Kinetics and Selectivities for the Solvolysis of *N,N*-Diphenylcarbamoyl Chloride[1]

Malcolm J. D'Souza and Dennis N. Kevill*

Department of Chemistry, Northern Illinois University, DeKalb, Illinois 60115

T. William Bentley* and Angela C. Devaney

Department of Chemistry, University of Wales, Swansea, Singleton Park,
Swansea SA2 8PP, United Kingdom

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Values for the specific rates of solvolysis of *N,N*-diphenylcarbamoyl chloride have been analyzed using the two-term Grunwald–Winstein equation, incorporating the N_T solvent nucleophilicity scale and the Y_{Cl} solvent ionizing power scale. The sensitivities of 0.23 ± 0.04 to changes in N_T and of 0.58 ± 0.03 to changes in Y_{Cl} are consistent with an S_N1 pathway with extensive internal nucleophilic assistance and a weak nucleophilic solvation of the developing carbocation. Product studies have been performed in mixtures of water with methanol, ethanol, and 2,2,2-trifluoroethanol (TFE) and in TFE–ethanol mixtures. Giving further support to the proposed S_N1 mechanism, both the sensitivity to changes in solvent nucleophilicity and the product selectivities in aqueous ethanol and methanol parallel closely those previously determined for solvolyses of *p*-methoxybenzoyl chloride.

Following a study of the hydrolysis of dimethylcarbamoyl chloride (**1**) in water and in aqueous dioxane, Hall and Lueck[2a] proposed an ionization mechanism, largely on the basis of the product ratio in the presence of azide ion being consistent with the competitive trapping by azide ion of a carbocationic intermediate and with the observation of catalysis by mercuric ion for hydrolysis of **1** but not for hydrolysis of *n*-butyl chloroformate or benzenesulfonyl chloride. On the basis of a comparison of the enthalpies, entropies, and heat capacities of activation for the hydrolysis of **1** with the corresponding values for hydrolyses of phenyl, methyl, and primary alkyl chloroformates, Queen[3] also proposed that **1** hydrolyzes by a unimolecular ionization mechanism. This proposal was given strong support by the observation[4] that the corresponding fluoride hydrolyzes about 10^6 times slower than **1**. However, in the presence of added amines, a superimposed bimolecular reaction was observed.[2]

Essentially identical behavior was found[5,6] for the hydrolysis and for the reaction with amines of *N,N*-diphenylcarbamoyl chloride (**2**). Initially, an S_N1 mechanism was proposed[5] for hydrolysis of **2**, favored by the stabilization of the incipient acylium ion by electron donation from nitrogen. This position was subsequently modified slightly[6] to allow for the possibility of a small amount of nucleophilic assistance by water, within the loose transition state of a reaction which was close to being unimolecular; a parallel transition state was also proposed for aminolysis.

A unimolecular mechanism was proposed by Bacaloglu, Dăescu, and Ostrogovich[7] for the solvolyses of a series of *N,N*-dialkylcarbamoyl chlorides in aqueous acetone, several alcohols, and formic acid. They found enhancement of the reactivity with increase in either the electron-donating ability of the alkyl groups or the solvent polarity. The observation of a rate depression upon addition of lithium chloride to solvolyses in ethanol or formic acid was considered to indicate, for these solvents, a common-ion effect upon product formation at the free (dissociated) ion stage. They found evidence for a rather complex pattern of solvation changes in going from the ground state of the carbamoyl chloride to the transition state for the solvolysis, with the possibility of two interaction mechanisms. Such a picture is consistent with the proposal[6] of a weak nucleophilic assistance accompanying the electrophilic solvation of the incipient chloride ion. Kim, Song, and Lee[8] suggested that **1** and other *N,N*-dialkylcarbamoyl chlorides react by an S_N2 mechanism but **2** by an S_N1 process.

