Nucleophilic Substitution Reaction of α-Methoxy-α-(trifluoromethyl)phenylacetyl Chloride in Alcohol-Water Mixtures

In Sun Koo,* Seong In Lee, Sun Kyoung An, Kiyull Yang, and Ikchoon Lee†

Department of Chemical Education, Gyeongsang National University, Chinju 660-701, Korea
†Department of Chemistry, Inha University, Incheon 402-751, Korea

Received August 26, 1999

Solvolyses of α-methoxy-α-(trifluoromethyl)phenylacetyl chloride in H_2O, D_2O, CH_3OD, 50% D_2O-CH_3OD, and in aqueous binary mixtures of acetone, dioxane, ethanol and methanol are investigated at 25.0 °C. The Grunwald-Winstein plots of first-order rate constants for α-methoxy-α-(trifluoromethyl)phenylacetyl chloride with Y_{Cl} show a dispersion phenomenon. Solvent nucleophilicity N has been shown to give considerable improvement when it is added as an lN term to the original Grunwald-Winstein for the solvolyses of α-methoxy-α-(trifluoromethyl)phenylacetyl chloride. The dispersions in the Grunwald-Winstein correlations in the present studies are caused by solvent nucleophilicity. The magnitude of l and m values associated with a change of solvent composition predicts the associative S_N2 transition state. The kinetic solvent isotope effects determined in deuterated water and methanol are consistent with the proposed mechanism of the general base catalyzed associative S_N2 or S_AN mechanism for the of α-methoxy-α-(trifluoromethyl)phenylacetyl chloride.

Introduction

The mechanism of nucleophilic substitution reaction of aroyl halides has been investigated intensively for many years experimentally[1] and theoretically.[2] Recent mechanistic work on the solvolysis of acyl chlorides in alcohol-water mixtures indicated that the reactions proceed by competing mechanisms involving two broad channels:[3,4] electron donation by an aryl group favors a carbocation or an S_N2-S_N1 process whereas electron withdrawal favours a general base catalysed process having a lower sensitivity to changes in solvent ionizing power. Lee *et al.*,[5] investigated the mechanism of the reactions of benzoyl fluorides and chlorides with anilines in methanol and acetonitrile. The results of all these works are reported to be consistent with a concerted displacement mechanism. Nucleophilic substitution reactions of furoyl chloride and thenoyl chloride were reported to proceed *via* different reaction mechanisms, the former by an addition-elimination and the latter by an S_N2 mechanism based on a product-rate study.[6,7] And also, nucleophilic substitution of para-substituted phenyl chloroformates has been reported to react *via* S_N2 like S_AN reaction mechanism based on kinetic solvent isotope effects (KSIE), quantum mechanical (QM) model and product study.[8]

In order to see the effects of highly electron deficient carbonyl center on the mechanism of solvolytic reactions, we chose α-methoxy-α-(trifluoromethyl) phenylacetyl chloride (**I,** PAC) in this work.

Competing nucleophilic substitution reactions in alcohol-water mixtures are interpreted in terms of product selectivities, S, defined from molar ratios of products and of solvents [Eq. (1)]. If these reactions simply involve competitive attack upon the substrate by either water or alcohol, S values would be independent of solvent composition.[9]

$$S = [\text{ester}][\text{water}]/[\text{acid}][\text{alcohol}] \qquad (1)$$

Dispersion into separate lines in the correlation of the specific rates of solvoysis of a substrate in various binary mixtures was documented[10-14] in early treatments using the Grunwald-Winstein Eq. (2).[15~17]

$$\log(k/k_o) = mY + c \qquad (2)$$

In general, dispersion effects in unimolecular solvoyses[18,19] make smaller contribution to the overall linear free energy relationship (LFER) than solvent nucleophilicity effects in bimolecular solvolyses. It was suggested that a second term which is governed by the sensitivity l to solvent nucleophilicity N, should be added to Eq. (1) for bimolecular solvolyses.[20] The resulting Eq. (3) is often referred to as the extended Grunwald-Winstein equation.[20]

