Dual Pathways in the Solvolyses of Isopropyl Chloroformate

Jin Burm Kyong,* Yong-Gun Kim, Dong Kook Kim, and Dennis N. Kevill†

Department of Chemistry, Hanyang University, Ansan, Kyunggi-Do 425-791, Korea
†Department of Chemistry and Biochemistry, Northern Illinois University, Dekalb, Illinois 60115-2862, U.S.A.

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Recently, we reported that the specific rates for the solvolyses of alkyl chloroformate (ROCOCl, R=CH_3-, CH_3CH_2-, C_6H_5-, $C_{10}H_{17}$-)[1-3] can be very well correlated using the extended Grunwald-Winstein equation [eq. (1)].[4-8]

$$\log (k/k_o) = lN_T + mY_{Cl} + c \qquad (1)$$

Leimu[9] showed a specific rate order of Me > Et > *i*-Pr for methanolysis of alkyl chloroformate, which is consistent with a bimolecular reaction in which bond formation to the attacking nucleophile is the dominant aspect. Crunden and Hudson[10] found a specific rate order of Me > Et < *i*-Pr in 35% aqueous acetone and a specific rate order of Me < Et << *i*-Pr in moist formic acid. They concluded that the isopropyl chloroformate reacted by a dominant unimolecular mechanism in both solvents, and ethyl chloroformate by a bimolecular mechanism in the aqueous acetone and by a unimolecular mechanism in the moist formic acid. Orlov[11] studied the ethanolysis of a series of halogenoformates, including isopropyl chloroformate, and concluded that they all reacted by a bimolecular mechanism, involving rate-determining addition of the nucleophile within an addition-elimination sequence. Evidence that this addition-elimination pathway often operates for the solvolyses of haloformate esters includes Cl/F leaving-group effects of close to unity or lower,[10b-13] consistent with the addition step being rate determining, and also the relatively high k_{H_2O}/k_{D_2O} solvent isotope effects and the large negative values for the entropies of activation.[10-14] Queen[14] proposed a unimolecular mechanism for hydrolysis of isopropyl chloroformate on the basis of a positive entropy of activation and a low solvent isotope effect. The tertiary 1-adamantyl chloroformate[1] solvolyzes by a unimolecular pathway over the full range of solvent compositions studied, which also involves loss of carbon dioxide.

In the present study, we report concerning the application of eq. (1) to the solvolyses of secondary isopropyl chloroformate in a wide range of solvent type, and also consider the specific rates for the solvolyses of primary, secondary and tertiary alkyl chloroformate in terms of the extended Grunwald-Winstein equation. In particular, we wish to see whether there is evidence from application of eq. (1) for a change in mechanism in the more and/or weakly nucleophilic solvents. This is the first time that this equation [eq. (1)] has been used as a tool in studies of isopropyl chloroformate solvolysis.

Results and Discussion

The specific rate constants of isopropyl chloroformate measured at 40.0 °C are reported in Table 1, together with the N_T and Y_{Cl} values.

Table 1. Specific rate constants of solvolysis (with standard deviations) of isopropyl chloroformate[a] in pure and aqueous solvents at 40.0 °C together with the appropriate N_T and Y_{Cl} values

