Rate and Product Studies of 1-Adamantylmethyl Haloformates

Bull. Korean Chem. Soc. **2012**, Vol. 33, No. 11   3657

Rate and Product Studies of 1-Adamantylmethyl Haloformates Under Solvolytic Conditions

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Reactions of 1-adamantylmethyl chloroformate (1-AdCH$_2$OCOCl, **1**) and 1-adamantylmethyl fluoroformate (1-AdCH$_2$OCOF, **2**) in hydroxylic solvents have been studied. Application of the extended Grunwald-Winstein (G-W) equation to solvolyses of **1** in a variety of pure and binary solvents indicates an addition-elimination pathway in the majority of the solvents except an ionization pathway in the solvents of relatively low nucleophilcity and high ionizing power. The solvolyses of **2** show an addition-elimination pathway in all of the mixed solvents. The leaving group effects (k_F/k_{Cl}), the kinetic solvent isotope effects (KSIEs, k_{MeOH}/k_{MeOD}), and the enthalpy and entropy of activation for the solvolyses of **1** and **2** were also calculated. The selectivity values (*S*) for each solvent composition are reported and discussed. These observations are compared with those previously reported for other alkyl haloformate esters.

Introduction

For several years, we have studied solvolysis reactions of alkyl and aryl haloformates, especially concerning the application of the Grunwald-Winstein (G-W) equation. The methyl-,[1] ethyl-,[2] *n*-propyl-,[3] and *n*-octyl-[4] chloroformates in hydroxylic solvents usually undergo attack at the acyl carbon (Scheme 1(a)). An ionization pathway (Scheme 1(b)) can only be detected in solvents of very low nucleophilicity and very high ionizing power. Secondary alkyl chloroformates (*i*-propyl-[5] and 2-adamantyl-[6]) follow the ionization pathway (Scheme 1(c)) in all of the solvents except for the more nucleophilic and less ionizing ones (ethanol, methanol, 90% ethanol, and 90% methanol). For tertiary 1-adamantyl chloroformate,[7] the ionization pathway (Scheme 1(c)) was dominant in all of the mixed solvents and a trace of the mixed carbonate was only detected in 100% ethanol. On the other hand, the solvolyses of primary and secondary alkyl fluoroformates (methyl-,[8] ethyl-,[9] *n*-propyl-,[10] *n*-octyl-,[4] and *i*-propyl-[11]) in all of the solvents show addition-elimination
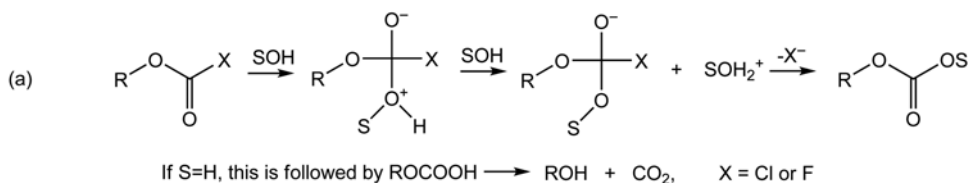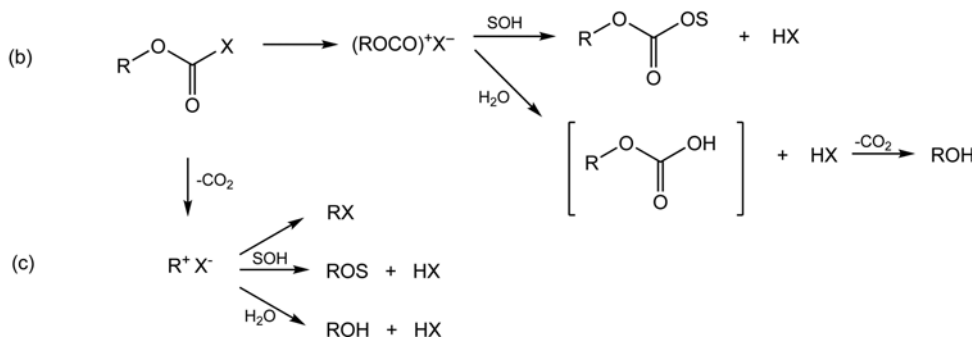
Scheme 1. Mechanisms of nucleophilic substitution at carbonyl compounds.

mechanisms (Scheme 1(a)), with the formation of a tetrahedral intermediate as the rate-determining step. Solvolyses of *t*-butyl fluoroformate[12] were found to proceed entirely by an ionization pathway (Scheme 1(c)) that included the loss of carbon dioxide to give the relatively stable *t*-butyl cation as an intermediate. Solvolyses of tertiary 1-adamantyl fluoroformate[13] led to two types of mechanisms, a bimolecular pathway (Scheme 1(a)) and an ionization pathway (Scheme 1(c)).

