Applications of Third Order Models in Solvolytic Reaction of Aliphatic Substituted Acyl Derivatives in 2,2,2-Trifluoroethanol-Ethanol Systems

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Rate constants at various temperatures and activation parameters are reported for solvolyses of acyl chlorides (RCOCl), with R = Me, Et, *i*-Pr, *t*-Bu, cyclopentylmethyl, benzyl, thiophenylmethyl, 2-phenylethyl, diphenylmethyl, and phenylthiomethyl in 100% ethanol, 100% 2,2,2-trifluoroethanol (TFE), 80% v/v ethanol/water and 97% w/w TFE/water. Additional rate constants for solvolyses with R = Me, *t*-Bu, and PhCH$_2$ are reported for TFE/water and TFE/ethanol mixtures, and for solvolyses with R = *t*-Bu, and PhCH$_2$ are reported for 1,1,1,3,3,3-hexafluoropropan-2-ol/water mixtures, as well as selected kinetic solvent isotope effects (MeOH/MeOD and TFE). Taft plots show that electron withdrawing groups (EWG) decrease reactivity significantly in TFE, but increase reactivity slightly in ethanol. Correlation of solvent effects using the extended Grunwald-Winstein (GW) equation shows an increasing sensitivity to solvent nucleophilicity for EWG. The effect of solvent stoichiometry in assumed third order reactions is evaluated for TFE/ethanol mixtures, which do not fit well in GW plots for R = Me, and *t*-Bu, and it is proposed that one molecule of TFE may have a specific role as electrophile; in contrast, reactions of substrates containing an EWG can be explained by third order reactions in which one molecule of solvent (ethanol or TFE) acts as a nucleophile, and a molecule of ethanol acts as a general base catalyst. Isokinetic relationships are also investigated.

Key Words : Solvolysis, Kinetics, Acyl chlorides, Solvent effects

Introduction

Studies of the stabilization of carbocation intermediates (C$^+$) and transition states for solvolytic reactions in aqueous organic solvent systems have been performed as one of the important projects for a long time. The main factors related to the stabilization have been found to be the polar solvent effect (the ionizing power, Y)[1] and the resonance effect,[2] recently Brönsted type solvation effect (*tertiary* alkyl cation)[3] and more a hydrophilic substituent effect,[4] have also been considered. Nucleophilic solvent participation on carbocations for solvolytic reactions has been interesting (so far)[5] since an appreciation of the nucleophilic solvation of C$^+$ in solvolyses of *tert*-butyl chloride (*t*-BuCl), which brought about a more suitable new S$_N$1 model compound, was reported by Kevill[6] and the nucleophilic and the electrophilic solvation effect for these reactions of benzyl[7,8] and benzoyl systems[9,10] (led by the introduction of C=O group into benzyl system) were also found out in fluorinated alcohol system favoring carbocation [including 2,2,2-trifluoroethanol (TFE)-ethanol system as medium].

Solvolyses of series of aliphatic acyl chlorides[11] (parent compound: CH$_3$COCl), were reported by Kevill[12,13] as S$_A$N mechanism in ethanolyses (highly nucleophilic media) and as (second) third order reactions by general base catalyzed (GBC) by a molecule of solvent in methanolyses, respectively. Whereas, in aqueous solvent systems, solvolytic reactions

for CH$_3$COCl and trimethyl acetyl chloride [(CH$_3$)$_3$COCl] possessing a bulky alkyl group, were evaluated by Bentley[14,15] as the bimolecular reaction (no GBC) and as the competing reaction channel, respectively according to the variation of the solvent composition. More recently, for solvolyses of substituted acetyl chlorides containing sulfur atoms in aqueous organic solvent systems including TFE-ethanol solvent systems, the same reactivity with relatively large nucleophilic solvation of the carbonyl group (C=O) relative to the electrophilic solvation were also investigated by Ryu.[16]

Other investigations for carbonyl compounds include the effect of the groups adjacent to the reaction center (C=O) in studies of kinetic and mechanism of aminolysis[17-19] and pyridinolysis[20,21] of substituted acylate compounds; observed effects are small, with substrates undergoing the same stepwise mechanism.

Our research has been conducted to obtain further information on the possible effect of adjacent groups and a possible application of third order models to solvolyses with nucleophilic participation in transition states (TS) with variable carbocation character. Aliphatic substituted acyl derivatives (Scheme) undergoing addition-elimination (S$_A$N)[12,13] and /or S$_N$2/S$_N$1[16] mechanism are chosen as the substrates for our work and the solvent systems chosen are as mentioned below.

TFE and ethanol are well known for contrasting[22,23] nucleophilicity and polarity: 100%TFE (solvent nucleophilicity, N$_T$[24,25] = −3.93 and solvent ionizing power, Y$_{Cl}$[26]: 2.79)
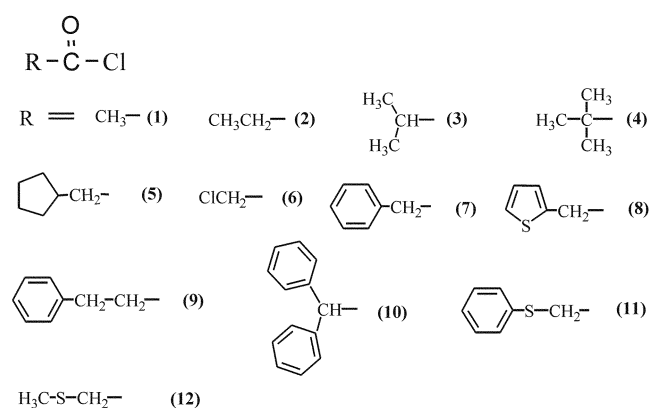
Scheme

and 100% ethanol ($N_T = 0.37$ and $Y_{Cl} = -2.5$). Kinetic studies of solvolyses in these alcohols probe for nucleophilic solvent assistance in solvolysis even though the two alcohols have dielectric constant which are closely similar ($\varepsilon_{TFE} = 26.14$ and $\varepsilon_{ethanol} = 24.32$ at 25 ℃).[27] Also 97% (w/w) 2,2,2-trifluoroethanol-water (97T) has a similar nucleophilic property to formic acid (N_{BS}[28] $= -2.59$ for 97T and -2.05 for HCO$_2$H)[29] and 80%(v/v) ethanol-water (80E) is the standard solvent for the solvent effects. As binary solvent mixtures for solvolyses, we studied TFE-ethanol solvent systems, which have a large negative gradient in the relationship[22] of solvent nucleophilicity (N) with solvent ionizing power (Y, based on 2-adamantyl tosylate) as their mixtures composition are varied, and TFE-water solvent systems with a drastic decrease in N[22,23] with an increase in TFE content. Additional solvent systems were chosen to be 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP)-water solvent systems (a relatively acidic solvent).

Solvolysis rates are analyzed by Taft's polar correlation,[30] Grunwald-Winstein plots,[26,31-33] third order reaction models, kinetic solvent isotopic effect (KSIE) and Leffler's isokinetic relationship[34] for the substrates shown in the scheme.

Results

Rate constants for solvolyses of substituted acyl derivatives of **1-11** in 100% ethanol, 80E, 100%TFE and 97T solvent systems at various temperatures and the activation parameters are shown Table 1 and rate constants for substituted acyl derivatives of **1**, **4** and **7** substituents in fluorinated alcohol systems at 0 ℃ are also shown in Table 2.