$$\log(k/k_o) = mY + lN \qquad (3)$$

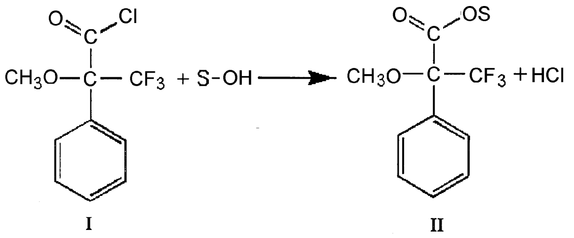
Another possible cause for the scatter could be the different solvation behavior of the charge that is developing on the aromatic substrate from that on the aliphatic standard compounds used for the determination of Y or Y_{Cl} scale.

Kevill *et. al.* recently suggested[21~24] that, since the dispersion seems to follow a consistent pattern, it should be possible to develop an aromatic ring parameter (I), which, as qualified by the appropriate sensitivity (h), can be added to Eqs. (2) or (3) to give Eqs. (4) or (5), respectively.[25,26]

$$\log(k/k_o) = mY + hI + c \qquad (4)$$

$$\log(k/k_o) = lN + mY + hI + c \qquad (5)$$

In this work, we determined rate constants and products selectivities for solvolysis of PAC in EtOH-H_2O, MeOH-H_2O, Acetone-H_2O, and Dioxane-H_2O mixtures at 25 °C, and transition state variation is discussed by applying the Grunwald-Winstein equation, extended Grunwald-Winstein equation, kinetic solvent isotope effect and selectivity.



Scheme 1

Result and Discussion

Solvent Effect. Rate constants for solvolysis of α-methoxy-α-(trifluoromethyl) phenylacetyl chloride (PAC, Scheme 1) in aqueous binary mixtures of dioxane, acetone, ethanol, methanol, and trifluoroethanol (TFE) and TFE-ethanol mixtures at 25 °C are reported at Tables 1 and 2.

Rate constants increase in the order TFE-H_2O < acetone-H_2O < dioxane-H_2O < ethanol-H_2O < methanol-H_2O. The rate increases slowly as the water content of the mixtures increases, and it means that the rate is slightly accelerated by the solvent with higher ionizing power, *Y*, suggesting little bobd-breaking in the transition state. The rate decreases remarkably with the TFE contents in the TFE-EtOH mixtures indicating that nucleophilicity decreases with increase in the trifluoroethanol contents in the mixture.

Table 1. Rate constants (k, s^{-1}) solvolyses of α-methoxy-α-(trifluoromethyl)phenylacetyl chloride in aqueous binary mixtures at 25 °C

v/v%	MeOH	EtOH	Acetone	Dioxane
	$k \times 10^2$			
100	1.07	0.157		
90	1.84	0.376		
80	3.18	0.511	0.199	0.365
70	3.57	0.675	0.339	0.598
60	4.55	0.887	0.572	0.965
50	6.88	1.24	0.777	1.57
40	8.22	2.21	1.52	1.95
30	11.8	4.65	2.89	4.19
20	14.1	6.15	3.84	7.35
10	8.97	12.4	8.22	10.3
H_2O	7.23	7.23	7.23	7.23

Table 2. Rate constants (k, s^{-1}) solvolyses of α-methoxy-α-(trifluoromethyl)phenylacetyl chloride in aqueous binary mixturesat 25 °C

v/v%	$k \times 10^4$
97TFE - $3H_2O$	0.0185
90TFE - $10H_2O$	0.291
70TFE - $30H_2O$	3.57
50TFE - $50H_2O$	15.6
80TFE - 20EtOH	0.407
60TFE - 40EtOH	2.06
40TFE - 60EtOH	5.47
20TFE - 80EtOH	10.7