To summarize, a general consensus has evolved that the mechanism for solvolysis of *N,N*-disubstituted carbamoyl chlorides is primarily S_N1 in character, favored by a powerful mesomeric electron-donation from nitrogen. Although it is considerably less well established, there does seem to be evidence, for some systems,[6–8] in favor of a weak nucleophilic participation by solvent toward a predominantly S_N1 solvolysis. Such behavior has recently been found to be relatively common,[9–12] and an S_N2 (intermediate) mechanism has been proposed.[13]

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A powerful tool for investigation of a possible weak nucleophilic participation by solvent toward a predominantly S_N1 process involves the use[14] of the extended (two-term) Grunwald–Winstein equation[15] (eq 1). Within

$$\log (k/k_0) = lN + mY + c \qquad (1)$$

eq 1, k and k_0 are the specific rates of solvolysis in the solvent under consideration and in 80% ethanol, respectively, m is the sensitivity of the specific rate of solvolysis to changes in solvent ionizing power Y, l is the sensitivity of the specific rate of solvolysis to changes in solvent nucleophilicity N, and c is a constant (residual) term. The original Y scale, based on *tert*-butyl chloride solvolysis, has been shown[9,12] to contain a nucleophilic component, and Y_X scales based on solvolysis of 1- or 2-adamantyl derivatives with the appropriate (X) leaving group are recommended.[16] In the present paper, the Y_X scale is used in conjunction with the N_T solvent nucleophilicity scale.[17,18]

The kinetic data can be complemented by studies of product selectivities, providing information about product-determining steps from which the nature of cationic intermediates may be deduced.[19] Solvolyses of 1- and 2-adamantyl substrates[20] and also of several acyl halides (such as *p*-methoxybenzoyl chloride[21,22] and 2,6-dimethylbenzoyl chloride[21]) show approximately constant selectivities in ethanol/water mixtures. Significantly $S < 1$, showing the importance of electrophilicity and bulk of solvent,[23] and the results may be explained by collapse of a solvent separated ion pair,[19,20–23] in which the leaving group may act as a general base catalyst.[22] In contrast, reactions via free carbocations show an increase in S as water is added to ethanol,[19,24] consistent with nucleophilic attack by one molecule of solvent being assisted by a second solvent molecule acting as general base catalyst.[24]

Results

Kinetic Studies. The specific rates of solvolysis of **2** at 62.5 °C have been determined in ethanol, in methanol, in 2,2,2-trifluoroethanol (TFE), in their binary mixtures with water, in aqueous acetone, in aqueous 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), and in TFE–ethanol mixtures. The 24 experimentally determined values together with 14 literature values[6,8] (interpolated or extrapolated from studies at other temperatures) are presented in Table 1. Also studied were the effects of adding pyridine to solvolyses in ethanol and TFE, the effects of adding perchloric acid to solvolyses in 50% TFE, and the effects of adding chloride ion to solvolyses in ethanol; these results are presented in Table 2.

Table 1. Specific Rates of Solvolysis of 2 at 62.5 °C

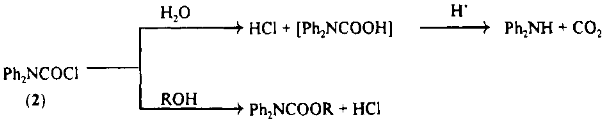
solvent[a]	10^5k,[b] s^{-1}	solvent[a]	10^5k,[b] s^{-1}
100% EtOH	0.057 ± 0.001	40% acetone	4.14[c]
90% EtOH	0.229 ± 0.008	30% acetone	13.7[c]
80% EtOH	0.441 ± 0.014	20% acetone	41.6[c]
50% EtOH	4.14 ± 0.15	10% acetone	120[c]
40% EtOH	9.42 ± 0.11	100% TFE	1.81 ± 0.52[e]
30% EtOH	20.0[c]	97% TFE[f]	4.79 ± 0.17
20% EtOH	59.7[c]	90% TFE[f]	5.71 ± 0.20
10% EtOH	150[c]	70% TFE[f]	10.8 ± 0.3
100% H_2O	218[d]	50% TFE[f]	20.1 ± 1.1
100% MeOH	0.382 ± 0.015	97% HFIP[f]	38.1 ± 1.1
90% MeOH	0.825 ± 0.014	90% HFIP[f]	27.2 ± 0.7
80% MeOH	1.63 ± 0.04	70% HFIP[f]	26.3 ± 0.4
60% MeOH	6.22 ± 0.18	50% HFIP[f]	30.8 ± 0.7
40% MeOH	23.7[c]	30% CH_3CN	14.0[c]
30% MeOH	44.8[c]	20% CH_3CN	39.3[c]
10% MeOH	145[c]	10% CH_3CN	138[c]
80% acetone	0.036 ± 0.001	80T–20E[g]	1.57 ± 0.05
60% acetone	0.433 ± 0.009	60T–40E[g]	0.543 ± 0.012