Discussion

Polar and steric relationships. This relationship was expressed as the two-term Taft eq. (1)[30] considered the role of both polar and steric effects, and has been extensively used for kinetics of the formation and hydrolysis of carboxylic ester.[36]

$$\log(k/k_o) = \rho^* \sigma^* + \delta E_s \qquad (1)$$

In eq. (1), k is the solvolytic rate constant for reaction of RCOCl, k_o is the rate constant for the standard compound [R

Table 1. First order rate constants[a] for solvolyses of aliphatic substituted acyl derivatives in solvent systems chosen at various temperatures (T) and the activation parameters

R in RCOCl	solvent	T, ℃	$k_{obs} \times 10^3/\text{s}^{-1}$	$\Delta H^{\ddagger b}$, kcal/mole	$\Delta S^{\ddagger b}$, eu
Me(**1**)-	100%EtOH[c]	-10.0	8.58 ± 0.01	12.9	-18.9
		-5.0	14.1 ± 0.1		
		0.0	21.9 ± 0.4		
	100%TFE[d]	-10.0	11.8 ± 0.1	11.2	-24.6
		-5.0	17.4 ± 0.5		
		0.0	26.8 ± 0.2		
	80%(v/v)EtOH[e]	-10.0	112 ± 1.0	13.8	-10.3
		-5.0	118 ± 1.0		
		0.0	305[f]		
	97%(w/w)TFE[g]	-13.6	18.7	13.7	-13.2
		-5.0	47.7 ± 1.0		
		0.0	57.3[f]		
		5.0	119		
Et(**2**)-	100%EtOH[c]	-12.8	7.79 ± 0.05	14.2	-13.4
		-10.0	10.5 ± 0.5		
		-5.0	17.8 ± 1.1		
		0.0	29.0 ± 0.7		
	100%TFE[d]	-12.6	6.74 ± 0.04	14.80	-11.5
		-10.0	8.50 ± 0.04		
		-5.0	15.4 ± 0.2		
		0.0	25.8 ± 0.4		
	80(v/v)%EtOH[e]	-12.4	57.1 ± 0.6	15.32	+5.14
		-10.0	78.3 ± 1.0		
		-5.0	141 ± 9.0		
		0.0	229 ± 3.0		
	97(w/w)%TFE[g]	-12.4	16.7 ± 0.2	13.1	-15.9
		-10.0	21.2 ± 0.7		
		-5.0	36.5 ± 0.1		
		0.0	55.5 ± 2.1		
i-Pr(**3**)-	100%EtOH[c]	-10.0	7.56 ± 0.1	10.6	-27.6
		0.0	16.9 ± 1.5		
		10.0	34.2[h]		
	100%TFE[d]	-10.0	5.6 ± 0.1		
		0.0	14.0 ± 0.7		
		10.0	32.8[h]		
	80%(v/v)EtOH[e]	-13.4	23.4 ± 0.6	13.8	-12.8
		-10.0	31.9 ± 0.3		
		0.0	81.8 ± 0.1		
		10.0	233[h]		
	97%(w/w)TFE[g]	-10.0	15.5 ± 0.2	12.1	-20.7
		-5.0	24.5 ± 0.1		
		0.0	37.1 ± 0.3		
		5.0	57.2 ± 1.0		
t-Bu(**4**)-	100%EtOH[c]	-10.0	1.14 ± 0.09	12.9	-22.7
		-5.0	1.89 ± 0.09		
		0.0	2.48 ± 0.01[i]		
		10.0	7.05 ± 0.27		
	100%TFE[d]	-10.0	1.34 ± 0.1	14.3	-17.2
		0.0	3.60 ± 0.01		
		10.0	9.93 ± 0.66		
	80%(v/v)EtOH[e]	-10.0	5.7 ± 0.3	13.1	-18.8
		0.0	13.4[j]		

Table 1. Continued

R in RCOCl	solvent	T, °C	$k_{obs} \times 10^3/s^{-1}$	$\Delta H^{\ddagger b}$, kcal/mole	$\Delta S^{\ddagger b}$, eu
t-Bu(**4**)-		25.0	120 ± 2.0[j]		
	97%(w/w)TFE[g]	-10.0	3.14 ± 0.04	13.4	-18.7
		0.0	8.66 ± 0.01		
		10.0	20.7 ± 0.2		
CPCH2(**5**)[k]-	100%EtOH[c]	-13.1	6.24 ± 0.01	14.6	-12.3
		-10.0	8.38 ± 0.12		
		-5.0	14.5 ± 0.5		
		0.0	25.2 ± 0.1		
	100%TFE[d]	-13.0	22.6 ± 0.3	13.4	-14.2
		-10.0	31.3 ± 1.6		
		-5.0	51.1 ± 1.0		
		0.0	82.7 ± 0.5		
	80(v/v)%EtOH[e]	-13.1	43.4 ± 0.6		
		-10.0	63.2 ± 0.4	16.0	-2.8
		-5.0	118 ± 2.0		
		0.0	200 ± 9		
	97(w/w)%TFE[g]	-13.6	40.4 ± 0.3	15.2	-6.1
		-10.0	63.1 ± 0.2		
		-5.0	106 ± 5		
		0.0	187 ± 8		
ClCH2(**6**)[l]	100%EtOH[c]	-10.0	101 ± 22		
PhCH2(**7**)-	100%EtOH[c]	0.0	20.4 ± 1.0	8.46	-35.2
		5.0	27.2 ± 0.3		
		10.0	36.7 ± 0.3		
	100%TFE[d]	-10.0	0.47 ± 0.005	12.6	-25.6
		-5.0	0.77 ± 0.04		
		0.0	1.18 ± 0.03		
	80%(v/v)EtOH[e]	-10.0	24.4 ± 0.07	11.2	-23.2
		0.0	54.7 ± 2.0		
		10.0	119 ± 2.0		
	97%(w/w)TFE[g]	0.0	3.04 ± 0.01	15.2	-14.2
		10.0	7.88 ± 0.01		
		20.0	22.1 ± 0.28		
TP-CH2(**8**)[m]-	100%EtOH[c]	-10.0	13.4 ± 0.07	9.90	-29.2
		0.0	29.3 ± 0.6		
		10.0	54.8[n]		
	100%TFE[d]	0.0	0.193 ± 0.01	13.9	-24.6
		10.0	0.423[n]		
		20.0	1.19 ± 0.05		
	80%(v/v)EtOH[e]	-10.0	36.8 ± 0.9	9.96	-28.6
		0.0	75.0		
		10.0	144[n]		
	97%(w/w)TFE[g]	0.0	0.59 ± 0.014	14.4	-20.5
		10.0	1.30[n]		
		20.0	3.75 ± 0.03		
		30.0	8.69 ± 0.19		
PhCH2CH2(**9**)-	100%EtOH[c]	-10.0	8.0 ± 0.006	13.0	-18.4
		0.0	22.0 ± 0.8		
		10.0	49.9 ± 0.1		
	100%TFE[d]	-10.0	2.29 ± 0.06	14.9	-13.9
		0.0	6.89 ± 0.08		
		10.0	18.3 ± 0.6		
	80%(v/v)EtOH[e]	-10.0	34.2 ± 0.7	13.1	-15.1