Such a phenomenon implies that the solvolysis of PAC proceeds by predominantly S_N2 or S_AN pathway with a tight transition state. First-order rate constants for solvolysis of PAC vary over seventy nine-fold range in alcohol-water mixtures, whereas the observed first-order rate constants for benzyl halide or thenoyl chloride vary over hundreds or thousands-fold range which is known to react *via* an S_N1 or S_N1 like-S_N2 reaction mechanism.[6,27,28] These results indicate that the rate determining step is not the bond breaking step as found in the reaction of benzyl halide[27,28] or thenoyl chloride[6] but the addition step for the reaction of PAC, since transition state is not sensitive to solvent ionizing power. These results are very similar to those of solvolytic reaction of *p*-nitrobenzoyl chloride,[12a,29] *p*-nitrobenzensulfonyl chloride[10,9,30] furoyl chloride[6] and ary1 chloroformates,[8,31] but they are different from the results of solvolytic reactions of thenoyl chloride,[6] *p*-methoxybenzoyl chloride[11,27] and benzyl halides.[6,27,28]

The Grunwald-Winstein plots of the rates in Table 1 are presented in Figure 1 using the solvent ionizing power scale Y_{Cl}, based on 2-adamantyl chloride.[32]

Examination of Figure 1 shows that the plots for the five binary mixtures exhibit dispersion into separate lines. The plot for alcohol-water and acetone-water binary mixtures shows a very small *m* value of *ca*. 0.25, and show very low reactivity for TFE-water and TFE-EtOH binary solvent mixtures. The low reactivity of TFE solvent mixtures shows a large deviation from the correlation of Grunwald-Winstein plots for aqueous alcohol and acetone. Rate ratios in solvents of the same Y_{Cl} value and different nucleophilicity provide measures of the minimum extent of nucleophilic solvent assistance (eg., $[k_{40EW}/k_{97TFE}]_Y = 119 \times 10^2$, EW = ethanol-water).[33] The low nucleophilicity and high ionizing power of the fluorinated alcohol, CF_3CH_2OH, show large deviations from Figure 1. Such a small *m* value and large value of k_{40EW}/k_{97TFE} implies that solvolysis of PAC in the binary

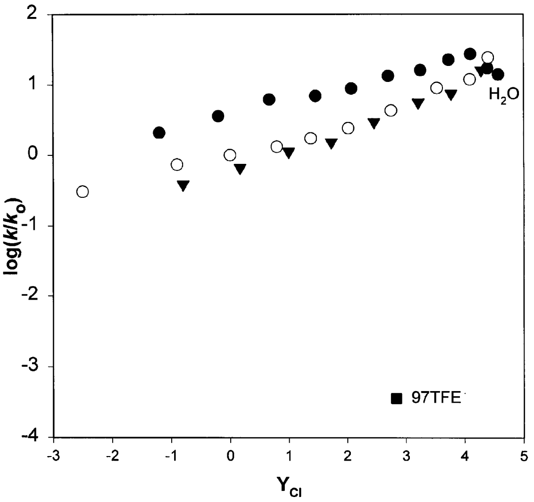


Figure 1. Logarithms of first-order rate constants for solvolyses of α-methoxy-α-(trifuoromethyl)phenylacetyl chloride at 25 °C log (k/k_o) *vs*. Y_{Cl} (solvent code: ● ; methanol, ○ ; ethanol, ▼; acetone, ■; TFE-H_2O).

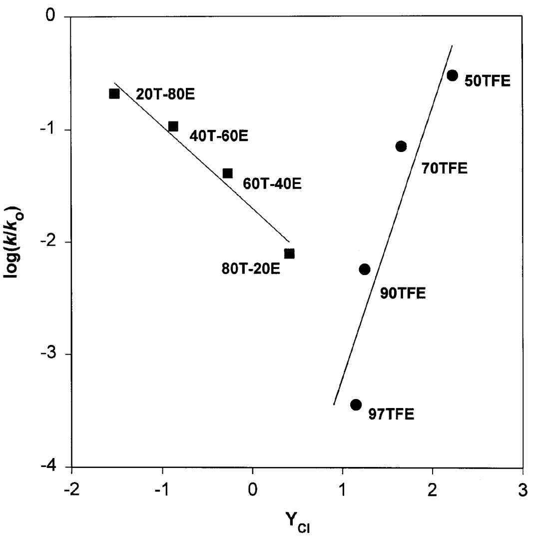


Figure 2. Logarithms of first-order rate constants for solvolyses of α-methoxy-α-(trifluoromethyl)phenylacetyl chloride at 25 °C log(k/k_o) *vs.* Y_{Cl} (solvent code: ■ ; TFE-EtOH, ● ; TFE-H_2O).