Linear free energy relationship (LFER) analysis with the original G-W equation [log $(k/k_o) = mY + c$][14] and the extended G-W Eq. (1)[15,16] has long been employed as a diagnostic tool for the study of solvent effects on solvolytic reactions.

$$\log (k/k_o) = lN + mY + c \qquad (1)$$

In Eq. (1), k and k_o are the specific rates for the solvolysis of a substrate in a given solvent and in 80% ethanol-water, respectively; m is the sensitivity towards changes in solvent ionizing power (Y),[17-19] l is the sensitivity towards changes in solvent nucleophilicity (N),[20,21] c is a constant (residual)

term. In Eq. (1), Application of Eq. (1) provides some of the best evidence for changes in reaction mechanisms from bimolecular to unimolecular.
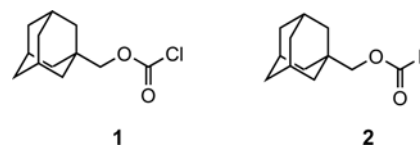
We have investigated the solvolysis reactions of **1** and **2** in a variety of pure and binary aqueous organic solvents using the extended G-W equation [Eq. (1)], which incorporates N_T and Y_{Cl}. We report the KSIEs, k_{MeOH}/k_{MeOD} for methanolysis, and the activation parameters and product data for solvolyses of **1** and **2**. These analyses were combined with a consideration of leaving group effects to arrive at reasonable mechanism.

Results and Discussion

The specific solvolyses rates of **1** and **2** at 40.0 °C are

Table 1. Specific rates of solvolysis of **1**[a] and **2**[b] in pure and binary solvents at 40.0 °C with the N_T and Y_{Cl} values for the solvents and the specific rate ratios (k_F/k_{Cl})

Solvent[c]	**1** $10^4 k$ (s^{-1})[d]	**2** $10^4 k$ (s^{-1})[d]	N_T[e]	Y_{Cl}[f]	k_F/k_{Cl}
100%MeOH	2.48±0.04[h]	1.64±0.04[i]	0.17	−1.17	0.66
90%MeOH	4.64±0.04	12.2±0.3	−0.01	−0.18	2.63
80%MeOH	6.54±0.06	32.5±0.4	−0.06	0.67	4.97
70%MeOH	8.66±0.04	66.8±0.3	−0.40	1.46	7.71
60%MeOH	10.2±0.2	85.9±0.03	−0.54	2.07	8.42
100%EtOH	0.767±0.004	0.384±0.004	0.37	−2.52	0.50
90%EtOH	1.55±0.03	5.19±0.05	0.16	−0.94	3.35
80%EtOH	2.11±0.03	11.3±0.4	0.00	0.00	5.36
70%EtOH	2.77±0.02	19.9±0.5	−0.20	0.78	7.18
60%EtOH	3.31±0.05	29.6±0.5	−0.38	1.38	8.94
50%EtOH	4.06±0.03	61.2±0.5	−0.58	2.02	15.1
90%Acetone	0.0855±0.0003	0.0651±0.0002	−0.35	−2.39	0.76
80%Acetone	0.250±0.005	0.587±0.004	−0.37	−0.80	2.35
70%Acetone	0.545±0.005	1.83±0.02	−0.42	0.17	3.36
60%Acetone	1.14±0.03	5.26±0.04	−0.52	1.00	4.61
97%TFE	0.0540±0.0005	0.00824±0.00005	−3.30	2.83	0.15
90%TFE	0.0611±0.0005	0.104±0.003	−2.55	2.85	1.70
70%TFE	0.209±0.003	0.973±0.003	−1.98	2.96	4.66
50%TFE	0.598±0.005	5.11±0.04	−1.73	3.16	8.55
80T-20E[g]	0.0251±0.0003	0.0440±0.0003	−1.76	1.89	1.75
60T-40E[g]	0.0990±0.0005	0.155±0.003	−0.94	0.63	1.57
40T-60E[g]	0.276±0.003	0.407±0.005	−0.34	−0.48	1.47
20T-80E[g]	0.526±0.005	0.573±0.004	0.08	−1.42	1.09
97%HFIP	1.12±0.03		−5.26	5.17	
90%HFIP	0.653±0.002	0.0212±0.0002	−3.84	4.31	0.032
70%HFIP	0.303±0.005	0.305±0.003	−2.94	3.83	1.01
50%HFIP	0.422±0.002	3.05±0.03	−2.49	3.80	7.23

[a]Substrate concentration of 3.602×10^{-4} mol dm^{-3}. [b]Substrate concentration of 3.983×10^{-4} mol dm^{-3}. [c]Volume/volume basis at 25.0 °C, except for TFE-H$_2$O and HFIP-H$_2$O mixtures, which are on a weight/weight basis. [d]The average of all integrated specific rates from duplicate runs, with associated standard deviation. [e]Values from ref. 22. [f]Values from ref. 17. [g]T-E are 2,2,2-trifluoroethanol-ethanol mixtures. [h]Value of $k_{MeOD} = 1.13 \pm 0.01$, and kinetic solvent isotope effect (k_{MeOH}/k_{MeOD}) of 2.19 ± 0.02. [i]Value of $k_{MeOD} = 0.468 \pm 0.02$, and kinetic solvent isotope effect (k_{MeOH}/k_{MeOD}) of 3.50 ± 0.04.

reported in Table 1. The solvents consisted of ethanol, methanol, binary mixtures of water with ethanol, methanol, 2,2,2-trifluoroethanol (TFE), acetone (Me$_2$CO), 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), and four binary mixtures of TFE and ethanol. The required N_T and Y_{Cl} values are also reported in Table 1 with the k_F/k_{Cl} ratios and the KSIE values of **1** and **2** in methanol-*d* (Table 3). Specific solvolysis rates of **1** and **2** were determined at three different temperatures in methanol, ethanol, 80% ethanol, 70% TFE, 97% HFIP and/ or 97% TFE. These values and the calculated enthalpies and entropies of activation are reported in Table 2. The products from the reactions of **1** and **2** under solvolytic conditions at 40.0 °C, in ethanol, binary mixtures of water with ethanol, acetone, TFE, and TFE-ethanol mixtures are reported in Tables 5 and 6.