[a] Unless otherwise stated, prepared on volume–volume basis at 25.0 °C, with other component water; concentration of **2** of 0.003–0.007 M. [b] With associated standard deviation for averaged values and associated standard error for extrapolated values. [c] Calculated from data at other temperatures (ref 8). [d] Extrapolated from data at 25.0 °C and 48.8 °C (ref 6). [e] Values fall during run, initial value determined by extrapolation; after the time estimated for 35% reaction, based on initial specific rate, only 19% of reaction had actually occurred. [f] Solvent prepared on weight–weight basis. [g] T–E are TFE–ethanol mixtures.

Product Studies. In aqueous alcohol, reaction of **2** with the water component will lead to diphenylamine[6,25] and with the alcohol component to a carbamate ester (eq 2). The $[Ph_2NCOOR]/[Ph_2NH]$ ratios and hence the selectivities (S), defined by eq 3, have been determined

$$S = \frac{[Ph_2NCOOR][H_2O]}{[Ph_2NH][ROH]} \qquad (3)$$

by HPLC after completion of 10 half-lives of reaction. The results are presented in Table 3 for aqueous ethanol, aqueous methanol, and aqueous TFE solvents. Also presented are two determinations in TFE–ethanol mixtures.



(2)

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Discussion

Kinetics of Solvolysis. The specific rates of solvolysis of **2** at 62.5 °C (Table 1) have been analyzed in terms of both the simple (eq 1 without the lN term) and extended (eq 1) Grunwald–Winstein equations. The details of the analyses are presented in Table 4, together with corresponding values from an analysis of literature values for the specific rates of solvolysis at 25.0 °C of **1** in 100, 90, 80, and 70% aqueous ethanol[8] (interpolated values of 10^5k, s^{-1}, of 1.23, 6.31, 22.3, and 54.1, respec-

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Table 2. Influence of Additives upon the Specific Rates of Solvolysis of 2 at 62.5 °C

solvent	additive	[additive], M	10^5k,[a] s^{-1}
100% EtOH	pyridine	0.0000	0.057 ± 0.001[b]
100% EtOH	pyridine	0.0050	0.355 ± 0.012
100% EtOH	pyridine	0.0100	0.470 ± 0.090
100% EtOH	pyridine	0.0200	1.25 ± 0.06
100% EtOH	pyridine	0.0400	1.94 ± 0.07
100% EtOH	pyridine	0.0810	3.35 ± 0.08
100% TFE	pyridine	0.0000	1.81 ± 0.52[b,c]
100% TFE	pyridine	0.0120	1.91 ± 0.11[c,d]
100% TFE	pyridine	0.0250	2.11 ± 0.14[e]
50% TFE[c]	$HClO_4$	0.000 00	20.1 ± 1.1[b]
50% TFE[c]	$HClO_4$	0.000 14	18.9 ± 0.6
50% TFE[c]	$HClO_4$	0.000 36	19.3 ± 1.0
50% TFE[c]	$HClO_4$	0.000 86	20.8 ± 1.1
50% TFE[c]	$HClO_4$	0.003 24	21.2 ± 0.7
100% EtOH	$NEt_4^+Cl^-$	0.0066	0.058 ± 0.003[c,f]
100% EtOH	$NEt_4^+Cl^-$	0.0192	0.056 ± 0.004[c,f]

[a] With associated standard deviation for averaged values and associated standard error for extrapolated values. [b] From Table 1. [c] Values fall during run; initial value obtained by extrapolation. [d] At 375 min, corresponding to 35% reaction based on the initial specific rate, 26% of possible solvolysis had occurred. [e] Average of values obtained during first 20% of reaction. [f] From a comparison for 0.0030 M substrate of the titer at equilibrium (taken after 17 days) with the theoretical titer for 100% solvolysis, values of 36% conversion to HCl with 0.0066 M NEt_4Cl present and of 31% conversion to HCl with 0.0192 M NEt_4Cl present can be calculated.

