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Solvolysis of *N,N*-dimethylthiocarbamoyl chloride: effect of sulfur-for-oxygen substitution upon kinetics and product partitioning

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ABSTRACT: A study of the solvolyses of *N,N*-dimethylcarbamoyl chloride (**1**) was extended to the solvolyses of *N,N*-dimethylthiocarbamoyl chloride (**2**). The specific rates of solvolysis of **2** at 0.0 °C are two to three orders of magnitude greater than those for **1**. Analysis of the data using the extended Grunwald–Winstein equation leads to sensitivities *l* and *m* and an *l/m* ratio which are lower for **2** than those previously reported for **1**. Product selectivities in mixtures of water with ethanol or methanol indicate a greater preference for reaction with alcohol for **2**. All observations can be rationalized in terms of the formation of a more stable carbocation from **2**, leading to an earlier transition state, reduced nucleophilic solvation and the possibility of extensive progression to a free carbocation prior to product formation. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: *N,N*-dimethylthiocarbamoyl chloride; solvolysis; Grunwald–Winstein equation; selectivity

INTRODUCTION

The extended Grunwald–Winstein equation[1,2] has been successfully applied previously to the specific rates of solvolysis of chloroformate esters,[3–7] *N,N*-disubstituted carbamoyl chlorides[8–11] and diaryl chlorophosphate esters:[12]

$$\log(k/k_0) = lN_T + mY_{Cl} + c \qquad (1)$$

where k and k_0 are the specific rates of solvolysis of a substrate in a given solvent and in the standard solvent (80% ethanol), respectively, l is the sensitivity to changes in solvent nucleophilicity (N_T value[2,13]), m is the sensitivity to changes in solvent ionizing power (Y_{Cl} value[14,15]) and c is a constant (residual) term.

For the solvolyses of phenyl chloroformate,[3] it was found that, on substitution of a sulfur atom for either oxygen atom,[4,7] the addition–elimination mechanism, which had been dominant over the full range of solvents studied, now dominated only in the more nucleophilic and less ionizing solvents. For solvents rich in fluoro alcohol [2,2,2-trifluoroethanol (TFE) or 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP)], an ionization mechanism became dominant. The trend towards ionization continued on introduction of a second sulfur atom and, for phenyl chlorodithioformate (PhSCSCl), the ionization mechanism was dominant over the full range of solvents.[7] A shift towards an ionization mechanism for solvolysis was also observed on going from ethyl chloroformate to ethyl chlorothioformate.[5]

The solvolyses of *N,N*-dimethylcarbamoyl chloride (**1**) were indicated to be S_N1 in nature,[9] but with a pronounced nucleophilic solvation of the developing carbocation ($l = 0.56 \pm 0.05$). For the solvolyses of *N,N*-diphenylcarbamoyl chloride, a much lower l value ($0.23 + 0.04$) was observed[8] and the solvolyses of *N*-methyl-*N*-phenylcarbamoyl chloride[11] gave an intermediate value of 0.40 ± 0.08.

A study of product selectivities (S):

$$S = \frac{[\text{ester}]_{prod}}{[\text{amine}]_{prod}} \cdot \frac{[H_2O]_{solv}}{[ROH]_{solv}} \qquad (2)$$

in aqueous ethanol or aqueous methanol led for **1** to S values that were fairly constant in value at about 0.5 in aqueous ethanol[9] and at about 1.1 in aqueous methanol.[10] These values are very similar to those observed for the competition between alcohol and water attack in solvolyses of *p*-methoxybenzoyl chloride[16] and 1-adamantyl derivatives[17] in these solvents. These S values have been rationalized in terms of product formation at the solvent-separated ion pair stage, and similar behavior was postulated for the solvolyses of **1**[9] and also of 4-