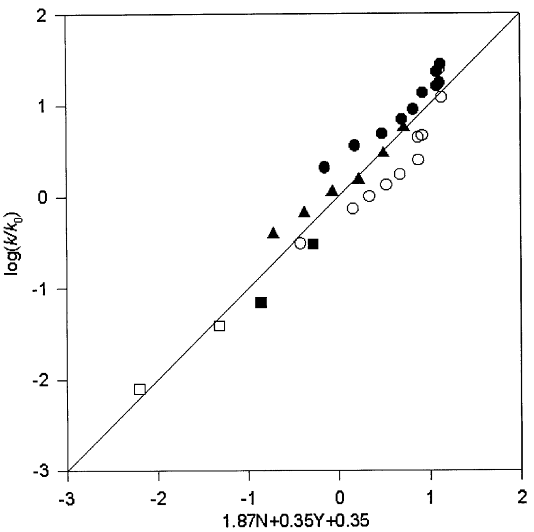


Figure 3. Plot of log(k/k_o) for α-methoxy-α-(trifluoromethyl) phenylacetyl chloride against (1.87N + 0.35Y + 0.35) (r = 0.938) (solvent codes: ● ; methanol, ○ ; ethanol, ▲ ; acetone, □ ; TFE-EtOH, ■ ; TFE-H_2O).

mixtures proceeds by an addition-elimination (S_AN) or associative S_N2 mechanism channel rather than by an S_N1 channel.

The Grunwald-Winstein plots of the rates in Table 2 for solvolysis of PAC in TFE-water and TFE-ethanol solvent mixtures are presented in Figure 2 using the solvent ionizing power scale Y_{Cl}, based on *t*-butyl chloride.[34] Examination of Figure 2 reveals an unusual correlation of substrate reactivity with solvent ionizing power. Reactivity decreases as solvent ionizing power of TFE-ethanol mixtures increases, and reactivity increases as solvent ionizing power for TFE-water mixtures increases.

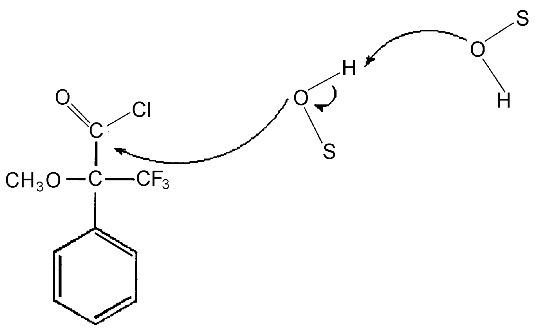
In spite of the higher ionizing power with increased contents of TFE in TFE-ethanol mixtures, low reactivity is an indication that bond-formation is important. However, for the TFE-water solvent mixtures, slightly increased reactivity is obtained as water content increases suggesting little bond-breaking in the transition state. These results imply that solvolysis of PAC in the binary mixtures proceeds by the addition-elimination (S_AN) or associative S_N2 mechanism with little bond-breaking in the transition state.

The rate data in Table 1 is correlated using the extended Grunwald-Winstein equation.[20,34] It has been shown that inclusion of the nucleophilicity parameter (N) results in considerable improvement when it is added as an lN term to the original Grunwald-Winstein equation.[16] The extended Grunwald-Winstein plots show good correlations (r = 0.938) for solvolysis of PAC (Figure 3) indicating an importance of solvent nucleophilicity compared to aromatic ring parameter. With use of the extended Grunwald-Winstein equation,[20,34] the l and m values are 1.87 and 0.35, respectively in this work. The magnitude of l and m values associated with a change of solvent composition therefore predicts an associative S_N2 or S_AN pathway with a relatively tight transition state, where bond formation is more progressed than bond cleavage of the leaving group. This results implies that negative charge of the carbonyl anion is stabilized by the strong electron withdrawing substituents, -CF_3 and -OCH_3, which are located at neighboring position of benzoyl carbonyl group in the transition state. Therefore, nucleophilic solvolysis of acid halides with strong electron withdrawing substituent at a neighboring position of carbonyl group proceeds predominantly by an associative S_N2 or S_AN reaction mechanism.