Table 3. Product Selectivities (eq 3) for Solvolyses of *N,N*-diphenylcarbamoyl Chloride at 62.5 °C[a]

solvent[b]	*S*	solvent[b]	*S*
90% EtOH	1.1	90% MeOH	1.4
80% EtOH	0.94	80% MeOH	1.4
70% EtOH	0.82	70% MeOH	1.3
60% EtOH	0.87	60% MeOH	1.4
50% EtOH	0.79	50% MeOH	1.4
40% EtOH	0.78	40% MeOH	1.5
30% EtOH	0.91	30% MeOH	1.3
20% EtOH	0.94	20% MeOH	1.5
10% EtOH	0.91	10% MeOH	1.4
		97% TFE	0.35
80T−20E	11.0[c]	90% TFE	0.33
60T−40E	11.3[c]	70% TFE	0.30
		50% TFE	0.32

[a] Determined by response-calibrated reversed-phase HPLC by duplicate analyses of duplicate solutions; errors typically ±5% (including calibration). [b] Solvents as in Table 1 are % v/v except for TFE which is % w/w trifluoroethanol/water. [c] $S = k_{EtOH}/k_{TFE}$.

Table 4. Correlation of the Specific Rates of Solvolysis of Carbamoyl Chlorides Using Both the Simple and Extended Grunwald−Winstein Equations and N_T and Y_{Cl} Scales

substrate	*n*[a]	*l*[b]	*m*[b]	*c*[b]	*R*[c]
1	8[d]		0.49 ± 0.03	−0.05 ± 0.18	0.989
1	8[d]	0.33 ± 0.06	0.60 ± 0.02	0.03 ± 0.08	0.998
2	36[e]		0.49 ± 0.03	−0.01 ± 0.33	0.944
2	36[e]	0.23 ± 0.04	0.58 ± 0.03	0.07 ± 0.24	0.971

[a] Number of solvents. [b] For definition, see eq 1 (with associated standard errors). [c] Correlation coefficient. [d] As presented in text (at 25.0 °C). [e] As listed in Table 1 (at 62.5 °C).

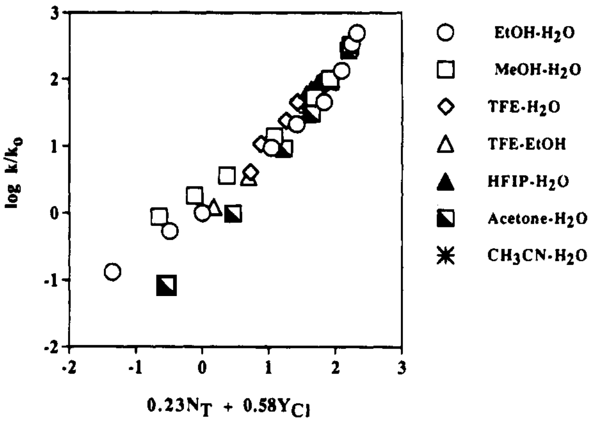

Figure 1. Plot of log (k/k_o) for *N,N*-diphenylcarbamoyl chloride (**2**) solvolysis against $l\,N_T + m\,Y_{Cl}$, where l has a value of 0.23 and m has a value of 0.58.

tively), water[3] (extrapolated value of 5170 × 10^{-5} s^{-1}), methanol[7] (interpolated value of 5.01 × 10^{-5} s^{-1}), 50% acetone,[7] and formic acid.[7] The plot, in terms of eq 1, of the data for solvolyses of **2** is shown in Figure 1.