Comparison with Specific Rates of 1 and 2. The choice of suitable rate ratios for various leaving groups is very important when studying the solvolytic reactivity of organic substrates in nucleophilic substitution reactions. Considering k_F/k_{Cl} ratios in nucleophilic substitution reactions has long been recognized as a useful tool in studying reaction mechanisms.[22]

For the ionization pathway, a value of $k_F/k_{Cl} = 1.3 \times 10^{-4}$ was observed for acetyl halide solvolyses,[23] and a low value of $k_F/k_{Cl} = 1.20 \times 10^{-5} \sim 3.17 \times 10^{-5}$ was observed for 1-adamantyl haloformate solvolyses.[7,13] Values for the k_F/k_{Cl}

ratios of 1.09 to 7.16 for the solvolysis of chloroformate and fluoroformate esters in 70% aqueous acetone at 30.1 °C have been reported.[24] As mentioned above, the specific rates for solvolysis of fluoroformate are somewhat faster for binary solvents, despite the stronger carbon-fluorine bond. As shown in Table 1, the k_F/k_{Cl} ratios for solvolyses of **1** and **2** are similar to those previously reported for all other the primary alkyl substrates.[4,8-10] This is true in all of the solvents except for very low nucleophilic solvents and very high ionizing solvents (*i.e.*, 90% HFIP, $k_F/k_{Cl} = 3.2 \times 10^{-2}$), which have been reported to proceed through a bimolecular pathway. The very low value for 90% HFIP is expected because of the previously demonstrated dominance of an ionization pathway for chloride solvolysis in this solvent. The k_F/k_{Cl} ratios are smaller for the 1-adamantyl substrates[7,13] that presumably proceed through a solvolysis-decomposition reaction (ionization pathway) in ethanol, methanol, and 80% ethanol.

The order of the specific rate for solvolyses of **1** and **2** in relation to those previously studied for primary,[8-10,25,26] secondary,[5,11] and tertiary[12] alkyl haloformates is $k_{Me} > k_{Et} \approx k_{n\text{-}Pr} \approx k_{i\text{-}Bu} \approx k_{1\text{-}AdCH_2} > k_{i\text{-}Pr} > k_{t\text{-}Bu}$ in 100% MeOH, 100% EtOH, and 80% EtOH, but not in 70% TFE. The increased bulk of the alkyl group (branching at the α-carbon group adjunct to the oxygen atom in alkyl haloformates) in ethyl, *i*-propyl, and *t*-butyl haloformates[2,5,9,11,12] decreases the rate of

Table 2. Specific rates for the solvolyses of 1-adamantylmethyl chloroformate (1-AdCH$_2$OCOCl, **1**) and 1-adamantylmethyl fluoroformate (1-AdCH$_2$OCOF, **2**) at various temperatures, enthalpies ($\Delta H^{\neq}$, kcal mol^{-1}), and entropies ($\Delta S^{\neq}$, cal mol^{-1}K^{-1}) of activation

Solvent (%)[a]	Temp. (°C)	**1**			**2**		
		$10^4 k$ (s^{-1})[b]	$\Delta H^{\neq}_{313}$[c]	$\Delta S^{\neq}_{313}$[c]	$10^4 k$ (s^{-1})[b]	$\Delta H^{\neq}_{313}$[c]	$\Delta S^{\neq}_{313}$[c]
100MeOH	40.0	2.48±0.04[d]	13.9±0.3	-30.7±1.1	1.64±0.04[d]	8.3±0.3	-49.5±0.8
	45.0	3.51±0.04			2.02±0.04		
	50.0	4.96±0.04			2.58±0.03		
	55.0	7.22±0.02			3.13±0.02		
100EtOH	40.0	0.767±0.004[d]	15.0±0.4	-29.6±1.3	0.384±0.004[d]	9.2±0.4	-49.4±1.4
	45.0	1.15±0.03			0.480±0.003		
	50.0	1.63±0.01			0.604±0.005		
	55.0	2.45±0.03			0.795±0.005		
80EtOH	40.0	2.11±0.03[d]	13.7±0.3	-31.6±1.0	11.3±0.4[d]	7.3±0.5	-48.8±1.5
	45.0	3.08±0.04			13.4±0.2		
	50.0	4.23±0.02			16.1±0.2		
	55.0	6.11±0.04			20.3±0.4		
70TFE	40.0	0.209±0.003[d]	19.6±0.6	-17.6±1.9	0.973±0.003[d]	12.1±0.5	-38.2±1.5
	45.0	0.353±0.004			1.28±0.03		
	50.0	0.547±0.003			1.83±0.04		
	55.0	0.938±0.003			2.45±0.05		
97TFE	40.0	0.0540±0.0005[d]	21.0±0.6	-15.7±1.8			
	60.0	0.474±0.003					
	65.0	0.717±0.005					
	70.0	1.10±0.03					
97HFIP	40.0	1.12±0.03[d]	22.2±0.4	-5.8±1.1			
	44.2	1.80±0.03					
	50.0	3.34±0.03					
	55.0	6.05±0.04					

[a,b]See footnotes in Table 1. [c]With associated standard error. [d]From Table 1.