Solvent[b]	$10^4\,k$ (s^{-1})	N_T[c]	Y_{Cl}[d]
100% MeOH[e]	1.54 ± 0.009[f]	0.17	-1.17
90% MeOH	3.07 ± 0.06	-0.01	-0.18
80% MeOH	4.97 ± 0.06	-0.06	0.67
70% MeOH	7.66 ± 0.08	-0.40	1.46
60% MeOH	12.0 ± 0.6	-0.54	2.07
100% EtOH	0.541 ± 0.001[g]	0.37	-2.52
90% EtOH	1.08 ± 0.005	0.16	-0.94
80% EtOH	1.86 ± 0.02	0.00	0.00
70% EtOH	3.13 ± 0.01	-0.20	0.78
60% EtOH	5.13 ± 0.004	-0.38	1.38
50% EtOH	9.65 ± 0.03	-0.58	2.02
100% H_2O	163[h]	-1.38	4.57
90% Me_2CO	0.108 ± 0.003	-0.35	-2.39
80% Me_2CO	0.427 ± 0.003	-0.37	-0.80
70% Me_2CO	1.18 ± 0.02	-0.42	0.17
60% Me_2CO	2.88 ± 0.02	-0.52	1.00
100% HCO_2H	17.9[i]	-2.44	3.20
97% TFE	7.16 ± 0.07	-3.30	2.83
90% TFE	7.47 ± 0.09	-2.55	2.85
70% TFE	11.7 ± 0.3	-1.98	2.96
80T-20E[j]	2.13 ± 0.07	-1.76	1.89
60T-40E[j]	0.787 ± 0.005	-0.94	0.63
40T-60E[j]	0.376 ± 0.002	-0.34	-0.48
20T-80E[j]	0.316 ± 0.005	0.08	-1.42

[a] Substrate concentration of *ca.* 5.2×10^{-3} M. [b] Volume/volume basis at 25.0 °C, except for TFE-H_2O mixtures, which are on a weight/weight basis. [c] From ref. 6. [d] From refs. 7 and 8. [e] k(0.393 ± 0.003) × 10^{-4} sec^{-1} at 25.0 °C, k=(0.985 ± 0.006) × 10^{-4} sec^{-1} at 35.0 °C, and k = (1.54 ± 0.009) × 10^{-4} sec^{-1} at 40.0 °C; $\Delta H^{\neq} = 57\ \mathrm{KJ \cdot mol^{-1}}$, $\Delta S^{\neq} = -101\ \mathrm{J \cdot mol^{-1} \cdot K}$. [f] Extrapolation of values in the range 15-35 °C (ref. 9) leads to a value of 1.55×10^{-4} sec^{-1}. [g] Interpolation within values of ref. 11 gives a value of 0.506×10^{-4} sec^{-1}. [h] By extrapolation, using the Arrhenius equation, of values in the range 2.591-24.54 °C (ref. 14). [i] By interpolation, using the Arrhenius equation, of values of 2.60×10^{-4} sec^{-1} at 24.0 °C (ref. 10b) and 54.0×10^{-4} sec^{-1} at 50.0 °C (ref. 10a). [j] T-E are TFE-ethanol mixtures.

An analysis of the 24 specific rates of Table 1 gives, in terms of the simple Grunwald-Winstein equation [eq. (1) without the lN_T term], values of 0.34 ± 0.03 for *m*, -0.11 ± 0.07 for *c*, 0.905 for the correlation coefficient, and 100 for the F-test value. A poor value was obtained for the correlation coefficient. Clearly, this equation does not correlate the data. Again, the correlation is considerably improved by the use of the full eq. (1), with values of 0.30 ± 0.08 for *l*, 0.46 ±

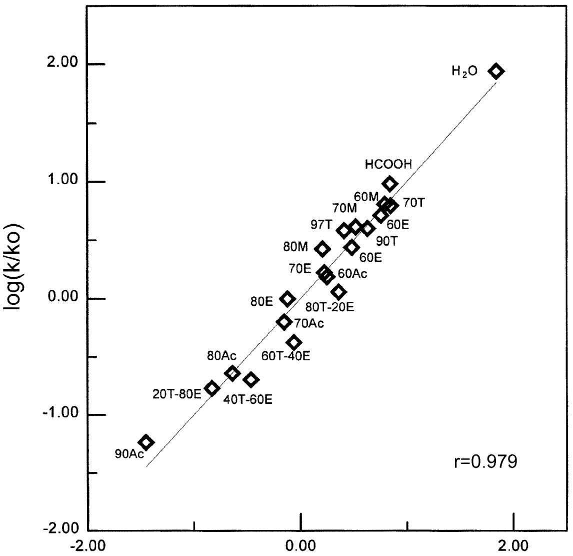

Figure 1. The plot of log(k/k_0) for solvolyses of isopropyl chloroformate at 40.0 °C against ($0.28N_T+0.52Y_{Cl}$). (Omission; EtOH, 90% EtOH, MeOH, and 90% MeOH).