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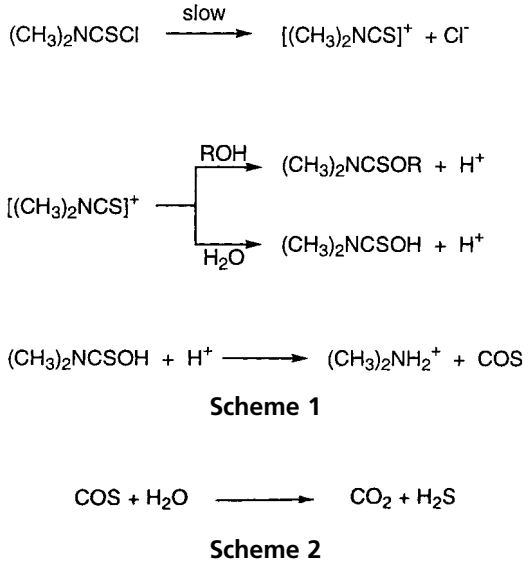
(chloroformyl)morpholine[10] and *N,N*-diphenylcarbamoyl chloride.[8]

We now report parallel studies of the kinetics and product selectivities for solvolyses of *N,N*-dimethylthiocarbamoyl chloride (**2**). Since, for chloroformate esters, the introduction of sulfur for oxygen brought about a considerable shift away from addition–elimination towards ionization, it will be of interest to see the effects of a parallel substitution into **1**, which already solvolyzes by an ionization mechanism.

We found only one previous study of the kinetics of solvolyses of *N,N*-disubstituted thiocarbamoyl chlorides, reporting on hydrolyses in 70% aqueous acetone at temperatures in the range of −5 to 30 °C for several substituents.[18] This study of substituent effects in a constant solvent is nicely complemented by our study of solvent effects for a constant structure.



Scheme 1

Scheme 2

RESULTS AND DISCUSSION

The specific rates of solvolysis of **2** at 0.0 °C and, so as to allow a direct comparison through *k*(2)/*k*(1) ratios, also those for **1** under identical conditions are reported in Table 1, together with the ratio. It can be seen that **2** solvolyzes two to three orders of magnitude faster than **1**. The observation that the ratio is solvent dependent, varying by about one order of magnitude, indicates that differences will be observed in the *l* and/or *m* values. The overall reaction scheme for solvolyses of **2** in an aqueous–alcohol solvent can be expressed according to Scheme 1.

The carbon oxysulfide formed during reaction involving capture by water slowly hydrolyzes to produce hydrogen sulfide:[18,19]

This reaction will not have any influence on either the kinetics or product studies, as carried out in this study.

When the solvent contains both an alcohol and water, a portion of the overall solvolysis produces the stable thiocarbamate ester, accompanied by acid. The other portion, reaction with water, leads to dimethylamine, which interacts with an equivalent amount of the formed acid to give the dimethylammonium ion, which is neutral under the titration conditions. The kinetics of the overall solvolysis can be obtained based on the experimental infinity titer. This infinity titer is dependent on solvent composition and it affords an accurate measure of the product partitioning occurring due to attack of either alcohol or water. These results are presented in Table 2 and are relative to the titer obtained in 100% ethanol,

Table 1. Specific rates of solvolysis of *N,N*-dimethylthiocarbamoyl chloride (**2**) and *N,N*-dimethylcarbamoyl chloride (**1**) in a variety of solvents at 0.0 °C

Solvent[a]	10^4 *k* (**2**) (s^{-1})[b]	10^6 *k* (**1**) (s^{-1})[b,c]	*k* (**2**) /*k* (**1**)
100% EtOH	0.550 ± 0.016	0.175 ± 0.007	314 ± 16
90% EtOH	4.75 ± 0.14	1.38 ± 0.04	344 ± 14
80% EtOH	12.6 ± 0.6	5.65 ± 0.08	223 ± 11
70% EtOH	26.9 ± 0.9	17.7 ± 0.6	152 ± 7
100% MeOH	2.66 ± 0.04	1.69 ± 0.04	157 ± 4
90% MeOH	10.5 ± 0.7	4.84 ± 0.15	217 ± 16
80% MeOH	20.0 ± 1.1	16.6 ± 0.7	120 ± 8
80% Acetone	1.14 ± 0.05		
70% Acetone	6.02 ± 0.33		
100% TFE	26.9 ± 0.6	6.01 ± 0.25	448 ± 21
97% TFE	48.0 ± 1.6	7.78 ± 0.34	617 ± 34
80T–20E	42.5 ± 1.7	2.56 ± 0.05	1660 ± 74
60T–40E	16.6 ± 0.7	1.40 ± 0.03	1186 ± 56
40T–60E	6.23 ± 0.32	0.712 ± 0.013	875 ± 48
20T–80E	1.96 ± 0.09	0.414 ± 0.006	473 ± 23