Table 3. Kinetic **s**olvent isotope effect values (k_{MeOH}/k_{MeOD}) of solvolysis of several alkyl chloroformates (ROCOCl) and alkyl fluoroformates (ROCOF) in methanol

Solvent[a]	R = methyl[b]	ethyl[c]	n-propyl[d]	i-butyl	1-admethyl[e]	i-propyl	t-butyl[f]
$(k_{MeOH}/k_{MeOD})_{Cl}$	2.14	2.22	2.17	2.00[g]	2.19	1.25[i]	-
$(k_{MeOH}/k_{MeOD})_F$	3.98	3.10	3.32	3.40[h]	3.50	2.53[j]	1.26

[a]On a volume/volume basis, at 25.0 °C. [b]From ref. 8. [c]From ref. 9. [d]From ref. 10. [e]This study. [f]From ref. 12. [g]From ref. 25. [h]From ref. 26. [i]k_{H_2O}/k_{D_2O} from ref. 5. [j]From ref. 11.

the reaction because the electrophilic carbonyl carbon center is less accessible to nucleophilic attack. The rate ratios for ethyl-,[2,9] n-propyl-,[3,10] i-butyl-,[25,26] and 1-adamantylmethyl haloformates (**1** and **2**) in 100% MeOH, 100% EtOH, and 80% EtOH are close to unity, suggesting that electronic and/ or steric influences due to a branching β-alkyl group adjacent to an oxygen atom in the alkyl haloformates can be neglected. The specific solvolysis rates of i-propyl[5,11] and t-butyl haloformates[12] in 70% TFE were somewhat higher than the specific rates for solvolyses of ethyl,[2,9] n-propyl,[3,10] i-butyl,[25,26] n-octyl,[4] and 1-adamantylmethyl haloformates. Higher rate ratios were found in 70% TFE relative to 100% MeOH, 100% EtOH, and 80% EtOH ($k_{i-PrOCOCl}/k_{EtOCOCl} \doteq 38$ and $k_{t-BuOCOF}/k_{EtOCOF} \doteq 10$ at 40.0 °C). This is likely because the solvolyses of i-propyl chloroformate[5] and t-butyl fluoroformate[12] (*via* the relatively stable i-propyl and t-butyl cations) are more favored by the electrophilic influence of the relatively acidic TFE than the other alkyl haloformates, which are believed to proceed by a bimolecular pathway. For secondary and tertiary alkyl haloformates that undergo solvolysis by ionization, an increase in the polarity of the solvent and/or its ion-solvation ability resulted in a significant increase in reaction rate. The specific solvolysis rate of t-butyl fluoroformate,[12] which has been reported to proceed through an ionization pathway, was found to be 4.0 × 10² times faster in 70% TFE ($Y_{Cl} = 2.96$) than in 100% EtOH ($Y_{Cl} = -2.52$). This is because in the ionization pathway, charge is developed and concentrated in the transition state.

The KSIE values for the methanolysis of **1** and **2** are of a magnitude that usually indicates nucleophilic attack by a methanol molecule assisted by general-base catalysis by a second methanol molecule (Table 3).[30-32] The value ($k_{MeOH}/k_{MeOD} = 3.50 \pm 0.04$ at 40.0 °C) for **2** is larger than the value for **1** ($k_{MeOH}/k_{MeOD} = 2.19 \pm 0.02$ at 40.0 °C). This further supports the proposal that bond formation is more advanced in the transition state for addition to fluoroformate than for addition to chloroformate. The KSIE has previously been studied for several solvolyses of haloformate esters (Table 3). In methanol, the k_{MeOH}/k_{MeOD} ratio was in the range of 2.00 to 3.98 for solvolyses of alkyl and aryl haloformates, which have been reported to proceed through a bimolecular mechanism.[1-4,8-11,30,31] The k_{ROH}/k_{ROD} values for i-propyl chloroformate and t-butyl fluoroformate in the range of an ionization mechanism were 1.25[5] in pure water (S=H) and 1.26[12] in methanol (S=Me), respectively.

Activation Parameters. The solvolyses were studied kinetically as functions of temperature (Table 2). The entro-

pies of activation (-38.2 to -49.5 cal mol⁻¹ K⁻¹) for the solvolysis of **2** in the four solvents are consistent with a bimolecular pathway. The activation parameters of **1** are consistent with a dual mechanism. Bimolecular attack at the acyl carbon is expected to dominate the solvolyses of **1** in methanol, ethanol, and 80% ethanol. The entropies of activation are in the range of -29.6 to -31.6 cal mol⁻¹ K⁻¹, which is consistent with this prediction. The relatively low enthalpies and appreciably negative entropies of activation for the solvolysis of **1** are similar to those for **2**. In 70% TFE, 97% TFE, and 97% HFIP, the activation values for **1** have slightly higher enthalpies with less negative entropies of activation (-5.8 to -17.6 cal mol⁻¹ K⁻¹). These values are similar to those (-8.0 to -14.7 cal mol⁻¹ K⁻¹) previously observed for the ionization pathway (solvolysis-decomposition) of 1-adamantyl fluoroformate in 97% TFE, 80% HFIP, and 70% HFIP.[13]

Application of the Extended Grunwald-Winstein (G-W) Equation. The extended G-W equation [Eqn. (1)] is very helpful in assessing the mechanisms of solvolysis reactions. A correlation analysis of the specific rates for the solvolyses of **1** and **2** was carried out using the extended G-W equation. The *l* and *m* values were compared with those previously obtained for the solvolyses of other haloformate esters (Table 4).[1-13]