Kinetic Solvent Isotope Effects. We have determined the kinetic solvent isotope effect (KSIE), k_{SOH}/k_{SOD}, for the solvoysis of PAC using deuterated water (D_2O), 50% D_2O-CH_3OD, and methanol-d (CH_3OD), and the results are presented in Table 3. Bentley reported a small KSIE value for the S_N2 solvolyses of methyl tosylate and S_N1 solvolysis of diphenyl chloromethane,[35~37] but he also found large l and KSIE value for the S_N2(P) solvolysis of $(PhO)_2POCl$.[38] Perhaps the small kinetic solvent isotope effects indicate an early transition state, and the large kinetic solvent isotope effects indicate a late transition state in typical S_N2 solvolyses.[37] Therefore, the large KSIE shows importance of bond-formation in the transition state of nucleophilic displacement reaction.[37] The KSIE is not a criterion of the reaction mechanism, but an indication of a degree of bond-formation in the transition state. Table 3 reveals that the magnitude of the KSIE varies from 2.4 (MeOH) to 5.3 (H_2O) at 25 °C. The KSIE in water solvent, which has the strongest ionizing power, is larger than that of methanol and 50% methanol sol-

Table 3. Rate constant (k, s^{-1}) and kinetic solvent isotope effects for solvolyses of α-methoxy-α-(trifluoromethyl)phenyl acetyl chloride in methanol, 50% methanol and water at 25 °C

v/v %	$k_{SOH} \times 10^{-3}$	$k_{SOD} \times 10^{-3}$	KSIE
Water	72.3	13.6	5.3
CH_3OD	10.7	4.42	2.4
50% D_2O-CH_3OD	68.8	25.9	2.7



Scheme 2

vents. This implies that bond formation in water has progressed extensively in the transition state. Thus general base catalysis is important for the solvolytic reaction of PAC in water solvent; especially (Scheme 2).

Product Study. Product selectivities [*S*, Eq. (1)] for solvolysis of **PAC** in aqueous alcohol mixtures at 25 °C are reported in Table 4. Table 4 shows that selectivity is increased as the water contents of aqueous alcohol mixtures increase, indicating that reactivity-selectivity principle (RSP)[39] is not obeyed: *S* values increase in water-rich media as the reactivity increases.[14,33,40b,41]

In general, selectivity values (*S*) in water-rich media are smaller than highly alcoholic mixture, because the amount of ester product by alcohol decreases and one of the acid product by water increases as water content of aqueous alcohol mixtures increases. This S value increase with the increase of alcohol content in aqueous alcohol mixtures can be interpreted to show that in alcohol-rich media alcohol as nucleophile. Such a phenomenon reveals that the bond-formation is more important than bond-breaking in the transition-state. These results of product study are consistent with the results of solvent effects and kinetic solvent isotope effect.

Cosolvent Effects. For solvolysis in water-cosolvent mixtures, interpretation based on a third order mechanism is more complex, but significant new information is available because cosolvent is acting as a general base catalyst. Thus, there are two possible third-order rate constants in the solvolysis reaction: (i) k_{ww} for a mechanism in which one molecule of water acts as a nucleophile and second molecule acts as a general base; (ii) k_{wc} in which water acts as a nucleophile and cosolvent acts as a general base.[31] Therefore, observed first-order rate constants in water-cosolvent mixtures are given by Eq. (6).

Table 4. Selectivity (*S*) for solvolyses of α-methoxy-α- (trifluoromethyl)phenylacetyl chloride in methanol-water at 25 °C

solvents[a]	(Ester/Acid)$_{raw}$	(Ester/Acid)$_{true}$	*S*
10% MeOH	0.0752	0.0621	1.25
20% MeOH	0.238	0.197	1.77
30% MeOH	0.386	0.319	1.67
40% MeOH	0.506	0.418	1.40
50% MeOH	1.14	0.938	2.10
60% MeOH	1.94	1.61	2.40