[a] Since substrate was added as a solution in acetone, actually 99.2% of the indicated composition together with 0.8% acetone; concentration of substrate, 0.00306 mol dm^{-3}.
[b] With associated standard deviation, based on all of the integrated rate coefficients from duplicate runs.
[c] These values were determined by A. G. Sell and I. Zdravkovic (University of Wisconsin–Waukesha).

Table 2. Percentage of the overall reaction of *N,N*-dimethylthiocarbamoyl chloride (**2**) in aqueous–organic solvents which is accompanied by development of acid and selectivity values (*S*)

Solvent[a]	Acid (%)	*S* (**2**)[b]	*S* (**1**)[c]
100% EtOH	100.0		
90% EtOH	91.8	3.9	0.53
80% EtOH	88.3	5.9	0.51
70% EtOH	86.4	8.5	0.50
100% MeOH	100.0		
90% MeOH	95.2	5.0	1.14
80% MeOH	82.6	2.7	1.05
80% Acetone	0.3		

[a] See footnote a in Table 1.
[b] As defined in Eqn. (2).
[c] From Refs 9 and 10.

when all reaction leads to acid production. It will be noted that, in 80% acetone, all reaction will be with water and, as expected, essentially zero acidity develops.

The two kinetic runs in aqueous acetone were carried out by adding portions of solution at appropriate time intervals into excess methanol, such that the subsequent solvolysis produces an amount of acid proportional to the amount of unreacted **2** at the time of sampling. That this affords an accurate way of following the kinetics is indicated by the observation that our specific rate of 6.02 ($\pm$0.33) $\times 10^{-4}$ s^{-1} at 0.0 °C is in excellent agreement with a value of 6.03×10^{-4} s^{-1} resulting from a modest extrapolation of values at 5–30 °C, obtained by measuring changes in electrical conductivity.[18]

A treatment of the 15 specific rates of solvolysis of **2** (Table 1) leads in terms of the simple Grunwald–Winstein equation [Eqn. (1) without the *lN* term] to values for *m* of 0.34 ± 0.04 and for *c* of -0.25 ± 0.25, with a correlation coefficient of 0.9053 and *F*-test value of 59. Using the full equation, values are obtained of 0.31 ± 0.07 for *l*, 0.57 ± 0.06 for *m* and -0.07 ± 0.16 for *c*, with a multiple correlation coefficient of 0.9674 and *F*-test value of 87. Inspection of the data shows a good correlation for all of the data, except the two water–acetone mixtures. That this is not experimental error, associated with the different procedure used to follow these two runs, is indicated by the excellent agreement of the value obtained in 70% acetone with a previous measurement.[18] When these two data points are excluded from the treatment using the full equation, correlation values are obtained of 0.29 ± 0.03 for *l*, 0.55 ± 0.03 for *m* and -0.03 ± 0.07 for *c*, with a multiple correlation coefficient of 0.9932 and *F*-test value of 362. The experimental specific rates of solvolysis in 80% and 70% acetone are, respectively, 3.0 and 2.5 times slower than the values calculated using these parameters. In Fig. 1, the plot is given based on the 13 solvents and the aqueous–acetone points are added to show the deviations.