The specific solvolysis rates of **1** have been studied in a wide range of solvents, including highly ionizing and weakly nucleophilic aqueous HFIP mixtures. Applying the extended G-W equation to 27 specific rates of solvolyses for **1** gave a very poor correlation, with a correlation coefficient of 0.636 (Table 4). The poor correlation and low *l* value suggest that, as with several other chloroformate esters, there is mechanism duality. An addition-elimination mechanism likely operates in highly nucleophilic and/or weakly ionizing solvents, and an ionization mechanism takes place in weakly nucleophilic and/or highly ionizing solvents. Good correlations are obtained when the 27 solvents are divided into two groups, the aqueous fluoroalcohol solvents together with 80T-20E (9 solvents) and the other solvents (18 solvents). An analysis of the specific solvolysis rates for **1** in the 18 solvents (Figure 1(a)) leads to good linear correlation with values of 1.84 ± 0.20 for *l*, 0.55 ± 0.05 for *m*, 0.23 ± 0.07 for *c*, and 0.951 for the correlation coefficient (*R*). For the fluoroalcohol solvents (the four HFIP-H₂O mixtures and the four TFE-H₂O and 80T-20E mixtures), the values were 0.36 ± 0.09 for *l*, 0.86 ± 0.11 for *m*, and -2.92 ± 0.23 for *c*. The correlation coefficient of 0.966 indicates an acceptable correlation (Figure 1(b)). The very negative value for *c* is

Table 4. Correlation of the specific rates for the solvolyses of 1-adamantylmethyl chloroformate (1-AdCH$_2$OCOCl, **1**) and 1-adamantylmethyl fluoroformate (1-AdCH$_2$OCOF, **2**), and a comparison with the corresponding values for the solvolyses of other haloformate esters using the extended Grunwald-Winstein equation

Substrate	n^a	l^b	m^b	c^b	l/m	R^c	ref^d
1-AdCH$_2$OCOCl	27^e	0.61±0.15	0.34±0.11	-0.18±0.14		0.636	
	18^f	1.84±0.20	0.55±0.05	0.23±0.07	3.35	0.951	A-E
	9^f	0.36±0.09	0.86±0.11	-2.92±0.23	0.42	0.966	I
MeOCOCl	19^g	1.59±0.09	0.58±0.05	0.16±0.07	2.74	0.977	A-E
EtOCOCl	28^h	1.56±0.09	0.55±0+.03	0.19±0.24	2.84	0.967	A-E
	7^h	0.69±0.13	0.82±0.16	-2.40±0.27	0.84	0.946	I
n-PrOCOCl	22^i	1.57±0.12	0.56±0.06	0.15±0.08	2.79	0.947	A-E
	6^i	0.40±0.12	0.64±0.13	-2.45±0.47	0.63	0.942	I
i-PrOCOCl	20^j	0.28±0.05	0.52±0.03	-0.12±0.05	0.54	0.979	I
i-BuOCOCl	18^k	1.82±0.15	0.53±0.05	0.18±0.07	3.43	0.957	A-E
1-AdOCOCl	15^l	~0	0.47±0.03	0.03±0.05	~0	0.985	I
1-AdCH$_2$OCOF	26^m	1.68±0.10	0.85±0.06	-0.08±0.09	1.98	0.959	A-E
	22^m	1.63±0.05	0.79±0.03	0.00±0.04	2.06	0.992	A-E
MeOCOF	14^n	1.33±0.09	0.73±0.06	-0.08±0.08	1.82	0.972	A-E
EtOCOF	17°	1.34±0.14	0.77±0.07	-0.06±0.10	1.74	0.942	A-E
n-PrOCOF	19^p	1.80±0.17	0.96±0.10	-0.01±0.11	1.88	0.940	A-E
n-OctOCOF	23^q	1.80±0.13	0.79±0.06	0.13±0.34	2.28	0.959	A-E
i-PrOCOF	20^r	1.59±0.16	0.80±0.06	-0.12±0.05	1.99	0.957	A-E
i-BuOCOF	18^s	1.68±0.07	0.80±0.04	0.01±0.05	2.10	0.989	A-E
t-BuOCOF	17^t	0.41±0.05	0.65±0.03	0.02±0.04	0.63	0.989	I
1-AdOCOF	10^u	2.78±0.21	1.01±0.06	0.09±0.16	2.78	0.987	A-E
	16^u	~0	0.70±0.01	-0.02±0.05	~0	0.999	I