0.05 for m, 0.02 ± 0.06 for c, 0.946 for the correlation coefficient, and 90 for the F-test value. The correlation coefficient is still rather poor at 0.946 and the F-test value is 90.

Inspection of the data showed considerable deviation for the more nucleophilic and less ionizing solvents (ethanol, 90% ethanol, methanol, and 90% methanol). A considerably improved correlation (Figure 1) results in when these four data points are omitted and values are obtained for 20 solvents of 0.28 ± 0.05 for l, 0.52 ± 0.03 for m, -0.12 ± 0.05 for c, 0.979 for the correlation coefficient, and 192 for the F-test value. These l and m values are similar to those obtained to reflect the ionization pathway within the analyses of the solvolyses of ethyl chloroformate, ethyl chlorothioformate, and 1-adamantyl chloroformate (Table 2),[1,2] where bond breaking (m-value) is more progressed than bond making (l-value).

Also, the values of the enthalpy and entropy of activation for the methanolysis of isopropyl chloroformate measured, as an example of the four exculded solvents (ethanol, 90% ethanol, methanol, and 90% methanol), are 57 kJ · mole^{-1} and -101 J · mole^{-1}K^{-1}, respectively. These values are consistent with the finding by Orlov[11] of similar activation parameters for the ethanolyses of methyl chloroformate, ethyl chloroformate, isopropyl chloroformate, and ethyl chlorothioformate, with a very negative entropy of activation. Presumably the bimolecular addition-elimination pathway is dominant in the four excluded solvents. One very compelling type of evidence for a rate determining addition, within an addition-elimination pathway, involves a study of chlorine/fluorine leaving-group effects. When the carbon-halogen bond is broken in a nucleophilic displacement reaction, the chloro-derivative reacts appreciably faster than the the fluoro-derivative, as much as 10^5 to 10^7 times faster for a unimolecular ionization[15,16] and some 10^1 to 10^3 times faster in concerted bimolecular displacements at a saturated carbon.[17] The previous observations[10b-13] that, when a bimolecular attack at an acyl carbon is operative, fluoroformate and chloroformate esters solvolyze at very similar rates, frequently with the fluoroformate ester the faster, have been uniformly rationalized in terms of the addition step of an addition-elimination mechanism being rate determining.

Solvent isotope effects (k_{H_2O}/k_{D_2O}), which have been measured, include values for aryl chloroformates of 2.19-2.24 in 10% acetone[18] and 1.79-1.89 for methyl, ethyl, and phenyl chloroformate in pure water.[14,19] These values are within the range predicted for a bimolecular solvolysis which is companied by general-base catalysis.[16,20-22] But the value for isopropyl chloroformate showed a smaller solvent isotope effect (k_{H_2O}/k_{D_2O}=1.25).[14] This is similar to a small solvent isotope effect value for the unimolecular pathway of diphenyl chloromethane.[23]

The correlation analyses of the specific rates for the solvolyses of primary, secondary and tertiary alkyl chloroformate esters are summerized in Table 2.