The selectivity values (Table 2) are calculated using Eqn. (2), with $[\text{ester}]_{\text{prod}}$ proportional to the acid titer and $[\text{amine}]_{\text{prod}}$ proportional to the difference between the acid titer for solvolysis in 100% ethanol and the corresponding titer when the 100% ethanol is replaced by the solvent under consideration. In contrast to the values for solvolyses of **1**, the *S* values are appreciably greater than unity, showing a marked preference for reaction with alcohol rather than water.

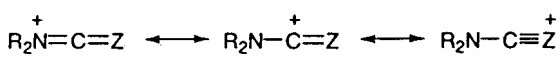
Before moving on to a consideration of the mechanistic implications of the analyses of the solvent effect on kinetic and product studies, we shall also outline the previously reported[18] analysis of substituent effects in terms of the Taft equation:[20]

$$\log(k/k_0) = \varrho^*\sigma^* + \delta E_s \qquad (3)$$

where k and k_0 are the rate coefficients in the presence of a given substituent and a methyl substituent, respectively, ϱ^* is the sensitivity to changes in the polar parameter σ^* and δ is the sensitivity to changes in the steric parameter E_s. Using the summation over the two substituents for σ^* and E_s, values were obtained[18] at 15 °C in 70% acetone of -1.73 for ϱ^* and 0.002 for δ, indicating essentially no sensitivity to changes in the steric environment and an appreciable sensitivity to changes in the polar environment, with faster reaction in the presence of electron-supplying substituents.

We can now consider the three types of evidence available for the solvolyses of **2** in terms of reaction mechanism, based in part on a comparison with the corresponding parameters for the solvolyses of **1**,[9,10,21] where a rate-determining ionization with a pronounced nucleophilic solvation of the developing cation, followed by product formation predominantly at the solvent-separated ion-pair stage, was proposed.[9]

The evidence obtained in this and previous work is all consistent with the mechanism presented in Scheme 1. This was also the mechanism proposed for the solvolyses of the oxygen-containing analog **1**. There are, however, appreciable quantitative differences between the solvolytic behavior of **1** and **2** in terms of both sensitivities within the linear free energy relationships and product selectivities. These can all be rationalized in terms of the carbocation from **2** being more stable than that formed from **1**. If the oxygen or sulfur is represented by Z, we can write the following resonance structures:



Scheme 3

The third contributor will be expected to make a larger contribution when Z = S, because sulfur can much better carry a positive charge in onium-type structures than oxygen. In turn, this will lead to an enhanced stability for the resonance hybrid.

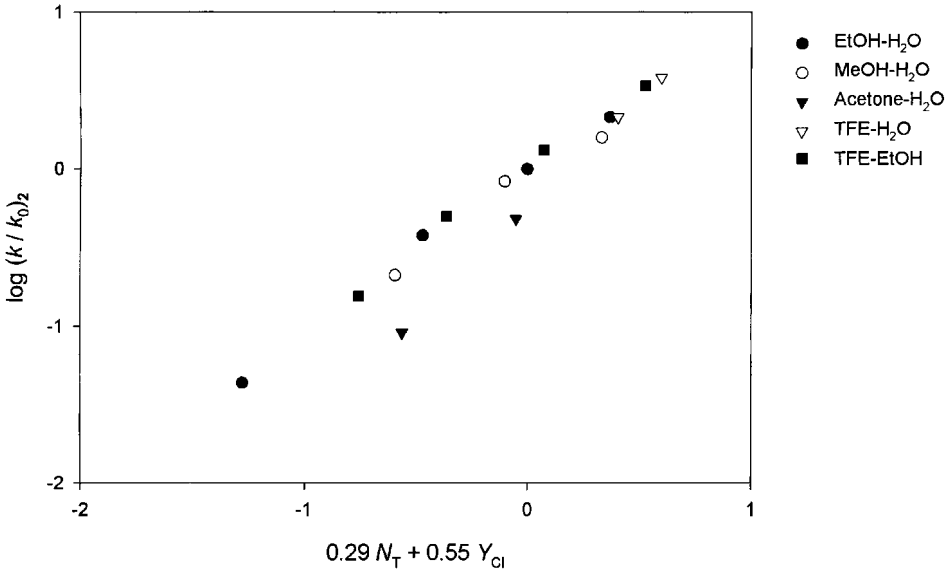


Figure 1. Plot of log (k/k_0) for solvolyses of *N,N*-dimethylthiocarbamoyl chloride (**2**) against $0.29N_T + 0.55Y_{Cl}$