Table 1. Continued

R in RCOCl	solvent	T, °C	$k_{obs} \times 10^3/s^{-1}$	$\Delta H^{\ddagger b}$, kcal/mole	$\Delta S^{\ddagger b}$, eu
PhCH2CH2 (**9**)-		0.0	89.2 ± 2.9		
		10.0	217 ± 2.0		
	97%(w/w)TFE[g]	-10.0	5.82 ± 0.05	14.1	-14.9
		0.0	15.9 ± 0.2		
		10.0	42.2 ± 0.4		
(Ph)2CH (**10**)-	100%EtOH[c]	0.0	9.01 ± 0.12	9.99	-31.2
		10.0	15.7[h]		
		20.0	37.8 ± 0.02		
		30.0	57.0 ± 0.01		
	100%TFE[d]	0.0	0.163 ± 0.06	15.6	-18.9
		10.0	0.370[h]		
		20.0	1.03 ± 0.04		
		30.0	3.02 ± 0.22		
	80(%v/v)EtOH[e]	0.0	22.6 ± 0.4	11.0	-25.6
		10.0	41.9[h]		
		20.0	97.2 ± 2.0		
	97%(w/w)TFE[g]	0.0	0.35 ± 0.01	14.7	-20.1
		10.0	0.94[h]		
		20.0	2.4 ± 0.1		
PhSCH2(**11**)-	100%EtOH[c]	-10.0	12.6 ± 0.3	9.92	-29.3
		0.0	27.5 ± 0.1		
		10.0	51.7[n]		
	100%TFE	0.0	0.143 ± 0.01	15.6	-19.1
		10.0	0.33[n]		
		20.0	1.09 ± 0.04		
	80%(v/v)EtOH[e]	-10.0	30.5 ± 1.0	10.3	-26.0
		0.0	68.0 ± 0.4		
		10.0	132[n]		
	97%(w/w)TFE[g]	0.0	0.485 ± 0.008	14.4	-20.9
		10.0	1.11[n]		
		20.0	3.04 ± 0.01		
		30.0	7.26 ± 0.29		

[a]Determined conductimetically at least in quadruplicate; typically injected 4 μL of 1%(w/w) substrate in dry acetonitrile into the kinetic apparatus with a turbo-stirrer containing 2 mL of each solvent systems: errors shown are the standard deviations. [b]Calculated from Eyring plots. [c]Pure ethanol solvent. [d]Pure 2,2,2-trifluoroethanol solvent. [e]80%(v/v) ethanol-water solvent system. [f]Data from ref. 14. [g]97%(w/w) trifluoroethanol-water solvent system measured exactly as 96.87%(w/w) by using a Karl Fisher Titrator. [h]Data from ref. 35. [i]Reported as $k = 2.49 \times 10^{-3}s^{-1}$ in ref. 15. [j]Data from ref. 15. [k]Presented as cyclophentyl acetyl chloride. [l]Solvolysis rate in 100% TFE solvent was too slow to measure under our experimental condition. [m]Presented as thiophenyl-2-acetyl chloride. [n]Data from ref. 16 [electronic supplementary information (ESI) available: TableS1-S3, see http//www.rsc.org/suppdata/p2/b2/b202664n/].

= Me-(**1**)], σ^* is a polar substituent parameter for R-, E_s is a steric parameter for R- and ρ^* and δ are susceptibilities for each substituent parameter, respectively.

Our work recognizes the formal similarity of solvolyses of acid chlorides and carboxylic esters, analyzed in terms of the eqn. (1). The results of correlation analysis involving multiple regression on ρ^* and δ are tabulated in Table 3.

Higher contributions of a polar effects ($0.65 < \rho^*$) relative to a steric effects (rather small: $0.18 < \delta < 0.50$) were obtained for solvolyses in pure ethanol and 80E (relatively

Table 2. First order rate constants ($k \times 10^3/\text{s}^{-1}$) for solvolyses of various substituted acyl chloride in aqueous fluorinated alcohol and trifluoroethanol (T)-ethanol (E) solvent mixtures at 0 °C[a]

Solvent[b]	1	4	7
90% TFE	209 ± 1.0	22.3 ± 0.1	9.17 ± 0.01
80% TFE	775 ± 2.0	54.9 ± 0.2	2.21 ± 0.09
70% TFE	1440[c]	164 ± 1.0	5.64 ± 0.1
60% TFE	–	268 ± 5.0	–
50% TFE	–	336 ± 3.0	1.12 ± 0.02
80T-20E[d,e]	36.3 ± 0.2	4.90 ± 0.06	4.86 ± 0.00
60T-40E[d,e]	33.7 ± 0.1	4.17 ± 0.01	7.64 ± 0.04
50T-50E[d,e]	31.4 ± 0.1	3.86 ± 0.03	9.46 ± 0.05
40T-60E[d,e]	29.5 ± 0.2	3.46 ± 0.01	11.7 ± 0.02
20T-80E[d,e]	26.2 ± 0.1	3.06 ± 0.01	16.1 ± 0.06
97% HFIP[f,g]	–	51.4 ± 0.1	7.52 ± 0.02
90% HFIP[f]	–	58.3 ± 0.1	14.6 ± 0.11
50% HFIP[f]	–	269 ± 0.4	106 ± 2

[a]Performed under the same condition as footnote a of Table 1. [b]Percentage of solvent composition based on weight/weight. [c]Data from ref. 14. [d]Percentage of solvent composition based on volume/volume. [e]T-E is 2,2,2-TFE-ethanol solvent systems. [f]HFIP is 1,1,1,3,3,3-hexafluoro-2-propanol-water solvent systems. [g]Measured exactly as 97.31% (w/w) by using a Karl Fisher.

Table 3. Correlation of $\log(k/k_{80E})$ and $\log(k/k_{Me-(1)})$ for solvolyses of series of aliphatic substituted acetyl chloride studied in this work at 0 °C with Taft's single (polar) and dual (polar-steric) parameters[a]

Solvent	parameters	n[b]	r[c]	ρ^{*}[d]	δ[d]	c[e]
ethanol	σ^{*}	5[f]	0.964	0.50		-0.593
	σ^{*}, E$_s$	7	0.955	0.70	0.49	0.12
TFE	σ^{*}	7	0.995	-2.27		-1.18
	σ^{*}, E$_s$	7	0.975	-2.08	0.62	-0.40
80% (v/v) ethanol-water	σ^{*}, E$_s$	7	0.924	0.66	0.19	-0.21
97% (w/w)	σ^{*}	7	0.974	-2.26		-0.760
TFE-water	σ^{*}, E$_s$	7	0.981	-2.07	0.77	-0.29

[a]Used by polar (σ^{*}) and steric (Es) parameters quoted from ref. 38 for aliphatic system within the range of all those known and $\log(k/k_{80E})$ were used for single regression parameter (σ^{*}) (k_{80E}; rate constant in 80%(v/v) ethanolwater solvent system) and $\log(k/k_{Me-(1)})$ was used for dual regression parameter (σ^{*} and E$_s$) ($k_{Me-(1)}$; rate constant for acetyl chloride). [b]Number of acyl derivatives used for correlation. [c]Correlation coefficient. [d]Susceptibility to each parameter chosen. [e]Value of constant obtained from the correlation. [f]Two points for **1** and **2** acyl derivatives were removed due to the deviation from correlation (as shown in Figure 1)

nucleophilic solvents). Our results for ethanolyses are appreciably different from those reported previously[12] (*e.g.* $\rho^{*} = 0.547$, $\delta = 0.527$ and r = 0.933). This is probably due to the different substituents analyzed (r = 0.955 for this work). As pure TFE and 97T are relatively acidic, weakly nucleophilic solvents, steric effects ($0.62 < \delta$) are of greater importance in determining the rates and more negative ρ^{*} values (−2.08) were obtained.

