

A Kinetic Study on Solvolysis of 9-Fluorenylmethyl Chloroformate

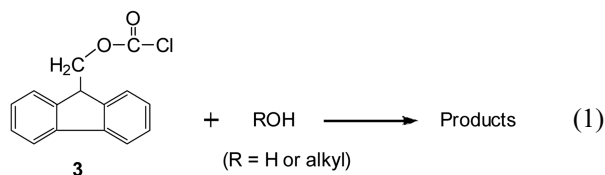
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Received July 25, 2011, Accepted August 20, 2011**Key Words :** 9-Fluorenylmethyl chloroformate, Extended Grunwald-Winstein equation, S_N2 mechanism, Kinetic solvent isotope effect

Chloroformate esters (ROCOCl, **1**) are known to hydrolyse much more slowly than other acyl chlorides (RCOCl). Initial-state stabilization through π -electron resonance (**2**) has been suggested to be responsible for the decreased reactivity of **1**, since such resonance interaction is not possible for RCOCl.¹ This resonance effect would be more significant as the R in **1** becomes a stronger electron donating group but be insignificant when R is a strong electron withdrawing group. The electronic nature of the R group would also cause a change in the reaction mechanism, *i.e.*, from rate limiting breakdown of a tetrahedral intermediate to rate-limiting formation of an intermediate upon introducing a strong electron donating group, R.²



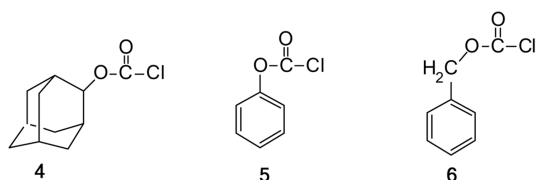
To gain further understanding of the mechanism of acyl transfer, we have carried out a kinetic study on the solvolysis of 9-fluorenylmethyl chloroformate (**3**) in a variety of pure and binary solvents at 45.0 °C, equation (1). We have deter-



mined the l and m values in the extended Grunwald-Winstein equation³ [eqn. (2)], together with the enthalpies and entropies of activation,

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

and solvent deuterium kinetic isotope effect (KIE). We have also compared our current results with those reported previously for solvolysis of 2-adamantyl chloroformate (2-AdOCOCl, **4**),⁴ phenyl chloroformate (C₆H₅OCOCl, **5**),⁵ and benzyl chloroformate (C₆H₅CH₂OCOCl, **6**)⁶ to investigate acyl-transfer reaction mechanisms.



Results and Discussion

The rate constants (k) for solvolysis of **3** in 34 pure and binary solvents at 45.0 °C are summarized in Table 1. As shown in the Table 1, k increases as the water content in the medium increases. This indicates that solvent-ionizing power is more important than solvent nucleophilicity, since water has much stronger ionizing power than other solvent employed in this study.³

The rate constant for ethanolysis of **3** measured in this study at 25.0 °C is $1.37 \times 10^{-4} \text{ s}^{-1}$ (Table 2), which is an order of magnitude smaller than that reported previously for phenyl chloroformate (PhOCOCl, **5**) ($k = 2.60 \times 10^{-3} \text{ s}^{-1}$ at 25.0 °C).⁵ This suggests that the 9-fluorenylmethyl group is less electron-withdrawing than the phenyl group (*i.e.*, less favorable for promoting nucleophilic attack at the electron-deficient carbonyl carbon).