The ϱ^* value of −1.73 for hydrolysis of thiocarbamoyl chlorides in 70% acetone at 15 °C is considerably lower in magnitude than the −4.11 for hydrolysis of carbamoyl chlorides in 50% acetone at 50 °C.[21] This is consistent with a reduced dependence on electron supply from nitrogen when it is also readily available from the sulfur atom.

The *l* and *m* values are both lower than the corresponding values[9] for solvolyses of **1** of 0.56 for *l* and 0.74 for *m*. This is consistent with an earlier transition state associated with the formation of a more stable intermediate, as is also indicated by the considerably faster solvolyses of **2** than **1**. The lower *l*/*m* ratio (0.53 for **2** and 0.76 for **1**) can be considered to reflect a reduced need for stabilization of the cation by solvation when an additional important source of internal stabilization is present. This reduced solvation can also explain the lower sensitivity to changes in the steric parameter E_s for solvolyses of **2**, relative to **1** (0.002 and 0.80).[18,21]

The product selectivities relate to step 2 of Scheme 1. For solvolyses of **1**, the values of about 0.5 for *S* [Eqn. (2)] for competition between water and ethanol were considered to reflect capture at the solvent-separated ion-pair stage, based on the similarity in value and the constancy of the value both mimicking the behavior for systems generally believed to involve capture at this stage.[9,16,17,22] The very different *S* values for solvolyses of **2**, which also vary considerably more with solvent composition than for **1**, of 3.9–8.3 for ethanol–water mixtures and 2.7–5.0 for methanol–water mixtures, strongly suggest that the capture is not at the solvent-separated ion-pair stage.

A survey of the literature shows that values of these magnitudes have been observed when capture by solvent is at the free-ion stage. Such a proposal is, of course, consistent with the idea of a more stable (less reactive) cation being formed, with the reduced reactivity providing the opportunity for progression to the free-ion stage before capture by solvent. The magnitude of *S* observed for previous systems believed to involve capture at the free-ion stage is illustrated by the following examples. Ta-Shma and Jencks[23] found, for capture of 4-$YC_6H_4CHCH_3^+$ ions in a 50:40:10 water–TFE–ethanol mixture, *S* values of 11.7 when Y is CH_3O and 27 when Y is $(CH_3)_2N$. In solvolyses of benzhydryl chloride in ethanol–water mixtures, Bentley and Ryu[24] found *S* values of 2.5–4.6 and, for solvolyses in methanol–water mixtures, *S* values of 4.2–7.7. Corresponding values for solvolyses of *p*-methoxybenzyl chloride were 1.7–4.8 and 3.6–7.2. Richard *et al.*[25] have found, for capture of several α-substituted 1-(4-methoxyphenyl)ethyl carbocations in 50% methanol, values in the range 5–22.

EXPERIMENTAL

The *N,N*-dimethylthiocarbamoyl chloride (Aldrich, 97%) was used without further purification. References for solvent purification have been presented previously.[13] Runs in the presence of an alcohol component in the solvent were carried out as described previously;[13] a stock solution of 3.10 g of the substrate in 65 ml of acetone was prepared and, at 0.0 °C, 0.200 ml was added to 25.0 ml of pure or mixed solvent under carefully controlled conditions. In this way, the infinity titer taken at 10 half-lives reflected accurately the partitioning between reaction with alcohol and, when present, water. Runs were performed in duplicate and two infinity titers were taken for each run.

The reactant solutions for runs in water–acetone

mixtures were made up in identical fashion but the 2 ml portions removed at appropriate time intervals were added to 10.0 ml of methanol and allowed to stand for in excess of 5 h before addition of 15 ml of acetone and titration in the usual manner.[10]

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