From the l and m values presented in Table 2, the solvolyses of phenyl[2a] and methyl[3] chloroformates are indicated to proceed by a bimolecular addition-elimination in all the solvents studied. In ethyl chloroformate solvolysis,[2b] an addi-

Table 2. Correlation of the specific rate constants of the solvolyses of methyl, ethyl, isopropyl, phenyl, and 1-adamantyl chloroformates and ethyl chlorothioformate using the extended Grunwald-Winstein equation

Substrate	Mechanism[a]	n[b]	l/m	l[c]	m[c]	c[c]	r[d]	F[e]
PhOCOCl	A-E	21[f]	2.95	1.68 ± 0.10	0.57 ± 0.06	0.12 ± 0.41	0.973	159
MeOCOCl	A-E	19[g]	2.74	1.59 ± 0.09	0.58 ± 0.05	0.16 ± 0.07	0.977	171
EtOCOCl	A-E	28[h]	2.84	1.56 ± 0.09	0.55 ± 0.03	0.19 ± 0.24	0.967	179
EtOCOCl	I	7[h]	0.84	0.69 ± 0.13	0.82 ± 0.16	-2.40 ± 0.27[i]	0.946	17
EtSCOCl	I	19[j]	0.71	0.66 ± 0.08	0.93 ± 0.07	-0.16 ± 0.31	0.961	96
i-PrOCOCl	I	20[k]	0.54	0.28 ± 0.05	0.52 ± 0.03	-0.12 ± 0.05	0.979	192
1-AdOCOCl	I	15[l]	~0	~0	0.47 ± 0.03	0.03 ± 0.05	0.985	97

[a] The two reaction channels are designated as addition-elimination (A-E) and ionization(I). [b] Number of solvent systems included in the correlation. [c] Using eq. 1, with standard errors for l and m values and with the standard error of the estimate accompanying the c value. [d] Correlation coefficient. [e] F-test value. [f] All solvent systems (ref. 2a). [g] The 21 solvent systems studied, with omission of 90% HFIP, and 100% HCO_2H (ref. 3). [h] The solvent systems divided into HCO_2H, 100% and 97% TFE and 97%-50% HFIP (n=7) and the remainder (n=28), (ref. 2b). [i] Large negative value for c because the experimental k_0 value is not for this reaction channel. [j] The 22 solvents systems studied, with omission of EtOH, 90% EtOH, and MeOH (ref. 2b). [k] The 24 solvents systems studied, with omission of EtOH, 90% EtOH, MeOH, and 90% MeOH. [l] Using the simple Grunwald-Winstein equation (ref. 4).

tion-elimination pathway dominates, and only in the more ionizing and less nucleophilic solvents does the principal reaction pathway involve ionization. For isopropyl chloroformate, the ionization pathway is dominant for the majority of solvents, only in ehtanol, 90% ethanol, methanol, and 90% mehanol is the major pathway bimolecular. The tertiary 1-adamantyl chloroformate[1] solvolyzes by an ionization pathway over the full range of solvents. The characteristics for the solvolyses of the ethyl and isopropyl chloroformate are intermediate between those for the methyl and 1-adamantyl chloroformate.

In conclusion, the specific rates of solvolysis of isopropyl chloroformate are very well correlated by the extended Grunwald-Winstein equation over a wide range of solvents. This substrate provides an evidence for two competing reaction channels. The solvolyses of isopropyl chloroformate are indicated to proceed by an ionizing pathway in all but the more nucleophilic and least ionizing solvents. In the more nucleophilicity-least ionizing combination (ethanol, 90% ethanol, methanol and 90% methanol) is there evidence for a dominant addition-elimination pathway. This behaviour is very similar to those analyzed of the specific rates for solvolyses of ethyl chlorothioformate over a wide range of solvents.

This study is able to divide into two reaction channels. In one channel, the l/m ratios of 2.74-2.95 are considered to reflect the operation of an addition elimination pathway. In the other channel, the l/m ratios of ≤ 0.84 are considered as being a consequence of an ionization pathway. Accordingly, these values (l/m ratios) will be very useful as reference values in extended Grunwald-Winstein treatments of the solvolyses of other chloroformate esters.

Experimental Section

Solvents were purified and the kinetic runs carried out as previously described.[1] Isopropyl chloroformate (Aldrich, 1.0 M solution in toluene) was used without further purification. All runs were performed at least in duplicate. The l and m values were calculated using the multiple regression analyses.

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