

Dual Pathways in the Solvolyses of Phenyl Chlorothioformate

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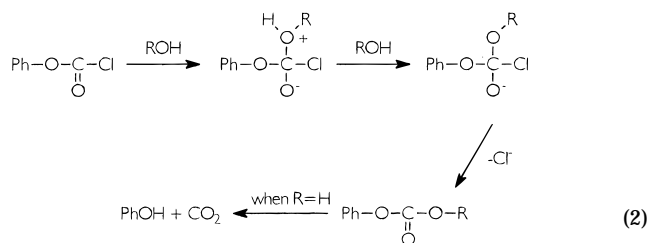
Recently, we reported¹ that the specific rates of solvolysis of phenyl chloroformate (PhOCOCl) at 25.0 °C can be very well correlated using the extended Grunwald–Winstein equation (eq 1), with an *l* value of 1.68 ± 0.10 and an *m* value of 0.57 ± 0.06 . In eq 1, *k* and *k*₀ are the

$$\log(k/k_0)_{\text{RCl}} = lN_{\text{T}} + mY_{\text{Cl}} + c \quad (1)$$

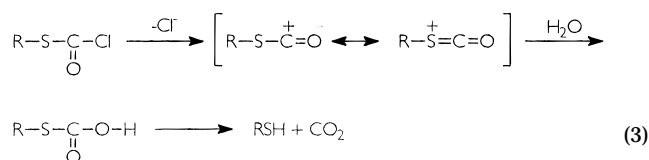
specific rates of solvolysis of RCl in the solvent under consideration and in the standard solvent, 80% ethanol, respectively; *l* is the sensitivity to changes in solvent nucleophilicity, here expressed as *N*_T values;² *m* is the sensitivity to changes in solvent ionizing power (*Y*_{Cl} for a chloride-ion leaving group);³ and *c* is a constant (residual) quantity.

Several other techniques had previously been applied to studies of the solvolyses of phenyl chloroformate, including F/Cl leaving group effects,^{4,5} Hammett treatments of substituent effects,^{6–8} solvent isotope effects,^{7–9} and consideration of the activation parameters.^{7–9} These techniques have all indicated a bimolecular mechanism, almost certainly of the addition–elimination (tetrahedral intermediate) type (eq 2) but possibly with the first-formed intermediate so unstable that the mechanism could be considered⁸ as an enforced concerted variant.¹⁰ Such a mechanism would proceed in one step, with the tetrahedral arrangement being a transition state rather than an intermediate. Accordingly, the *l* and *m* values obtained are useful reference values for studies of other chloroformate ester solvolyses.

One interesting substrate for consideration of this type is the formally closely related phenyl chlorothioformate (PhSCOCl, **1**). In a study of the hydrolysis of **1**, Queen



found^{11,12} that the reaction was slower than the corresponding hydrolysis of PhOCOCl. Increases in rate as one goes from phenyl to primary to secondary to tertiary alkyl for the R group within RSCOCl, coupled with a positive entropy of activation for hydrolysis of the methyl ester, were considered^{11,13} to give strong support to an S_N1 mechanism for the hydrolyses of chlorothioformate esters (eq 3).



A fairly delicate balance between the unimolecular and bimolecular pathways on replacement of the oxygen atoms of PhOCOCl with sulfur atoms was indicated by the observation that, while the hydrolysis in aqueous acetone of chlorodithioformate esters (RSCSCL) had the characteristics of an ionization process (S_N1 mechanism),¹³ the addition of azide ion led to a bimolecular attack by the anion.¹⁴ Mechanistic changes within the bimolecular pathway could be associated with changes in the stability of the tetrahedral intermediate, with the enforced concerted mechanism lying at one extreme.

It was decided that it would be of interest to see whether the claim of a unimolecular hydrolysis for **1** would be supported by a study of solvent variation, with application of the extended Grunwald–Winstein equation. Further, assuming the claim was supported, it would also be of interest to see whether the mechanism could revert to the bimolecular mechanism observed for PhOCOCl when the solvent was changed to one of higher solvent nucleophilicity and/or lower solvent ionizing power.

Results

The specific rates of solvolysis of phenyl chlorothioformate were determined, at 25.0 °C, in ethanol and methanol and their binary mixtures with water. Acetone and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) were used in binary mixtures with water, and 2,2,2-trifluoroethanol (TFE) was used in binary mixtures with both water and ethanol. Constant integrated specific rates were obtained over the 50–80% of possible reaction that was followed.