Considering only polar (σ^{*}) parameter and of replacing k_o for Me-(**1**) group by k_{80E} for R-groups in 80E solvent system, led to the eq. (2).

$$\log(k/k_{80E}) = \rho^{*}\, \sigma^{*} \qquad (2)$$
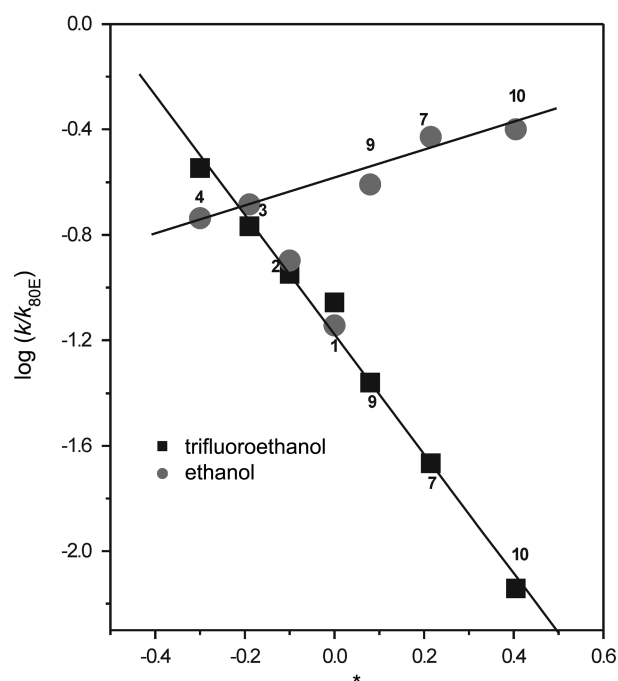
Figure 1. Taft's polar relationship using the eq. (2) for solvolyses of aliphatic substituted acyl derivatives in chosen solvent systems according to structural change in the substitutents at 0 °C.

Equation (2) permits the efficient interpretation of the effect of adjacent groups (especially the downward deviation shown in Figure 1). Solvolyses in TFE give a good the $\rho\,\sigma^{*}$ plot (slope −2.27, Table 3), showing reactions disfavoured by electron-withdrawing groups (EWG). For pure ethanol solvent, the points for **1**, **2** and **3** laid surprisingly on the same correlation line as TFE (Figure 1), indicating similar solvolysis rates in TFE and ethanol solvents. In contrast, other ethanolyses gave a correlation of small positive slope [slope (ρ^{*}) = 0.50, n = 5 and r = 0.964; except for **1** and **2**].

Grunwald-Winstein (GW) correlations. Correlation of solvolysis rates with changes in solvent composition has been evaluated by an one term Grunwald-Winstein (GW) eq. (3).[26,31a]

$$\log(k/k_{80E}) = mY_{Cl} + c \qquad (3)$$

In the equation (3), k and k_{80E} are solvolysis rates in a given solvent and 80E solvent system as a standard solvent, respectively and Y_{Cl}[20] is a solvent ionizing power parameter based on solvolysis rates of 1-adamantyl chloride[1] as a standard substrate with m = 1.00 and the sensitivity to the change in those parameters, respectively, and c is a residual (constant) term. Equation (3) has performed satisfactorily in the role as a tool of mechanistic criteria on the basis of the degree of electrophilic solvation on the ionization TS (unimolecular character) with respect to the change of solvent composition.

Introduction of lN_T term, corresponding solvent nucleophilicity term (bimolecular character), into the eq. (3) led to the two terms (extended) GW eq. (4).[31b,32]

$$\log(k/k_o) = mY_{Cl} + lN_T + c \qquad (4)$$

In eqn. (4), l is the sensitivity to change in solvent nucleophilicity N_T (based on solvolysis rates of S-methyl dibenzothiophenium ion[24]).[6,25] Multiple correlation using eq. (4) have been highly successful for solvolyses of acid
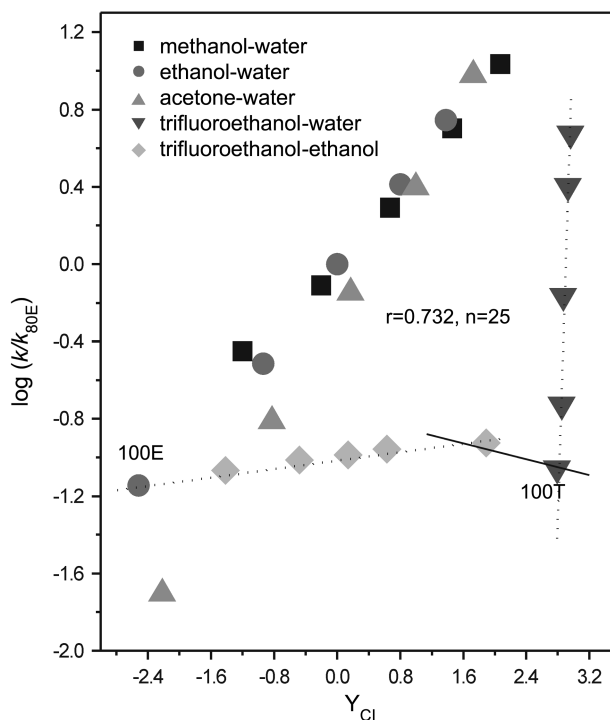
Figure 2. Grunwald-Winstein plot for solvolyses of Acetyl chloride (1) at 0 °C. (kinetic data were quoted from ref. 14 and Table 2 in this work).
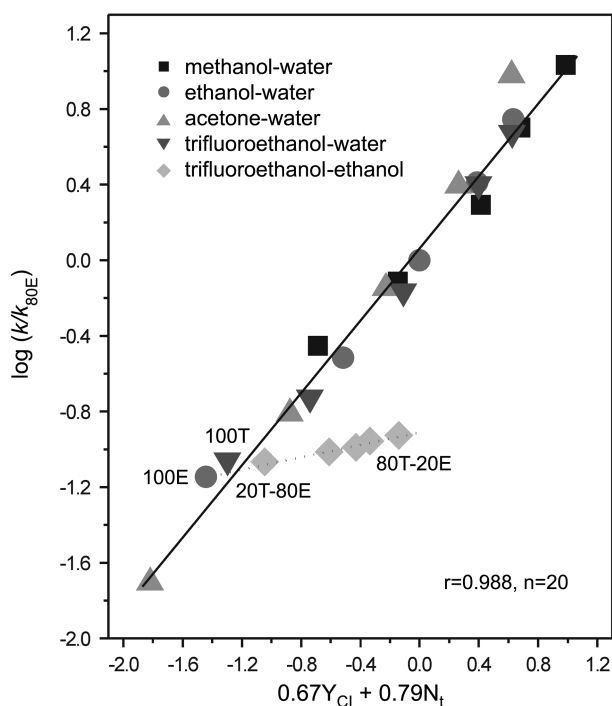
Figure 3. Extended Grunwald-Winstein plot for solvolyses of Acetyl chloride at 0 °C. (condition analysed were shown in g and h footnote of Table 4).

chlorides[37-39] reacting via a single mechanism over the range of organic solvents, and nucleophilic solvation is one cause of dispersed Grunwald-Winstein correlation (eq. 3). Further investigation of the differential reactivity in ethanolysis separated according to whether substituent is alkyl or arylaliphatic group was attempted using an one-term (eq. 3) and the two-terms (extended) Grunwald-Winstein equation (eq. 4).