^{a}Number of solvent systems included in the correlation. ^{b}Using equation 1, with standard errors for l and m values and with standard errors of the estimate accompanying the c values. ^{c}Correlation coefficient. ^{d}Addition-elimination (A-E) and ionization (I). ^{e}This study for all solvents. ^{f}This study. The solvent systems divided into 97-50% TFE, 97-50% HFIP and 80T-20E ($n = 9$) and the remainder ($n = 18$). ^{g}From ref. 1. ^{h}From ref. 2. The solvent systems divided into HCOOH, 100% and 97% TFE, and 97-50% HFIP ($n = 7$) and the remainder ($n = 28$). ^{i}From ref. 3. The solvent systems divided into 100% TFE, 97% TFE, and all HFIP-H$_2$O mixtures ($n = 6$). ^{j}From ref. 5. ^{k}From ref. 25. ^{l}From ref. 7. ^{m}This study. Omitting the TFE-ethanol solvents ($n = 22$). ^{n}From ref. 8. ^{o}From ref. 9. ^{p}From ref. 10. ^{q}From ref. 4. ^{r}From ref. 11. ^{s}From ref. 26. ^{t}From ref. 12. ^{u}From ref. 13. The 26 solvent systems divided into 16 aqueous fluoroalcohol solvents and the remainder.
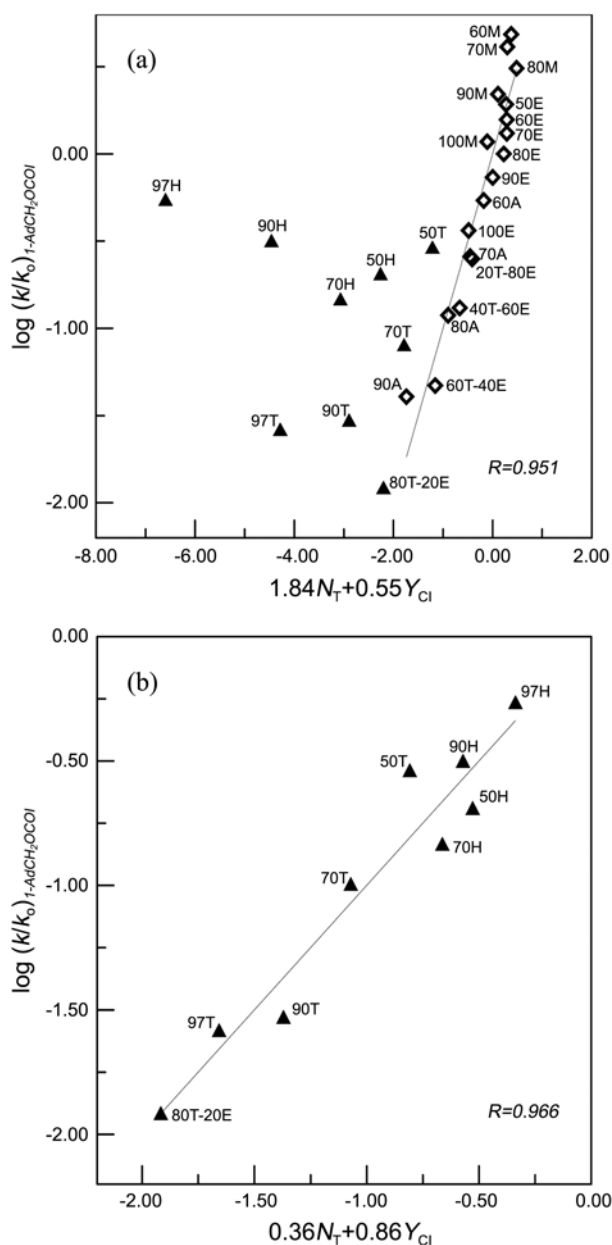
due to the experimental k_o value relating to the alternative mechanism.[2]

Table 4 also shows values obtained from the analysis of the specific solvolysis rates for **2**. As shown in Figure 2, the plot corresponding to this correlation shows that the four data points for the solvolyses in the TFE-ethanol mixtures moderately deviate from the linear plot. This has previously been discussed in detail for applying the extended G-W Eq. (1) to the specific solvolysis rates of alkyl and acyl haloformate esters in binary TFE-ethanol solvents.[5,13,32,33] Correlations were carried out both with and without the TFE-ethanol data. Data analysis using the extended G-W Eq. (1) for the specific rates of solvolysis for **2** in all solvents led to an acceptable linear correlation with values of 1.68 ± 0.10 for l, 0.85 ± 0.06 for m, -0.08 ± 0.09 for c, and 0.959 for the correlation coefficient. Recalculation with omission of the four data points for the TFE-ethanol mixtures led to a considerably improved linear correlation with values of 1.63 ± 0.05 for l, 0.79 ± 0.03 for m, 0.01 ± 0.04 for c, and 0.992 for the correlation coefficient (Table 4).
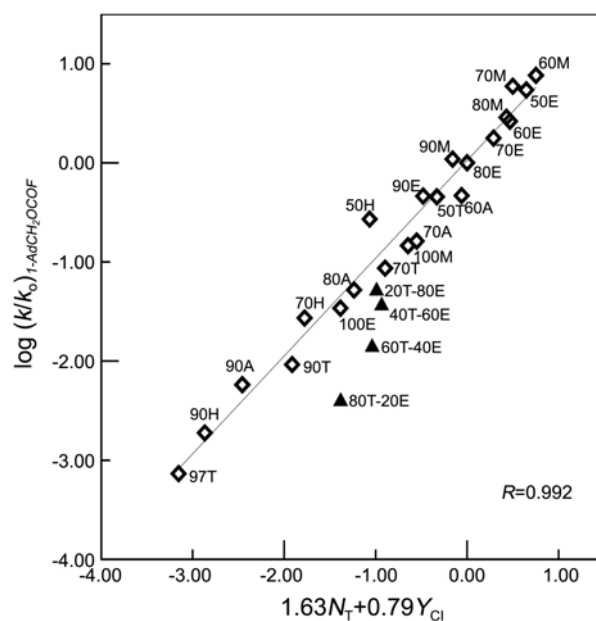
The relative magnitude of l and m has often been suggested as useful mechanistic criteria. The l and m values of alkyl chloroformates in Table 4 divide clearly into two classes, values of 2.7 to 3.4 for those entries postulated to represent an addition-elimination (A-E, Scheme 1a) mechanism and values below 0.84 for those believed to represent an ionization (I, Scheme 1b and 1c) mechanism. Table 4 shows that the l and m values [l/m = 3.35 (A-E) and 0.42 (I)] of **1** are similar to those previously reported for all other primary alkyl chloroformates in all of the solvents, except for aqueous fluoroalcohol solvents. The value for **2** [l/m = 2.06 (A-E)] is similar to those for all other primary and secondary alkyl fluoroformates in all of the solvents, despite the increasing chain length in primary alkyl fluoroformates,[4,8-10,26] the influence of a branched-chain alkyl group (*i.e.*, EtO-[9] and *i*-PrO-[11]), and the steric effect of a bridgehead compound of adamantane in all of the solvents except for aqueous fluoroalcohol solvents (*i.e.*, 1-AdO-[13]). Higher m values for the addition-elimination solvolyses of **2** relative to **1** may reflect the need for increased solvation of the developing negative charge on the carbonyl oxygen in the presence of the fluorine attached at the carbonyl carbon.[4,8-11,34,35]