In Table 1 are presented the 22 specific rates of solvolysis incorporated into the correlations using eq 1, comparisons with the corresponding specific rates of solvolysis of PhOCOCl, and *N*_T and *Y*_{Cl} values.^{2,3}

(11) Queen, A.; Nour, T. A.; Paddon-Row, M. N.; Preston, K. *Can. J. Chem.* **1970**, *48*, 522.

(12) Queen, A.; Nour, T. A.; Bock, E. *Can. J. Chem.* **1969**, *47*, 343.

(13) McKinnon, D. M.; Queen, A. *Can. J. Chem.* **1972**, *50*, 1401.

(14) (a) Queen, A.; Matts, T. C. *Tetrahedron Lett.* **1975**, 1503. (b) Queen, A.; McKinnon, D. M.; Bell, A. W. *Can. J. Chem.* **1976**, *54*, 1906.

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(1) Kevill, D. N.; D'Souza, M. J. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1721.

(2) (a) Kevill, D. N.; Anderson, S. W. *J. Org. Chem.* **1991**, *56*, 1845.

(b) Kevill, D. N. In *Advances in Quantitative Structure–Property Relationships*; Charton, M., Ed.; JAI Press: Greenwich, CT, 1996; Vol. 1, pp. 81–115.

(3) (a) Bentley, T. W.; Carter, G. E. *J. Am. Chem. Soc.* **1982**, *104*, 5741. (b) Bentley, T. W.; Llewellyn, G. *Prog. Phys. Org. Chem.* **1990**, *17*, 121. (c) Kevill, D. N.; D'Souza, M. J. *J. Chem. Res., Synop.* **1993**, 174. (d) Koo, I. S.; Bentley, T. W.; Kang, D. H.; Lee, I. *J. Chem. Soc., Perkin Trans. 2* **1991**, 296.

(4) Queen, A.; Nour, T. A. *J. Chem. Soc., Perkin Trans. 2* **1976**, 935.

(5) Orlov, S. I.; Chimishkyan, A. L.; Grabarnik, M. S. *J. Org. Chem. U.S.S.R. (Engl. Transl.)* **1983**, *19*, 1981.

(6) Butler, A. R.; Robertson, I. H.; Bacaloglu, R. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1733.

(7) (a) Ostrogovich, G.; Csunderlik, C.; Bacaloglu, R. *J. Prakt. Chem.* **1975**, *317*, 62. (b) Csunderlik, C.; Bacaloglu, R.; Ostrogovich, G. *J. Prakt. Chem.* **1975**, *317*, 81.

(8) Yew, K. H.; Koh, H. J.; Lee, H. W.; Lee, I. *J. Chem. Soc., Perkin Trans. 2* **1995**, 2263.

(9) Queen, A. *Can. J. Chem.* **1967**, *45*, 1619.

(10) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345.

Table 1. Specific Rates of Solvolysis of Phenyl Chlorothioformate (1)^a at 25.0 °C, Comparison with Corresponding Specific Rates for PhOCOCl,^b and Solvent Nucleophilicity and Ionizing Power Values

solvent ^c	10 ⁵ <i>k</i> , s ⁻¹ ^d	<i>k</i> / <i>k</i> _{PhOCOCl}	<i>N</i> _T ^e	<i>Y</i> _{Cl} ^f
100% EtOH	6.73 ± 0.15	0.026	+0.37	-2.52
90% EtOH	11.5 ± 0.6	0.029	+0.16	-0.94
80% EtOH	14.6 ± 0.6 ^g	0.029	0.00	0.00
70% EtOH	16.0 ± 0.6	0.029	-0.20	0.78
60% EtOH	18.1 ± 0.8	0.028	-0.38	1.38
50% EtOH	23.0 ± 0.8		-0.58	2.02
100% MeOH	29.1 ± 0.9	0.042	+0.17	-1.17
90% MeOH	47.6 ± 1.3		-0.01	-0.18
80% MeOH	55.1 ± 1.2		-0.06	0.67
80T-20E ^h	0.252 ± 0.009	0.10	-1.76	1.89
60T-40E	0.574 ± 0.019	0.033	-0.94	0.63
40T-60E	2.11 ± 0.18		-0.34	-0.48
20T-80E	3.94 ± 0.10		+0.08	-1.42
80% acetone	2.82 ± 0.08	0.042	-0.37	-0.80
70% acetone	4.86 ± 0.14		-0.42	0.17
60% acetone	7.40 ± 0.42		-0.52	1.00
97% TFE ⁱ	0.345 ± 0.009	5.9	-3.30	2.83
90% TFE ⁱ	0.561 ± 0.016	0.50	-2.55	2.85
70% TFE ⁱ	2.22 ± 0.09		-1.98	2.96
50% TFE ⁱ	6.22 ± 0.08		-1.73	3.16
90% HFIP ⁱ	2.70 ± 0.06	16	-3.84	4.31
50% HFIP ⁱ	6.93 ± 0.20	0.22	-2.49	3.80