[a] Solvents are % v/v methanol/water; molar conentration of methanol and water are calculated by ignoring the small volume of mixing as follows ([MeOH], [H_2O]. 10M, 2.47, 49.94; 20M, 4.94, 44.41; 30M, 7.41, 38.85; 40M, 9.88, 33.31; 50M, 12.35, 27.75; 60M, 14.82, 22.20.

$$k_{obs} = k_{ww}\,[\text{water}]^2 + k_{wc}\,[\text{water}][\text{cosolvent}]$$

$$\frac{k_{obs}}{[\text{water}]^2} = k_{ww} + k_{wc}\frac{[\text{cosolvent}]}{[\text{water}]} \qquad (6)$$

Plots (Figures 4 and 5) of third-order rate constants against molar ratios of [cosolvent]/[water] for solvolysis of PAC in acetone-water (slope = 0.78) and dioxane-water (slope = 1.57) mixtures show that the k_{wc} value for the dioxane-water solvent mixture is two times greater than that for acetone-water solvent mixtures. This suggests that the role of cosolvent as a general base catalyst is more important in dioxane than in acetone.

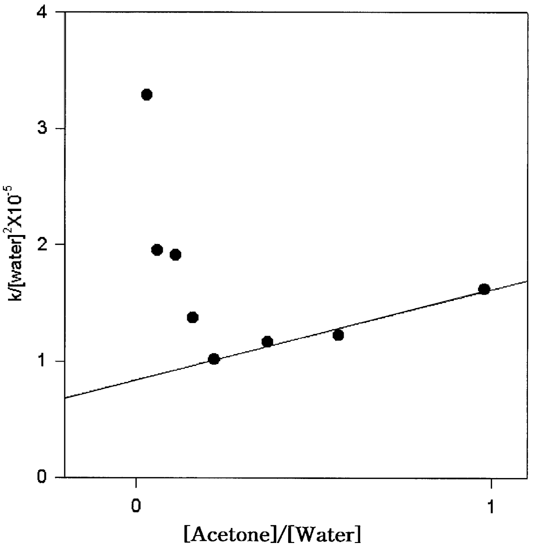


Figure 4. Plot of $k/[\text{water}]^2 \times 10^{-5}$ for α-methoxy-α-(trifluoromethyl)phenylacetyl chloride against [acetone]/[water](k_{wc} = 0.78).

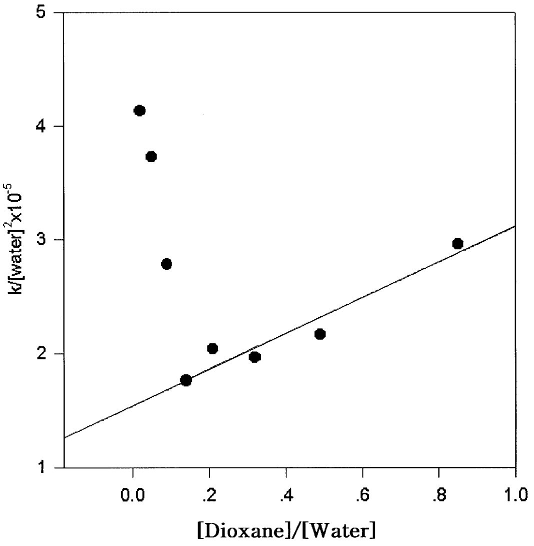
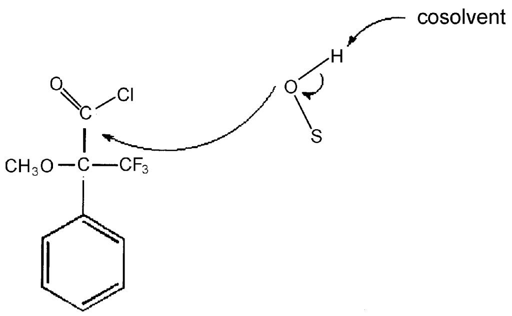


Figure 5. Plot of $k/[\text{water}]^2 \times 10^{-5}$ for α-methoxy-α-(trifluoromethyl)phenylacetyl chloride against [dioxane]/[water] (k_{wc} = 1.57).