Product Studies. The percentage compositions and selectivity (S) values for reactions of **1** in ethanol and aqueous ethanol are reported in Table 5. The 1.1% of 1-adamantanemethanol (1-AdCH$_2$OH) after solvolysis in 100% ethanol is

Figure 2. Plot of $\log(k/k_o)$ for the solvolyses of 1-adamantylmethyl fluoroformate (**2**) at 40.0 °C against $(1.63N_T + 0.79Y_{Cl})$. The log (k/k_o) values for the four TFE-EtOH mixtures are not included in the correlation. They are added to show their moderate deviation from the correlation line.

Figure 1. Plots of $\log(k/k_o)$ for the solvolyses of 1-adamantyl-methyl chloroformate (**1**) at 40.0 °C (a) against $(1.84N_T + 0.55Y_{Cl})$ and (b) against $(0.36N_T + 0.86Y_{Cl})$ in the aqueous TFE, HFIP, and 80T-20E mixtures. Data points for aqueous TFE, HFIP, and the 80T-20E mixtures are not included in the correlation for (a).

similar to the 2.7% found after ethanolysis of 1-adamantyl chloroformate[7] and the 1.3% found after ethanolysis of 2-adamantyl chloroformate.[6] As previously proposed, this probably results from the substrate reacting with moisture during manipulation.

For solvolyses in aqueous ethanol, the S values increase steadily from 2.4 in 80% ethanol to 4.2 in 50% ethanol (Table 5). These values are remarkably similar to those observed in the corresponding solvolyses of benzyl chloroformate $(S=2.0\text{-}4.1)$,[30] benzyl fluoroformate $(S=2.2\text{-}3.6)$,[31] and p-substituted benzoyl chlorides $(S=2.0\text{-}4.2)$,[36,37] which are believed to follow the addition-elimination pathway.[38]

The product studies for the solvolysis of **2** (Table 6) are also consistent with an addition-elimination pathway. All of the products can result from mixed carbonate esters formed from reaction with either a pure alcohol or an alcohol component of a mixed solvent. When reacting with water, 1-

Table 5. Percentage of products formed in the solvolyses of 1-adamantylmethyl chloroformate (1-AdCH$_2$OCOCl, **1**) in various hydroxylic solvents at 40.0 °C and the calculated selectivity (S) values

Solvent[a] (%)	1-AdCH$_2$Cl 2.007[b]	1-AdCH$_2$OEt 4.520[b]	1-AdCH$_2$OH 4.780[b]	1-AdCH$_2$OCO$_2$Et 7.863[b]	S^c_{acyl}
100EtOH	trace[d]		1.1371	98.8629	
80EtOH	0.374		24.9178	74.7082	2.43
70EtOH	0.5019		31.1696	68.3285	3.05
60EtOH	0.8606	2.4300	36.4269	60.2824	3.58
50EtOH	0.9651	3.9663	41.4201	53.6485	4.20

[a]Volume-volume basis at 25.0 °C. [b]Retention time (min) under the GC conditions. [c]Selectivity involved in solvent attack at the acyl carbon, *i.e.*, $(S_{acyl})_{EtOH} = $ [1-adamantylmethyl alkyl carbonate][water]/[1-adamantylmethanol][alcohol]. [d]Less than 0.1%.

Table 6. Percentage of products formed in the solvolyses of 1-adamantylmethyl fluoroformate (1-AdCH$_2$OCOF, **2**) in various hydroxylic solvents at 40.0 $^{\circ}$C and the calculated selectivity (*S*) values

Solvent[a] (%)	1-AdCH$_2$OCO$_2$TFE 3.915[b]	1-AdCH$_2$OH 4.780[b]	1-AdCH$_2$OCO$_2$Et 7.863[b]	S^c_{acyl}
100EtOH		trace[d]	100.000	
80EtOH		28.1607	71.8393	2.07
60EtOH		41.2192	58.7808	3.08
90Acetone		100.000		
90TFE	30.7066	69.2994		0.27
70TFE	9.8131	90.1868		0.25
80T-20E	15.4332	1.7387	82.8281	0.068

[a,b,c,d]See footnotes to Table 5.