The activation parameters, ΔH^\ddagger and ΔS^\ddagger , calculated from the k values at 4-different temperatures for solvolysis of **3** in pure EtOH and MeOH, and in 80%EtOH and 50%TFE are shown in Table 2. One can find relatively low ΔH^\ddagger (11.2 to 13.1 kcal·mol⁻¹) and large negative ΔS^\ddagger values (-31.1 to -38.6 cal·mol⁻¹·K⁻¹), which are within the ranges of those reported previously for a normal S_N2 reaction.^{5,7} In deuterated methanol (MeOD), a kinetic solvent isotope effect ($k_{\text{MeOH}}/k_{\text{MeOD}}$) of 2.20 ± 0.03 is observed. This is within the KIE values of 1.58-2.31 reported for the corresponding methanolyses of *n*-propyl chloroformate and a series of benzenesulfonyl chlorides at 25.0 °C, in which the reactions are believed to be S_N2 in character.^{8,9}

The extended Grunwald-Winstein equation [eqn. (2)] is useful to determine the extent of nucleophilic participation by the solvent, since the magnitude of l and m in equation (2) is an indicator to determine whether a nucleophilic substitution reaction proceeds through a unimolecular, S_N1 (*e.g.*, $l \approx 0$ and $m \approx 1$) or a bimolecular reaction, S_N2 (*e.g.*, $l \approx 1$ and $m \approx 0.5$). Therefore, the determination of l and m values would provide valuable information concerning the structure of the transition state for solvolyses.⁸

The l and m values obtained in this study are 0.95 ± 0.07 and 0.39 ± 0.04 , respectively (Table 3). Since the data points for solvolysis in TFE-ethanol mixtures fell somewhat below the best-fit line, Figure 1 (this behavior has been discussed previously),¹⁰ the correlation was carried out without the data points.

Table 1. Rate constants of solvolysis of 9-fluorenylmethyl chloroformate (**3**)^a in a variety of pure and mixed solvents at 45.0 °C and the N_T and the Y_{Cl} values for the solvents

Solvent ^b	$10^3 k^c$ (s ⁻¹)	N_T^d	Y_{Cl}^d
100%EtOH	0.457 ± 0.003	0.37	-2.52
90%EtOH	0.955 ± 0.004	0.16	-0.94
80%EtOH	1.35 ± 0.03	0.0	0.0
70%EtOH	1.66 ± 0.03	-0.20	0.78
60%EtOH	1.86 ± 0.02	-0.38	1.38
50%EtOH	2.04 ± 0.03	-0.58	2.02
40%EtOH	2.29 ± 0.03	-0.74	2.75
20%EtOH	3.09 ± 0.02	-1.16	4.09
100%MeOH ^e	1.38 ± 0.02	0.17	-1.20
90%MeOH	2.75 ± 0.04	-0.01	-0.20
80%MeOH	3.63 ± 0.02	-0.06	0.67
70%MeOH	4.11 ± 0.03	-0.40	1.46
50%MeOH	4.90 ± 0.05	-0.75	2.70
40%MeOH	5.25 ± 0.06	-0.87	3.25
20%MeOH	5.75 ± 0.03	-1.23	4.10
90%Acetone	0.0550 ± 0.0004	-0.35	-2.39
80%Acetone	0.162 ± 0.002	-0.37	-0.83
70%Acetone	0.257 ± 0.003	-0.42	0.17
60%Acetone	0.447 ± 0.002	-0.52	1.00
50%Acetone	0.603 ± 0.005	-0.70	1.73
40%Acetone	0.933 ± 0.004	-0.83	2.46
30%Acetone	1.91 ± 0.02	-0.96	3.21
20%Acetone	3.89 ± 0.03	-1.11	3.77
90%TFE ^f	0.0794 ± 0.0005	-2.55	2.85
80%TFE	0.240 ± 0.003	-2.19	2.90
70%TFE	0.490 ± 0.004	-1.98	2.96
50%TFE	0.977 ± 0.005	-1.73	3.16
90%HFIP ^f	0.0155 ± 0.0002	-3.84	4.31
70%HFIP	0.0447 ± 0.0003	-2.94	3.83
50%HFIP	0.186 ± 0.003	-2.49	3.80
80T-20E ^g	0.0275 ± 0.0003	-1.76	1.89
60T-40E	0.0692 ± 0.0004	-0.94	0.63
40T-60E	0.155 ± 0.002	-0.34	-0.48
20T-80E	0.286 ± 0.003	0.08	-1.42