^a Substrate concentration of 0.004–0.006 mol dm⁻³. ^b From ref 1. ^c Unless otherwise stated, binary solvents are on a volume–volume basis at 25.0 °C. ^d With associated standard deviation. ^e From ref 2. ^f From ref 3. ^g Measured at three substrate concentrations; values of 10⁵ *k* of 14.3 ± 0.4 at 0.0197 mol dm⁻³, 14.6 ± 0.6 at 0.0055 mol dm⁻³, and 14.8 ± 0.2 at 0.0025 mol dm⁻³. ^h T–E are TFE–ethanol mixtures. ⁱ On weight–weight basis.

Discussion

A comparison of the specific rates of solvolysis of **1** with those for phenyl chloroformate solvolysis shows that the replacement of oxygen by sulfur leads, in ethanol, methanol, and binary solvents not containing fluoro alcohol, to a retardation by a factor of about 30. Introduction of fluoro alcohol reduces this retardation, and eventually **1** becomes the most reactive, by a factor of 6 in 97% TFE and by a factor of 16 in 90% HFIP. Similar behavior for the methyl esters in aqueous acetonitrile and aqueous acetone, with the chlorothioformate solvolysis fastest in the highly aqueous region but the chloroformate solvolysis faster in the solvents rich in the organic component,¹⁵ was rationalized in terms of a usual bimolecular reaction being replaced by a predominantly unimolecular pathway for solvolyses of chlorothioformate in the more aqueous solvents. It had previously been proposed¹¹ that the hydrolysis of methyl chlorothioformate in pure water was S_N1 in character.

A change in the mechanism for the solvolyses of **1** as the solvent composition is varied, unlike the unity of mechanism for phenyl chloroformate solvolysis,¹ is indicated from an analysis in terms of the extended Grunwald–Winstein equation (eq 1). The correlation of all 22 solvents of Table 1 in this way leads to values of 0.79 ± 0.17 for *l*, 0.34 ± 0.11 for *m*, and -0.04 ± 0.46 for *c*. Low values were obtained for both the correlation coefficient (0.755) and the *F*-test value (12.6). Inspection showed considerable deviation for the data points for TFE–H₂O and HFIP–H₂O binary solvents.

Repeating the correlation, with omission of the six aqueous fluoro alcohol solvents, gave a considerably improved correlation (Figure 1) with values of 1.74 ± 0.17

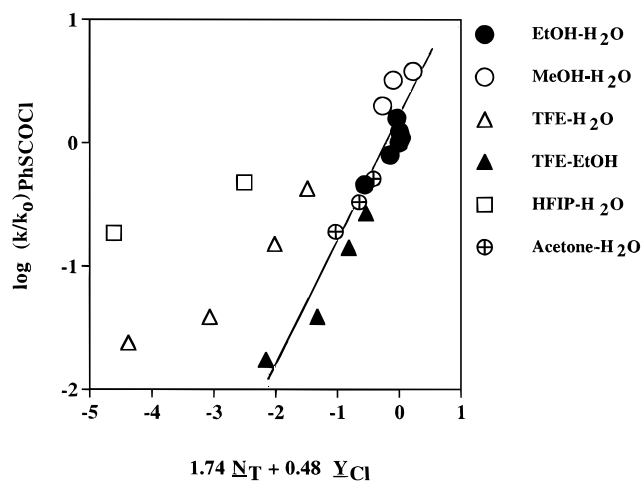


Figure 1. Plot of $\log(k/k_0)$ for solvolyses of phenyl chlorothioformate at 25.0 °C against $(1.74N_T + 0.48Y_{Cl})$. The six $\log(k/k_0)$ values for the TFE–H₂O and HFIP–H₂O solvents are not included in the correlation; they are added to show their considerable deviation from the correlation line.