Solvolyses of aliphatic substituted acyl derivatives were studied over a wide the range of aqueous organic solvents including TFE-ethanol to inquire further into the reactivity in terms of the solvent effect. These results of correlation analyses involving multiple regression on Y_{Cl} and N_T (eqns. 3 and 4) are described in Table 4 and the previous results reported so far for acid chlorides are also included in Table 4 (and /or in footnotes). Typical correlations for one-term and two-terms GW parameter correlation in solvolyses of acetyl chloride (**1**) at 0 °C are plotted in Figure 2 and 3 respectively.

Comparison between Figure 2 and 3 exhibited that the separate linear correlation in TFE-water solvent system (Figure 2) became a single linear correlation with $\log(k/k_{80E})$ = $(0.67 \pm 0.03)Y_{Cl}$ + $(0.79 \pm 0.04)N_T$ + 0.09 ± 0.04 (r = 0.988 and n = 20) see Figure 3. When solvolyses rates in all solvent systems including TFE-ethanol solvent system are analyzed by eq. (4), an unacceptable correlation coefficient (r = 0.934 and n = 25) was obtained, so that separate discussion is needed for these solvolyses. Anyway, from a single correlation in aqueous organic solvent systems

Table 4. Correlation analyses of $\log(k/k_{80E})$ for solvolyses of various acetyl chlorides with the multiple parameter Grunwald Winstein equation [(3)and (4)][a]

R in RCOCl	parameter	solvent	n[b]	r[c]	m[d]	l[d]	c[e]
1[f,g] (0 °C)	Y_{Cl}, N_T	all	20	0.988	0.67	0.79	0.09
3[h] (10 °C)	Y_{Cl}, N_T	f[i]	6	0.982	0.81	0.72	
4[g,i,j] (0 °C)	Y_{Cl}, N_T	all	18	0.994	0.90	0.75	-0.258
4 (0 °C)	Y_{Cl}, N_T	f[i]	9	0.981	0.92	0.74	-0.331
4[h] (10 °C)	Y_{Cl}, N_T	f[i]	7	0.987	0.97	0.74	
7 (0 °C)	Y_{Cl}, N_T	f[i]	9	0.989	0.79	0.95	-0.950
8[k] (10 °C)	Y_{Cl}, N_T	all	33	0.959	0.42	1.03	0.031
11[k] (10 °C)	Y_{Cl}, N_T	all	35	0.963	0.39	1.02	0.002
12[k] (10 °C)	Y_{Cl}, N_T	all	33	0.964	0.46	1.02	-0.016
ρ-NO$_2$Ph-[l] (25 °C)	Y_{Cl}, N_T	all	34	0.969	0.54	1.78	0.110

[a]The multiple regression analysis was performed using Origin 6.0 program using the values of solvent parameter for Y_{Cl} and N_t quoted from ref. 26 and ref. 6, 25. [b]Number of solvents. [c]Correlation coefficient. [d]Susceptibility to each solvent parameter chosen. [e]Value of constant obtained from the correlation. [f]Result analyzed using data from ref. 14 and Table 2. And the result in agreement with those reported Bentley (the m = 0.86 and the l = 0.68) in aqueous solvent system including acetic acid solvent. [g]Except for trifluoroethanol-ethanol solvent systems in correlation. [h]For aqueous fluorinated alcohol and data quoted from ref. 35. [i]Result analyzed using data from ref.15 and Table 2. [j]Solvent systems chosen for correlation is only higher aqueous binary mixtures known as the range of S_N1 mechanism (the dual reaction channel) (ref. 15 and ref. 16). [k]Result analysed using data from ref. 16 [l]Quoted from ref. 37b and the m- and the l- values for solvolyses of acid chloride S_AN pathway; 0.57, 1.68 for PhOCOCl (ref. 37b), 0.58, 1.59 for MeOCOCl (ref. 40) and 0.46, 1.61 for ρ-NO$_2$PhCH$_2$OCOCl (ref. 37c), respectively.
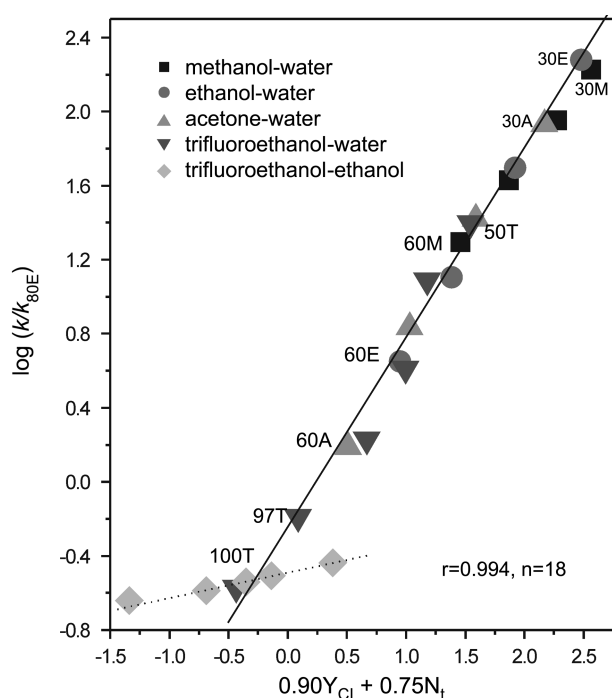
Figure 4. Extended Grunwald-Winstein plot for solvolyses of trimethylacetyl chloride (**4**) at 0 °C. [in case of including TFE-ethanol system, r = 0.975 (n = 23) was obtained and condition analyzed are shown in g, i and j footnote of Table 4].

meaning a single reaction channel, the solvent effects for this reaction with a loose type S_N2 mechanism (reported by Bentley[14]) quantitatively dissected into the contribution from solvent ionizing power (m = 0.67) consistent with C-Cl cleavage and solvent nucleophilicity (l = 0.79). But, for TFE-ethanol solvent systems, not containing water, no major change of correlation patterns were observed in Figure 2 and Figure 3.

A similar pattern to those discussed above for **1** is also seen in solvolyses of **4** (dual reaction channel) within a range of S_N1 solvent systems at 0 °C. The plot for this result from multiple regression analysis with log(k/k_{80E}) = (0.90 ± 0.03)Y_{Cl} +(0.75 ± 0.03)N_T + (0.2 ± 0.095) (r = 0.994 and n = 18) is shown in Figure 4.

Considering on the basis of the multiple correlation of *t*-BuCl (m = 0.86 and l = 0.38 for S_N1 standard compound)[6] with nucleophilically-solvated cation intermediate, those of trimethylacetyl chloride (*t*-BuCOCl, **4**), led by the introduction of C=O group into *t*-BuCl, in rich aqueous media was considered as being a consequence of the ionization mechanism with considerably nucleophilic solvent participation (about relatively two fold the l value) on developing carbocation. A greater m value for **4** relative to those for **1** would be consistent with the dominant electronic effect to be expected in the presence of three methyl groups. As shown in Figure 3, the deviation (like **1**) from the TFE-ethanol correlation also was displayed for solvolysis rates of **4**.