Scheme 3

General base catalysis by cosolvent is not favoured in the mixture with a stronger hydrogen-bond acceptor cosolvent [acetone ($\beta = 0.48$) > dioxane ($\beta = 0.37$)].[42] This result shows that the hydrogen bond between cosolvent and water is stronger in acetone-water mixture than that in dioxane-water mixture in ground state. Therefore, general base catalytic ability is decreased in solvent with higher hydrogen-bond accepter basicity.

Experimental Section

Methanol, ethanol, acetone, and dioxane were Merck GR grade (< 0.1% H_2O), and D_2O and CH_3OD were from Aldrich (99.9% D). Distilled water was redistilled with Buchi Fontavapor 210 and treated using ELGA UHQ PS to obtain specific conductivity of less than 1×10^{-6} mhos/cm. α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (PAC) was Aldrich GR grade (> 99%). The rate were measured conductometrically at 25(± 0.03) °C at least in duplicate as described previously,[40] with substrate concentrations of substrate *ca.* 10^{-3} M. The solvolysis products, ester and acid, were determined by HPLC analysis described previously,[30] and the product selectivity (*S*) were calculated from Eq. (5). The *S* values calculated from the observed peak area ratios of ester and acid gave S_{raw} values, which were divided by a response factor [(methyl ester/acid) = 1.21] to afford at true *S* values. Eluent solvent used was 68% methanol-water mixture and flow rate adjusted to 1mL/min. The HPLC system used was Hewlett-Packard 1050 Series with 125 × 4 mm Spherisorb ODS reversed phase column, and wave length of UV detector is fixed to 256 nm.

Reference

1. (a) Bender, M. L. *Chem. Rev.* **1960**, *60*, 53. (b) *The Chemistry of the Carbonyl Group*; Patai, S., Ed.; Intersience: New York, 1966; Vols. 1~2, p 1970. (c) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1968. (d) Jencks, W. P. *Acc. Chem. Res*. **1980**, *13*, 161. (e) Guthrie, J. P. *Acc. Chem. Res*. **1983**, *16*, 22. (f) Baer, S.; Brinkman, E. A.; Brauman, J. I. *J. Am. Chem. Soc*. **1991**, *113*, 805. (g) Williams, A. *Chem. Soc. Rev.* **1994**, *23*, 93.
2. (a) Yamabe, S.; Minato, S. *J. Org. Chem*. **1983**, *48*, 2972. (b) Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc*. **1987**, *109*, 3856. (c) Madura, J. D.; Jorgensen, W. L. *J. Am. Chem. Soc*. **1986**, *108*, 2517. (d) Park, Y. S.; Kim, C. K.; Lee, B. S.; Lee, I.; Lim, W. M.; Kim, W. K. *J. Phys. Org. Chem*. **1995**, *8*, 35.
3. (a) Bentley, T. W.; Shim, C. S. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1659. (b) Bentley, T. W.; Koo, I. S. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1385.
4. Jedrzejczak, M.; Motie, R. E.; Satchell, D. P. N.; Satchell, R. S.; Wassef, W. N. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1471.
5. (a) Lee, I.; Shim, C. S.; Chung, S. Y.; Kim, H. Y.; Lee, H. W. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1919. (b) Lee, I.; Koh, H. J.; Lee, B. C. *J. Phys. Org. Chem*. **1994**, *7*, 50.
6. Oh, J.; Yang, K.; Koo, I. S.; Lee, I. *J. Chem. Res*. **1993**, 310.
7. Jedrzejczak, M.; Moite, R. E.; Satchell, D. P. N. *J. Chem. Soc., Perkin Trans. 2* **1993**, 599.
8. Koo, I. S.; Yang, K.; Kang, K.; Lee, I. *Bull. Korean Chem. Soc.* **1998**, *19*, 968.
9. Bentley, T. W.; Jones, R. O.; Koo, I. S. *J. Chem. Soc., Perkin Trans. 2* **1994**, 753.
10. Koo, I. S.; Bentley, T. W.; Kang, D. H.; Lee, I. *J. Chem. Soc., Perkin Trans. 2* **1991**, 175.
11. Bentley, T. W.; Koo, I. S. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1385
12. Bentley, T. W.; Carter, G. E. *J. Am. Chem. Soc.* **1982**, 5741.
13. Bentley, T. W.; Harris, H. C.; Koo, I. S. *J. Chem. Soc., Perkin Trans. 2* **1988**, 783.
14. Bentley, T. W.; Harris, H. C. *J. Chem. Soc., Perkin Trans. 2* **1986**, 619.
15. Winstein, S.; Grunwald, E. *J. Am. Chem. Soc*. **1948**, *70*, 846.
16. Bentley, T. W.; Dau-Schmidt, J.-P.; Llewellyn, G.; Mayr, H. *J. Org. Chem.* **1992,** *57*, 2387.
17. Bentley, T. W.; Bowen, C. T.; Morten, D. H.; Schleyer. P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5466.
18. Winstein, S.; Fainberg, A. H.; Grunwald, E. *J. Am. Chem. Soc.* **1957**, *79*, 4146.
19. Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc*. **1957**, *79*, 1957.
20. Winstein, S.; Grunwald, E.; Jones, H. W. *J. Am. Chem. Soc.* **1951**, *73*, 2700.
21. Kevil, D. N.; Ismail, N. HJ; D' Souza, M. J. *J. Org. Chem*. **1994**, *59*, 6303.
22. Kevil, D. N.; D'Souza, M. J. *J. Chem. Soc., Perkin Trans. 2* **1995**, 973.
23. Kevill, D. N.; Anderson, S. W. *J. Am. Chem. Soc.* **1986**, *108*, 1597.
24. Kevil, D. N.; Bond, M. W.; D'Souza, M. J. *J. Org. Chem.* **1997**, *62*, 7869.
25. Sneen, R. A.; Felt, G. R.; Dickason, W. C. *J. Am. Chem. Soc*. **1973**, *95*, 638.
26. Friedberger, M. P.; Thornton, E. R. *J. Am. Chem. Soc.* **1976**, *98*, 2861.
27. Bentley, T. W.; Koo, I. S.; Norman, S. *J. Org. Chem*. **1991**, *56*, 1604.
28. Liu, K-T.; Duann, Y-F.; Hou, S-J. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2181.
29. Bentley, T. W.; Harris, H. C. *J. Org. Chem*. **1988**, *53*, 724.
30. (a) Bentley, T. W.; Jones, R. O. *J. Chem. Soc., Perkin Trans. 2* **1992**, 743. (b) Jones, R. O. M. Phil. Thesis. University of Wales, **1991**.