AdCH$_2$OH is formed after carbon dioxide loss from an initially formed hydrogen carbonate (Scheme 1a). There was no evidence for 1-adamantylmethyl fluoride (1-AdCH$_2$F) from a competing decomposition. There was also no evidence for the appropriate mixed ether, which would have formed by an ionization pathway involving loss of carbon dioxide, followed by carbocation reaction with an alcohol component of the solvent. Small amounts of 1-AdCH$_2$OH (1.74% and 3.32%) were found in TFE-ethanol mixtures. Since no 1-AdCH$_2$OH was found for the reaction in 100% ethanol, its presence in the TFE-ethanol mixtures is likely due to the presence of a small concentration of water in the TFE.

In 80% and 60% ethanol, the *S* values are 2.1 and 3.1, respectively. These values are also similar to those previously observed for other haloformates solvolyses which are believed to follow the addition-elimination pathway. For the reactions in aqueous TFE and TFE-ethanol mixtures, the selectivity (*S*) values are 0.25-0.27 and 0.068-0.14, respectively. These values are very similar to the values for benzyl fluoroformate (*S* = 0.12 and 0.19 in aqueous TFE, *S* = 0.043 in 80T-20E)[31] and *p*-nitrobenzyl chloroformate (*S* = 0.16 in 80% TFE, *S* = 0.0035 in 80T-20E)[30] and are within the addition-elimination region.

In conclusion, the solvolyses of **1** occur by two major reaction pathways. In fluoroalcohol solvents (four HFIP-H$_2$O mixtures, four TFE-H$_2$O mixtures, and 80T-20E mixtures), the reactions of **1** solvolyze by an ionization pathway (Scheme 1(c)) which gives an *l* value of 0.36 and an *m* value of 0.86. In all solvents except the aqueous fluoroalcohol and 80T-20E binary solvents, these solvolyses (*l* = 1.84, *m* = 0.55) are similar to values previously observed for the solvolyses of ethyl- and *n*-propyl chloroformates, which proceeds by an addition-elimination pathway (Scheme 1(a)). Multiple correlation analysis of the specific rates of solvolysis of **2** in all the solvents showed sensitivity toward changes in solvent nucleophilicity (*l* value of 1.63) and sensitivity toward changes in solvent ionizing power (*m* value of 0.79). These reactions are similar to those observed for the solvolyses of **1** in 18 pure and binary solvents. The results are consistent with the large negative entropies of activation (Table 2), the leaving group effects of close to unity (Table 1), and the relatively high kinetic solvent isotope effects (KSIEs, Table 3).

Experimental

Materials. The 1-adamantylmethyl chloroformate was prepared by the procedure described earlier.[6] A solution of 3.00 g of triphosgene in 20 mL of toluene at 0-4 $^{\circ}$C (ice bath) was added to a room temperature solution of 1.500 g of 1-adamantanemethanol and 0.800 mL of pyridine in 20 mL of toluene over a 1 h period. The mixture was then washed with 3 × 50 mL of ice water and dried (anhydrous MgSO$_4$). It was passed through a glass filter, and the toluene was removed using a rotary evaporator. The residue was recrystallized twice from anhydrous *n*-hexane to give 1.75 g (67.6% yield) of white crystalline 1-adamantylmethyl chloroformate (**1**), mp 46.4-47.5 $^{\circ}$C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.564-1.763 (m, 12H, CH$_2$ in adamantyl), 2.023 (s, 3H, CH in adamantyl), 3.930 (s, 2H). ^{13}C NMR δ 27.99, 33.72, 36.90, 38.95, 81.66, 151.2. IR (KBr) includes 2905, 2849, 1777 (C=O), 1151(C-O) cm^{-1}. 1-Adamantylmethyl fluoroformate (**2**, mp 56.4-58.0 $^{\circ}$C) was prepared from 1-adamantanemethanol *via* reaction with 1-chloroethyl chloroformate by the procedure described earlier.[39] For the ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.570-1.766 (m, 12H, CH$_2$ in adamantyl), 2.025 (s, 3H, CH in adamantyl), 3.891 (s, 2H). ^{13}C NMR δ 27.95, 33.58, 36.89, 38.85, 81.11, 145.1, 147.3. IR (KBr) includes 2906, 2851, 1828 (C=O), 1258 (C-O) cm^{-1}.

The solvents used were purified as previously described.[40] The kinetic runs were carried out as previously described,[26] and the *l* and *m* values were calculated using multiple regression analysis.

Product Studies. The products from reactions **1** and **2** under solvolytic conditions were analyzed after 10 half-lives by gas chromatography (GC) with response-calibrated FID (Shimazu GC-9A). A 2.1 m glass column containing 10% Carbowax 20M was used on Chromosorb WAW 80/100 with an injection temperature of 210 $^{\circ}$C and a column temperature 170 $^{\circ}$C. The retention times (min) of the observed products are reported in Tables 5 and 6. Small quantities of the solvolysis, solvolysis-decomposition, and decomposition products required for calibration purposes were prepared as previously described.[6,13] The 1-adamantanemethanol (1-AdCH$_2$OH, Aldrich) used in response calibration was recrystallized commercial material. A solution in ethanol of 1-AdCH$_2$OH showed only one solute peak in GC. It is

possible, indeed probable, that in the product percentages, presented in Table 5, the small amounts of products formed by collapse of an intermediate carbocation with chloride ion or with solvent involve an initial capture of the 3-homoadamantyl cation, formed by an energetically favorable rearrangement. However, since there are offsetting influences of carbenium ion stability and ring strain, it is possible that an eventual thermodynamic control could lead to some degree of conversion to products with the 1-adamantylmethyl group contained.[41,42] Since these types of products make up only a very small percentage of the overall product formation, we did not attempt further characterization.

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