In turn, an acceptable linear correlation in aqueous organic solvents including TFE-ethanol solvent systems have been reported previously for solvolyses of substituted acyl

derivatives[16] containing S-atom, para-substituted benzoyl derivatives (*p*-XC₆H₅COCl)[37d] and chloroformate systems (ROCOCl)[37b,c,40] and these results are described in Table 4 (and/or footnotes). Such phenomena can be explained by the similarity of mechanism caused by the similarity of the role of solvent molecules (as a nucleophile) in aqueous organic and TFE-ethanol solvent systems to stabilize TS structure.

Although solvolyses of cyclopropylcarbinyl and cyclobutyl bromides were reported by Kevill[5] as the reaction proceeding via the ionization mechanism with an appreciate nucleophilic solvation of carbocation (like *t*-BuCOCl), the correlation lines including the points of TFE-ethanol solvent systems (slightly below one) were shown in these solvolyses.

Consequently, solvolyses of **1** and **4** having two separate correlation lines using eqn. (4), for aqueous media or non aqueous media (TFE-ethanol solvents), can be rationalized in terms of two different modes of nucleophilic attack on the C=O group (see below).

Two third order reaction models. Nucleophilic attack by the molecule of solvent has been quantitatively evaluated by a third order reaction model,[35,41] based on a general base catalyzed (GBC) reaction involving another molecule of solvent. For solvolyses in TFE-ethanol solvents,[35,41b] we could establish eq. (5) having four possible third order reactions:

$$k_{obs} = k_{EE}[ethanol]^2 + k_{TT}[TFE]^2 + (k_{ET} + k_{TE})[ethanol][TFE] \quad (5)$$

the letter described in the subscript of third order rate constants (k) in eq. (5) represents the role of solvents as a nucleophile (first letter) and/or as a general base (second one) (E: a molecule of ethanol and T: a molecule of TFE. e.g. k_{ET} term; E as a nucleophile and T as a general base). In cases where it is established that yields of trifluoroethylated products are low, equation (5) has been simplified by assuming that the main factor determining the rate constants is nucleophilic attack by ethanol, assisted by another molecule of ethanol.[41c] More generally, we have shown that the rates of solvolyses of acyl chlorides, containing aromatic rings or other EWG, can be explained using eqn. (6) (in which only the k_{TT} term is ignored),[35] in these cases, k_{obs}/ [ethanol]^2 is linearly related to the solvent ratio [TFE]/ [ethanol] (Table 5), and solvolysis rates in ethanol are significantly faster than in TFE (see k_E/k_T ratios for substrates **7-12** and others in Table 5).

$$k_{obs}/[ethanol]^2 = k_{EE} + (k_{ET} + k_{TE})[TFE]/[ethanol] \quad (6)$$

The slightly negative slope of the correlation using eq. (6) (Table 5) observed for solvolyses of *p*-nitrobenzoyl chloride at 10 °C could be an expression of dominant dependence on two ethanol molecules (k_{EE} term) compared with other solvent molecules.[41c] Benzoyl chloride showed an excellent correlation (r = 0.998 and n = 4) with a slightly positive slope.

However, solvolyses of substrates **1-4** in TFE/ethanol mixtures give low k_E/k_T ratios (Table 5), and are not well correlated using eq. (4) (see Figures 3 and 4). In contrast,

Table 5. Results analysed using third order model equations [(6) and (7)] and selectivity (k_E/k_T) values for solvolysis rates of aliphatic substituted acetyl chloride in trifluoroethanol-ethanol solvent mixtures

| R in RCOCl | $k/10^{-4}s^{-1}L^2mol^{-2}$ | | r[b] | slope/intercept[c] | k_E/k_T[d] |
	slope[a]	intercept[a]			
1[e] (0 °C)	4.33 ± 0.14 (4.37)[f]	1.41 ± 0.15 (1.39)[g]	0.998	3.07	0.817
2[h] (0 °C)					1.12
3[h] (0 °C)					1.21
3[i] (10 °C)	5.84 ± 0.29 (5.14)[f]	1.75 ± 0.31 (1.70)[g]	0.996	3.34	1.04
4[e] (0 °C)	0.488 ± 0.017 (1.06)[f]	0.213 ± 0.017 (0.197)[g]	0.998	2.29	0.647
4[i] (10 °C)	1.64 ± 0.08	0.500 ± 0.08 (0.514)[g]	0.997	3.29	0.710
7[e] (0 °C)	1.08 ± 0.06	0.548 ± 0.094 (0.703)[j]	0.993	1.98	17.3
8[k] (10 °C)	0.665 ± 0.081	2.22 ± 0.10 (1.89)[j]	0.972	0.30	129
10[i] (10 °C)	0.803	0.557 (0.541)[j]	0.996	1.44	42.4
11[k,l] (10 °C)	0.480 ± 0.10	0.960 ± 0.160 (1.78)[j]	0.942	0.16	157
12[k] (10 °C)	1.16 ± 0.06	1.93 ± 0.09 (1.82)[j]	0.994	0.6	77.9
MeOPhCH$_2$-[i] (10 °C)	3.44	1.49	0.99	2.31	7.42
PhCOCl[m]- (10 °C)	$(1.31 \pm 0.06) \times 10^{-2}$	$(6.72 \pm 0.21) \times 10^{-2}$ (6.54×10^{-2})[j]	0.998	1.94	2[n]
P-NO$_2$PhCOCl[m]- (10 °C)	$-(4.32 \pm 0.76) \times 10^{-2}$	0.128 ± 0.003 (0.126)[j]	0.970		120[n]

[a]In case of **1**, **3** and **4** groups, the slope and the intercept obtained from the plot using eq. 7 (including pure TFE, but excepted 40T-E solvent system) correspond to ($k_{ET} + k_{TE}$) term and k_{TT} term, respectively, but except for these compounds, the intercept is required to be changed as k_{EE} term obtained from the plot using eq. 6 (whole the range of TFE-ethanol studied in this work for correlation). [b]Correlation coefficient. [c]Corresponded to the k_{TE}/k_{TT} ratio.for **1**, **3** and **4** groups and to the k_{TE}/k_{TT} ratio for other compounds. [d]Ratio of solvolysis rates between those corresponding for pure ethanol (k_E) and pure TFE solvent (k_T). [e]Result obtained from Table 2. [f]Data quoted for methanolyses in acetonitrile at 0 °C from Table 2 of ref. 13 [g]Calculated by $k_{TT} = k_{obs}/[TFE]^2$. [h]Data from Table 1. [i]Result obtained from ref. 35. [j]Calculated by $k_{EE} = k_{obs}/[EtOH]^2$. [k]Result obtained from ref. 16. [l]Removed the point for 80T-E solvent system. [m]Result obtained from ref. 9 (using Kinetic data in 40T-E, 30T-E, 20T-E and 100E). [n]Data from ref. 9.
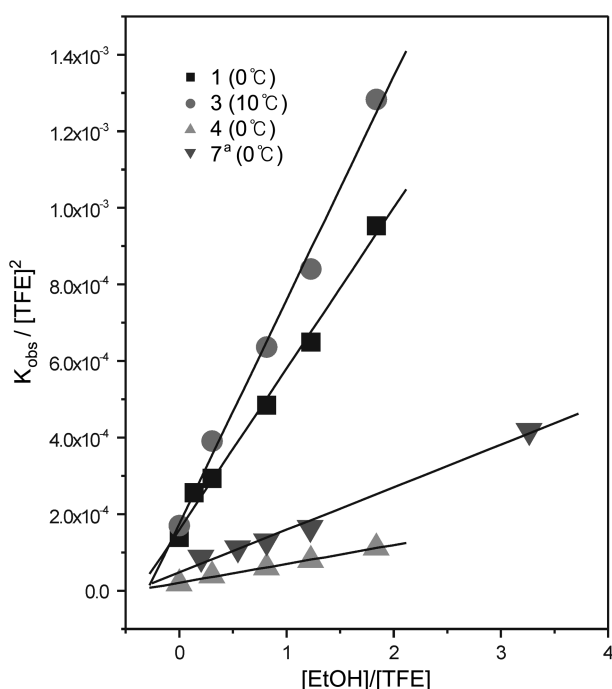
Figure 5. Plots of $k_{obs}/[TFE]^2$ *vs.* molar ratio of ethanol and TFE for solvolysis of aliphatic substituted acetyl chloride chosen in TFE-ethanol system. [a]Plotted using eq. (6).

