systems were prepared by volume percentage (v/v%).

$\alpha$ -Methylthioacetyl chloride (MeSCH<sub>2</sub>COCl) was prepared from the reaction of  $\alpha$ -methylthioacetic acid in two drops of DMF with thionyl chloride, and then the products was purified by distillation under reduced pressure.<sup>11,25</sup>  $\alpha$ -Phenylthioacetyl chloride (PhSCH<sub>2</sub>COCl) used Aldrich reagents (AR: 97%); trimethylacetyl chloride (**2**) used Aldrich reagents (AR: 99.6 %); isobutyryl chloride (**3**) used Aldrich reagents (AR: 98%); diphenylacetyl chloride (**4**) used Aldrich reagents (AR: 97%); *p*-methoxyphenylacetyl chloride (**5**) used Aldrich reagents (AR: 98%); and phenylacetyl chloride (PhCH<sub>2</sub>COCl) used Aldrich reagents (AR: 98%) without distillation and/or recrystallization.

**Kinetic methods.** Conductimetric measurements were made using a digital multiple converter, which was set up under computer control (MS-Pentium: A/D converter interface program) collecting up to 1000 readings from a stirrer conductivity cell to solve the problems of fast reactions ( $t_{1/2} < 4$  min.) and problems of low solubilities of substrates. Calculations of rate constants were performed automatically by the Origin 6.0 program using the Guggenheim equation<sup>26</sup> from the data monitor.

### Conclusion

An evaluation of rate-rate profiles and the multiple regression analysis incorporating Y<sub>Cl</sub> scale and the appropriate N<sub>T</sub> scale [(equation (2))] plotted so far with respect to the aqueous fluorinated solvent mixtures, irrespective of the kind of neighboring group in the reaction site, can be described as the similarity of solvation effect on the

solvolytic reaction with the same mechanism.

In the case of TFE-ethanol solvent systems, according to whether substituted acetyl chloride have aromatic rings (Ph-) or alkyl groups (CH<sub>3</sub>-), a quite different solvation with a predominant stoichiometric effect (third order reaction mechanism by GBC) for Ph- groups (**4** and **5**) and the same effect as those shown in TFE-water solvent systems (loose S<sub>N</sub>2 type mechanism by electrophilic solvation) for CH<sub>3</sub>-groups (**2** and **3**) were exhibited.

The result of a regression analysis between KSIE values and  $\sigma_1$  parameters indicated that the differences in solvation are responsible for the inductive effect (electron withdrawing ability) except for sterically-hindered compounds.

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