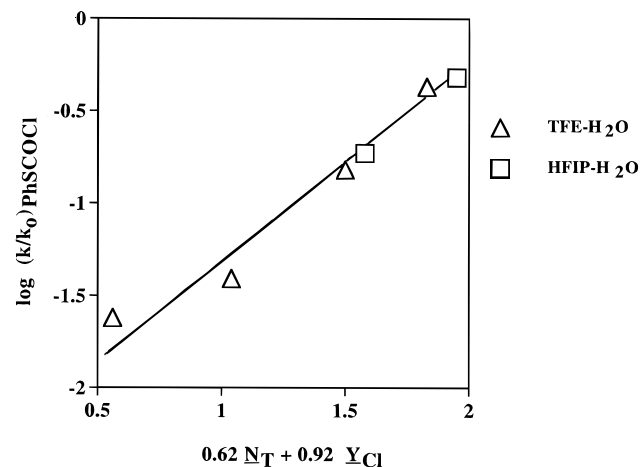


Figure 2. Plot of $\log(k/k_0)$ for solvolyses of phenyl chlorothioformate at 25.0 °C against $(0.62N_T + 0.92Y_{Cl})$.

for *l*, 0.48 ± 0.07 for *m*, and 0.19 ± 0.23 for *c*; the correlation coefficient increased to 0.946, and the *F*-test value increased to 55. These *l* and *m* values are extremely similar to those obtained¹ for solvolysis of phenyl chloroformate over the full range of solvent composition (*l* = 1.68 ± 0.10 and *m* = 0.57 ± 0.06), suggesting that the addition–elimination pathway, well established for solvolyses of phenyl chloroformate, also applies to phenyl chlorothioformate solvolysis in this range of solvents.

The specific rates of solvolysis of **1** in the six aqueous fluoro alcohol solvents have also been correlated using eq 1 (Figure 2). The values obtained are 0.62 ± 0.08 for *l*, 0.92 ± 0.11 for *m*, and -2.29 ± 0.13 for *c*. The large *c* value is a consequence of the experimental *k*₀ value not applying to this mechanism, and indeed the *c* value can be used to estimate a *k*₀ value (specific rate of solvolysis by this mechanism in 80% ethanol) of 7.4 × 10⁻⁷ s⁻¹ at the 25.0 °C temperature of the study. Values are obtained of 0.983 for the correlation coefficient and of 44 for the *F*-test.

In a previous comparison¹¹ of the specific rates of hydrolysis of **1** and phenyl chloroformate, it was assumed that the sulfur of the RS group would have a lower

(15) La, S.; Koh, K. S.; Lee, I. *Taehan Hwahakhoe Chi* **1980**, *24*, 8; *Chem. Abstr.* **1980**, *93*, 203581h.

tendency than the oxygen of the RO group to use its lone-pair electrons in the formation of the partial π bond to carbon within the ionization channel (eq 3). However, recent high-level calculations of cation stabilization have strongly suggested that the heavy element π donation is not less effective.¹⁶ Accordingly, if solvent influences are excluded, one should carry out a comparison of the element effect upon the ionization (S_N1) reaction solely in terms of the retarding inductive effects of phenoxy and phenylthio groups. While, when both react by S_N1 reaction, the chlorothioformate would be expected to react the more rapidly, the comparison of the specific rates of hydrolysis of the phenyl esters is between the S_N1 reaction of the chlorothioformate and an efficient S_N2 reaction¹ for the chloroformate, leading to a faster reaction for the chloroformate.^{11,12}

One aspect of the chlorothioformate ester study by Queen and co-workers which puzzled the authors was that, for the methyl and ethyl esters, the replacement of chlorine by fluorine led to a slightly faster reaction, which was obviously not consistent with a uniformly S_N1 reaction, where Cl/F rate ratios of as high as 10^5 – 10^7 would be predicted.¹⁷ Since the hydrolysis of **1** was studied¹¹ only at one lower temperature (4.6 °C), it is not possible to include the measured specific rate in the present study of solvent effects. We can, however, using eq 1, calculate the specific rates of solvolysis by the addition–elimination pathway (k_{A-E}) and by the ionization pathway (k_I). For solvolysis in water ($N_T = -1.38$;² $Y_{Cl} = 4.37$), values are obtained, at 25.0 °C, of $11 \times 10^{-5} \text{ s}^{-1}$ for k_{A-E} and $110 \times 10^{-5} \text{ s}^{-1}$ for k_I , corresponding to a 9% contribution from addition–elimination to a predominantly ionization reaction. On substitution of fluorine, the k_I value would become negligible,¹⁷ but an increase in the k_{A-E} value of only a little over 10-fold would be sufficient to lead to an overall F/Cl rate ratio of > 1 . That such an increase is reasonable is indicated by the F/Cl rate ratio of 32 for the hydrolysis of the 4-methoxyphenyl haloformates in 60% dioxane.⁴