^aUnless otherwise indicated, a 1.0 mol dm⁻³ solution of the substrate in the indicated solvent, containing 0.1% CH₃CN. ^bOn a volume-volume content at 25.0 °C, other component is water. ^cWith associated standard deviations. ^dValues from ref. 3. ^eValues of $k = 6.27(\pm 0.03) \times 10^{-4}$ s⁻¹ in deuterated methanol (MeOD), corresponding to k_{MeOH}/k_{MeOD} value of 2.20 ± 0.03 (with associated standard error).¹¹ ^fSolvent prepared on a weight-weight basis at 25.0 °C, other component is water. ^gT-E represents TFE-ethanol mixtures.

The l and m values for the solvolysis of **3** are smaller than those reported recently for reactions reported to proceed through an addition-elimination mechanism ($l = 1.59$ - 1.95 and $m = 0.57$ - 0.58 , Table 3). Therefore, one can conclude that solvolysis of **3** proceeds through an S_N2 mechanism, in which bond making is more progressed than bond breaking on the basis of the magnitude of l and m .⁸ This conclusion can be further supported from the fact that the reactivity of **3** increases with increasing the water content (Table 1), **3** is *ca.* 10 times less reactive than **5**, the activation parameters

Table 2. Rate constants and activation parameters for the solvolysis of 9-fluorenylmethyl chloroformate^a at various temperatures

Solvent	Temp. (°C)	$10^4 k^b$ (s ⁻¹)	ΔH^\ddagger (kcal·mol ⁻¹) ^c	$-\Delta S^\ddagger$ (cal·mol ⁻¹ ·K ⁻¹) ^c
100%EtOH	25.0	1.37 ± 0.02	11.2 ± 0.3	38.6 ± 0.9
	35.0	2.54 ± 0.03		
	45.0	4.57 ± 0.03		
	55.0	8.56 ± 0.03		
80%EtOH ^d	25.0	3.84 ± 0.04	11.6 ± 0.3	35.1 ± 0.9
	35.0	7.14 ± 0.03		
	45.0	13.5 ± 0.3		
	55.0	25.3 ± 0.2		
100%MeOH	25.0	3.54 ± 0.003	12.6 ± 0.3	32.0 ± 1.0
	35.0	6.93 ± 0.005		
	45.0	13.8 ± 0.2		
	55.0	27.2 ± 0.3		
50%TFE ^e	25.0	1.60 ± 0.02	13.1 ± 0.4	31.1 ± 1.4
	35.0	3.89 ± 0.03		
	45.0	9.77 ± 0.05		
	55.0	24.4 ± 0.3		

^aA 1.0 mol dm⁻³ solution of the substrate in the indicated solvent, also containing 0.1% CH₃CN. ^bAverages of three or more runs, with standard deviation. ^cThe activation parameters are accompanied by the standard error. ^dOn a volume-volume content at 25.0 °C, other component is water. ^eSolvent prepared on a weight-weight basis at 25.0 °C, other component is water.