31. Koo, I. S.; Yang, K.; Kang, K.; Lee, I.; Bentley, T. W. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1175.
32. Bently, T. W.; Llewllyn, G. *Adv. Phys. Org. Chem*. **1990**, *17*, 121.
33. Bentley, T. W.; Carter, G. E.; Harris, H. C. *J. Chem. Soc. Trans. 2* **1985**, 983.
34. Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7667.
35. Robertson, R. E. *Prog. Phys. Org. Chem.* **1963**, *4*, 213.
36. Kruz, J. L.; Lee, J.; Love, M. E.; Rhodes, S. *J. Am. Chem. Soc.* **1986**, *108*, 2960.
37. Bentley, T. W.; Llewellyn, G.; Ryu, Z. H. *J. Org. Chem.* **1998**, *63*, 4654.
38. Bentley, T. W.; Ebdon, D.; Llewellyn, G.; Abduljaber, M. H.; Miller, B.; Kevill, D. N. *J. Chem. Soc., Dalton Trans.* **1997**, 3819.
39. Exner, O. *J. Chem. Soc., Perkin Trans. 2* **1993**, 973.
40. (a) Bentley, T. W.; Carter, G. E.; Harris, H. C. *J. Chem. Soc., Perkin Trans. 2* **1985**, 938. (b) Bentley, T. W.; Koo, I. S. *J. Chem. Soc., Chem. Commun.* **1988**, 41.
41. Ta-Shma, R.; Rappoport, Z. *Adv. Phys. Org. Chem.* **1992**, *27*, 239.
42. Kamlet, M. J.; Abboud, J. L. M.; Taft, R. W. *Prog. Phys. Org. Chem*. **1981**, *13*, 485.