solvolyses of **12** are well correlated using eq. (4).[16] To explain the results for **1-4**, we now propose an alternative third order mechanism in which the solvent molecule assisting nucleophilic attack acts as an electrophile (not as

general base). In support of this proposal, electrophilic assistance by phenol accelerates solvolyses of acetyl chloride, but retards solvolyses of chloroacetyl chloride.[13] As TFE is a better electrophile than ethanol, if the k_{EE} term in eq. (5) is ignored, we then obtain eq. (7). Consequently, $k_{obs}/[TFE]^2$ should be linearly related to the solvent ratio [ethanol]/[TFE], as found (Figure 5, Table 5).

$$k_{obs}/[TFE]^2 = k_{TT} + (k_{ET} + k_{TE})[ethanol]/[TFE] \quad (7)$$

The different values of the k_E/k_T ratio for **4** from those values for other acyl chloride with alkyl groups is responsible for dual reaction channel depending on the characteristic of solvents. Relatively large *l*-values in solvolysis of aliphatic substituted acyl derivative do not seem to be a conclusive clue to the type of assistance to nucleophilic solvation (third order reactions with GBC or electrophilic assistance).

Kinetic solvent isotope effects (KSIEs). In the studies on acid chloride solvolyses proceeding *via* S$_A$N mechanisms, the determination of the values for KSIE (KSIE in methanol $\geq$ 2.0),[41a-c,42] presented as k_{ROH}/k_{ROD} rate ratios, provided convincing evidence for third order reactions, based on powerful GBC by one molecule of solvent. High values (>1.6)[43] as (possible) third order[6b,c] reactions and low values ($\leq$ 1.2)[44,45] as S$_N$1 or S$_N$2 reactions have been proposed, respectively.

KSIE values determined for this work are given in Table 6 (along with selected literatures values). New results for CF$_3$CH$_2$OD are included, and values corresponding to the range of S$_N$2/S$_N$1 reaction mechanisms were observed. These results support the exclusion of the k_{TT} term (proposed in eq.

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Table 6. First order constants (k/s^{-1}) in methanol and trifluoro-ethanol for kinetic solvent isotope effect (KSIEs)[a]

R in RCOCl	methanol	methanol-D[b]	k_{ROH}/k_{ROD}[c]
2 (0 °C)	$(4.06 \pm 0.03) \times 10^{-2}$	$(2.85 \pm 0.07) \times 10^{-2}$	1.42
5 (0 °C)	$(4.33 \pm 0.09) \times 10^{-2}$	$(3.12 \pm 0.07) \times 10^{-2}$	1 38
8 (10 °C)			1.80[d]
9 (0 °C)	$(7.99 \pm 0.04) \times 10^{-2}$	$(5.41 \pm 0.20) \times 10^{-2}$	1.48
10 (10 °C)			1.61[d]
ρ-NO$_2$Ph- (25 °C)			2.27[e]
11 (10 °C)			1.68[d]
12 (10 °C)			1.48[d]
	trifluoroethanol	trifluoroethanol-D[f]	
1 (0 °C)	$(2.67 \pm 0.01) \times 10^{-2}$	$(2.64 \pm 0.02) \times 10^{-2}$	1.01[g]
3 (0 °C)	$(1.40 \pm 0.07) \times 10^{-2}$	$(1.34 \pm 0.03) \times 10^{-2}$	1.04[h]
4 (0 °C)	$(3.60 \pm 0.01) \times 10^{-3}$	$(3.53 \pm 0.01) \times 10^{-3}$	1.02[i]
7 (0 °C)	$(1.23 \pm 0.01) \times 10^{-3i}$	$(1.23 \pm 0.01) \times 10^{-3}$	1.00[k]
CDPM[l] (0 °C)	$(1.16 \pm 0.02) \times 10^{-1}$	$(1.04 \pm 0.02) \times 10^{-1}$	1.12[m]

[a]Determined under the same conditions as shown in footnote a in Table 5. [b]Methanol-D was Aldrich (>99.5% D). [c]Kinetic solvent isotope effect. [d]Data from ref 16. [e]Data from ref. 41b. [f]Trifluoroethanol-D was Aldrich (>99% D). [g]1.32 of KSIE in methanol from ref. 16. [h]1.37 of KSIE in methanol from ref. 16. [i]1.46 of KSIE in methanol from ref. 16 and 1.55 for PhCOCl from ref.14. [j]Rate constant measured for KSIE was within the range of standard deviation, when compared previous the result of rate constant [$k = (1.18 \pm 0.06) \times 10^{-3}$] obtained as shown in Table 1. [k]1.40 of KSIE in methanol from ref. 16. [l]Chlorodiphenyl methane. [m]1.06 of KSIE in methanol at 35 °C from ref. 46.

6), and show the absence of GBC by a TFE molecule. The slightly higher value of 1.12 for chlorodiphenylmethane (CDPM)[46] can be rationalized as the result of a degree of electrophilic assistance.

Leffler's isokinetic relationship[33] (eq. 8), a linear relationship showing the compensation effect between activation enthalpies and entropies of a series of reactions related by structural change, was applied to solvolyses of acetyl chloride over a wide range of substituents.

$$\delta\Delta H^{\ddagger} = \beta\delta\Delta S^{\ddagger} \qquad (8)$$

For the plot for pure ethanol and TFE solvents, a linear plot with the isokinetic temperature ($\beta = 268.2$ K; r = 0.996 and n = 12 in Figure 6) separates these relationship into two parts, one having a good linear correlation and another showing deviations above the line. Most points form a straight line consisting of activation parameters for all ethanolyses of all substrates (except for **4**). This result means that these ethanolyses are within the same series of reactions controlled by structural changes in a bimolecular TS. The points for solvolyses of **1**, **2** and **3** in pure TFE lie on this same line (like Figure 1) with similar slope ($\beta = 254.5$ K), but a different intercept was observed for **4** possibly due to steric hindrance.[47]