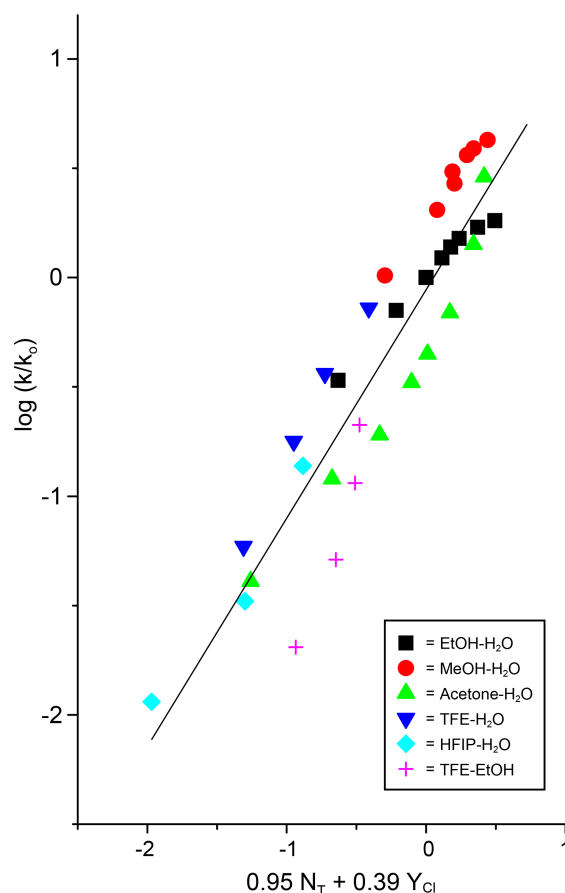
**Figure 1.** Plot of $\log(k/k_0)$ versus $0.95 N_T + 0.39 Y_{Cl}$ for the solvolysis of 9-fluorenylmethyl chloroformate, **3**.

Table 3. Extended Grunwald-Winstein correlations of the kinetics of solvolytic displacement of chloride

Substrate	n ^a	l ^b	m ^b	R ^c
2-AdOCOCI ⁽⁴⁾	19	~0	0.47 ± 0.03	0.970
C ₆ H ₅ CH ₂ OCOCI ⁽⁶⁾	11	0.25 ± 0.05	0.66 ± 0.06	0.976
<i>i</i> -PrOCOCI ⁽¹²⁾	20	0.28 ± 0.05	0.52 ± 0.03	0.979
C ₆ H ₅ CH ₂ SO ₂ Cl ⁽¹³⁾	30	0.61 ± 0.04	0.34 ± 0.02	0.954
9-Fluorenyl-OCOCI ^d	30	0.95 ± 0.07	0.39 ± 0.04	0.941
C ₆ H ₅ SO ₂ Cl ⁽¹⁴⁾	37	1.10 ± 0.17	0.61 ± 0.04	0.959
((CH ₃) ₂ N) ₂ POCl ⁽¹⁰⁾	27	1.14 ± 0.05	0.63 ± 0.03	0.982
CH ₃ SO ₂ Cl ⁽¹⁴⁾	43	1.20 ± 0.05	0.52 ± 0.03	0.969
(CH ₃) ₂ NSO ₂ Cl ⁽¹⁴⁾	32	1.20 ± 0.04	0.72 ± 0.03	0.985
CH ₃ OCOCI ⁽¹⁵⁾	19	1.59 ± 0.09	0.58 ± 0.05	0.977
C ₆ H ₅ OCOCI ⁽⁵⁾	21	1.68 ± 0.10	0.57 ± 0.06	0.973
C ₆ H ₅ CH ₂ OCOCI ⁽⁶⁾	15	1.95 ± 0.16	0.57 ± 0.05	0.966

^aNumber of solvents. ^bFrom equation (2) and with associated standard error. ^cMultiple correlation coefficient. ^d9-Fluorenylmethyl chloroformate.

(relatively small ΔH^\ddagger and large negative ΔS^\ddagger), and the solvent KIE (2.20).

Experimental

Solvents were purified as previously described.⁸ The 9-fluorenylmethyl chloroformate (**3**, Aldrich 98%) was used as received. The kinetic experiments were carried out by allowing a conductivity cell containing 12.5 mL of solvent to equilibrate, with stirring, in a constant-temperature water bath. A 12 μ L portion of a 1.0 mol dm⁻³ stock solution of **3** in acetonitrile was then added. The monitoring of increases in conductivity with time and the calculation of the rate constants (first-order coefficients) were conducted as previously reported.⁸ The multiple regression analyses were performed using commercially available packages.

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