The k_{A-E} and k_I contributions have also been calculated for each of the 22 solvents of the study (Table 2). Because of the very different combinations of l and m values for the two mechanisms, in only one instance (80% TFE–20% ethanol) is there less than an 88% contribution from one or the other of the mechanisms, consistent with the analysis in terms of the two plots of Figures 1 and 2. The mechanism designated as ionization has a very typical m value (0.92) for an ionization reaction (unity by definition for the solvolyses of 1-adamantyl chloride³). However, the rather large sensitivity to changes in solvent nucleophilicity (l value) of 0.62 requires some comment. The solvolyses of *tert*-butyl chloride are well-established as involving ionization, and indeed this was the original standard substrate chosen by Grunwald and Winstein for establishing a Y scale.¹⁸ Nonetheless, an analysis for 46 solvents in terms of eq 1 leads^{3c} to an l value of 0.38. Especially relevant to the present study, even larger l values have been obtained for effects believed to be due to nucleophilic solvation of the developing carbocation for the less sterically hindered situation of ionization from a carbonyl chloride derivative; for example, an l value of 0.74 has been obtained from

Table 2. Calculated Contributions^a from the Two Solvolysis Mechanisms for Solvolysis of **1 at 25.0 °C and Percentage by the Mechanism Designated as Addition–Elimination (A–E)**

solvent	$10^5 k_{A-E}, \text{ s}^{-1}{}^b$	$10^5 k_I, \text{ s}^{-1}{}^c$	%A–E ^d
100% EtOH	6.23	0.001	100
90% EtOH	15.2	0.013	100
80% EtOH	22.6	0.075	100
70% EtOH	23.7	0.298	99
60% EtOH	22.6	0.800	97
50% EtOH	21.1	2.36	90
100% MeOH	12.4	0.008	100
90% MeOH	17.6	0.050	100
80% MeOH	37.7	0.289	99
80T–20E	0.159	0.334	32
60T–40E	1.04	0.075	93
40T–60E	3.42	0.017	100
20T–80E	6.50	0.004	100
80% acetone	2.14	0.008	100
70% acetone	5.08	0.059	99
60% acetone	8.60	0.298	97
97% TFE	0.001	0.268	0
90% TFE	0.019	0.825	2
70% TFE	0.216	2.33	9
50% TFE	0.732	5.15	12
90% HFIP	0.001	2.88	0
50% HFIP	0.070	6.77	1

^a Using eq 1, with N_T and Y_{Cl} values from Table 1. ^b From $\log k_{A-E} = 1.74N_T + 0.48Y_{Cl} - 3.65$. ^c From $\log k_I = 0.62N_T + 0.92Y_{Cl} - 6.13$. ^d Using calculated values within $100k_{A-E}/(k_{A-E} + k_I)$.

an extended Grunwald–Winstein equation correlation of the rates of solvolysis of 4-(chloroformyl)morpholine.¹⁹ Accordingly, it appears that an l value as large as 0.6 is not incompatible with a solvolysis of **1** by a rate-determining ionization process.^{11,15}

Whereas phenyl chloroformate solvolyzes by an addition–elimination mechanism over a wide range of solvent composition, this mechanism is dominant for phenyl chlorothioformate solvolysis only in solvents of low ionizing power and/or high nucleophilicity. In water or in solvents rich in fluoro alcohol, an alternate mechanism dominates. This mechanism is believed to involve ionization, but with a rather high degree of stabilization of the transition state by solvation of the developing acylium ion. This study is believed to be the first in which the extended Grunwald–Winstein equation has been used to demonstrate the existence of two reaction channels within a solvolysis reaction. In situations where the two channels have very different combinations of l and m values, this promises to be a powerful technique, and other systems believed to be of this general type are under investigation.

Experimental Section

Phenyl chlorothioformate (Acros Organics, 98%) was used without further purification. Solvents were purified and the kinetic runs carried out as previously described.^{2a} The multiple regression analyses were performed using the ABSTAT statistical package (Anderson–Bell, Arvada, CO).

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(16) Kapp, J.; Schade, C.; El-Nahasa, A. M.; Schleyer, P. v. R. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2236.

(17) (a) Swain, C. G.; Scott, C. B. *J. Am. Chem. Soc.* **1953**, *75*, 246.

(b) Song, B. D.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 8470.

(18) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc.* **1948**, *70*, 846.

(19) Kevill, D. N.; Casamassa, A. J.; D'Souza, M. J. *J. Chem. Res., Synop.* **1996**, 472.