For all solvolyses of arylaliphatic substrates (**7**-**11**) in TFE, the scattered points again show positive deviations from the linear correlation and the degree of the deviation appears to be related to the k_E/k_T (>1) terms and/or the $(k_{ET} + k_{TE})/k_{EE}$ term. Such phenomena are attributed to the lesser role of TFE as nucleophile at the formation of TS structure.
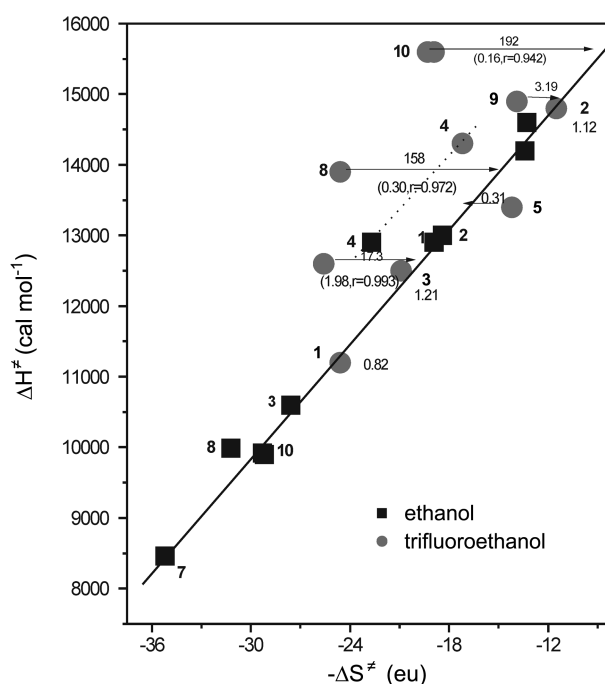
Figure 6. Isokinetic relationship: plots of $\Delta H^{\ddagger}$ *vs.* $\Delta S^{\ddagger}$ for solvolyses of aliphatic substituted acyl derivatives in 100% ethanol and 100% trifluoroethanol solvent systems according to structural change in substituents [numerals; (k_E/k_T, parenthesis; ($k_{ET} + k_{TE}$)/k_{EE}].
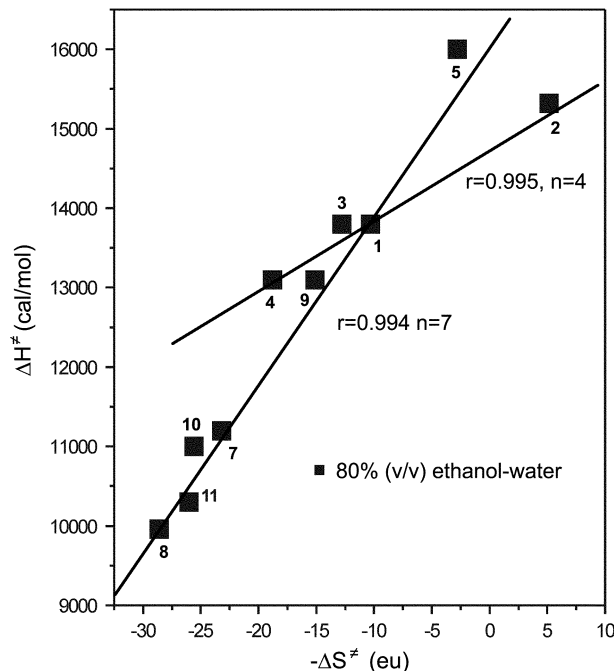
Figure 7. Isokinetic relationship: plots of $\Delta H^{\ddagger}$ *vs.* $\Delta S^{\ddagger}$ for solvolyses of aliphatic substituted acyl derivatives in 80%(v/v) ethanol-water solvent systems according to structural change in substituents. Isokinetic temperature, $\beta = 226.7°$ (r = 0.994, n = 7) and $\beta = 91.38$ °C (r = 0.995, n = 4).

For 80% (v/v) ethanol-water, two separate linear correlations with $\beta = 226.7$ K (r = 0.994 and n = 7) for arylaliphatic substrates (as well as for **1** and **5**) and with $\beta = 91.4$ K

(r = 0.995 and n = 4) for **1**, **2**, **3** and **4**, were observed (Figure 7). Isokinetic relationships for substituted acyl derivatives in our work show a high sensitivity to polar aqueous media (particularly alkyl groups). Consequently, in this solvent system, these reaction depended on the solvent effect (rather than electronic effect) were controlled by entropy ($\Delta S^{\ddagger}$) value because the β values are less than the experimental temperature ($\beta < T_{exp}$).[33]

Conclusion

Successful applications of third order models using the eqns. (6) and (7) for solvolyses of aliphatic substituted acyl derivatives (S_N2/S_N1 process) in TFE-ethanol solvent systems depend on whether arylaliphatic or alkyl groups are present. The different contributions of third order rate constants obtained from linear correlation with positive slopes were shown to be the k_{EE} and the k_{TE} terms for arylaliphatic and the k_{TT} and k_{ET} (TFE molecule in a specific role as an electrophile) terms for alkyl groups, respectively. The contributions from the $(k_{ET}+k_{TE})/k_{EE}$ terms analyzed for arylaliphatic substituted acyl derivatives increase in the order **9** < **7** < **10** < **8** < **11** group, providing strong support for the fact that the ratio of those third rate constants are not dependent on the degree of the solvent nucleophilic participation (the l values) in the rate determining step (rds) but TS structure favoring electrophilic solvation. Solvolytic reactions of those derivatives with alkyl groups undergoing the positive charge developing on the C=O group in the rds fit eq. (7) and could be mainly controlled a molecule of TFE solvent acting as a electrophile.

Taft's polar correlation (Figure 1) and isokinetic relationship (Figure 6) with the phenomena of collinearity, the results analyzed by Grunwald-Winstein parameter and KSIE effects have confirmed as the nucleophilic solvent participation (reflected alkyl groups favoring carbocation TS) in solvolyses of those derivatives with alkyl group, but for arylaliphatic substituted acyl derivatives, solvolyses which proceed through the nucleophilic solvation of TS with no the adjacent effect were observed.

Experimental Section

Materials. Solvents used for kinetics were dried and distilled by standard methods except for 1,1,1,3,3,3-hexa-fluoro-2-propanol (HFIP, 99%), methanol-*D* (>99.5% D) and trifluoroethanol-*D* (>99%D) which used Aldrich reagents without distillation. 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 (Model: ORION AF instrument) using (Hydranal composite 5 K reagent (precision: 0.3% at 1mg H_2O). TFE-ethanol and other solvent mixtures were prepared by volume percentage (%v/v).

Solvolyses of aliphatic substitutes acetyl chlorides (RCOCl) used Aldrich reagents for: R = Me (**1**, purity 98%);

R = Et (**2**, 98%); R = *i*-Pr (**3**, 98%); R = *t*-Bu (**4**, 99.6%); R = chloromethyl (**6**, 98%); R = benzyl (**7**, 98%); R = thiophenylmethyl (**8**, 98%) R =; 2-phenethyl (**9**, 98%); R = diphenylmethyl (**10**, 97%); and R = phenylthiomethyl (**11**, 97%), and used Lancaster reagents for R = cyclophenyl-methyl (**5**, 98%); without distillation and/or recrystallization.

Kinetic methods. The rate constants were determined using a general conductimetric method,[35] which were performed by the Origin 6.0 program using the Guggenheim equation[49] from data monitor automatically..

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