The analysis of the eight solvolyses of **1** shows that a very good correlation is obtained ($r = 0.992$) using only the simple (one-term) Grunwald−Winstein equation, but with some improvement ($R = 0.997$) on using the full form of eq 1. The analysis of the solvolyses of **2** in 36 solvents includes several measurements in fluoro alcohol-containing solvents, important in considerations in terms of sensitivity to solvent nucleophilicity because of their low nucleophilicity but relatively high ionizing power.[16,27] In terms of the one-term Grunwald−Winstein equation, solvolyses of **2** show a reasonable correlation (0.943), but this is considerably improved ($r = 0.971$) when the two-term equation (eq 1) is used. Despite the differences in the number and types of solvents used the sensitivities toward solvent ionizing power and solvent nucleophilicity using the two-term equation are very similar for the solvolyses of **1** and **2**. This suggests, contrary to a previous proposal,[8] that **1** and **2** have similar structures at the transition state for the rate-determining step. It must, however, be emphasized that, in the study of the solvolysis of **1**, very heavy weight is given to the specific rate of formolysis. An extension to other solvent systems is currently underway.

The values for l (sensitivity to changes in solvent nucleophilicity) of 0.23 and 0.33 suggest that the S_N1 pathway is favored for the solvolyses. Sensitivities slightly higher than this, such as 0.38 for *tert*-butyl chloride solvolysis[12] and 0.35 for cyclohexyl *p*-toluenesulfonate solvolysis,[11] have been proposed to reflect a nucleophilic solvation of the developing carbocation within an S_N1 ionization, and a modest nucleophilic assistance, which can be visualized either as a nucleophilic solvation or as an S_N2 (intermediate) mechanism,[13] can also be proposed for solvolyses of **1** and **2**. However, low values for l are usually associated with m values only slightly reduced below unity (0.86 for *tert*-butyl chloride solvolysis and 0.85 for cyclohexyl *p*-toluenesulfonate solvolysis), in contrast to the values of 0.60 and 0.58 in the present studies. The m values observed are similar to those observed in S_N2 reactions, and such values for unimolecular ionizations are frequently taken as reflecting a substantial internal nucleophilic assistance (comparable to the assistance from the attacking nucleophile in an S_N2 reaction). The relatively low m value is, therefore, nicely consistent with the proposed stabilization of the developing acylium ion by mesomeric interac-

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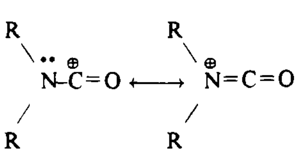
tion of the lone pair of electrons on the nitrogen[5,7] (eq 4),



$$\mathrm{R_2\ddot{N}{-}\overset{\oplus}{C}{=}O \longleftrightarrow R_2\overset{\oplus}{N}{=}C{=}O} \qquad (4)$$

such that at the transition state the extent of bond breaking to the departing chloride ion is comparable to that in S_N2 reactions of alkyl derivatives. An essentially identical *m* value of 0.55 has been obtained[17] when the specific rates of solvolysis of methyl *p*-toluenesulfonate at 50 °C[28] have been correlated, using eq 1, against N_T[17] and Y_{OTS}[27] values. The k_Δ processes[29] of mustard chlorohydrin and related compounds[30] also exhibit[31] very low or negligible *l* values, together with *m* values of close to 0.43, when treated using eq 1.

An extrapolated value (from measurements[7] at 40–60 °C) of 45.7×10^{-5} s^{-1} for the specific rate of ethanolysis of **1** at 62.5 °C can be compared with our value (Table 1) of 0.057×10^{-5} s^{-1} for the corresponding ethanolysis of **2** to give a rate ratio of 802 for solvolysis of **1** relative to solvolysis of **2**. Similarly, in water at 0.1 °C, an experimental value[2] of 160×10^{-5} s^{-1} for hydrolysis of **1** can be compared with an extrapolated value (from measurements[6] at 25–49 °C) of 0.091×10^{-5} s^{-1} for hydrolysis of **2**, to give a corresponding ratio of 1765. That *N*-methyl substituents are more favorable than *N*-phenyl substituents, in regard to the rate of an essentially S_N1 solvolysis, is contrary to observations when the substituents are directly attached, at the transition state, to an incipient electron-deficient carbocation.[32] In the present instance, the groups are attached to a nitrogen which has developed considerable positive charge within the incipient mesomeric cation (eq 4), but which has not lost its octet of electrons. Under these conditions inductive effects will dominate and the Taft polar substituent constants (σ^*) of zero for a methyl group (by definition) and of +0.60 for a phenyl group[33] are consistent with a destabilization, relative to the effect of methyl groups, of the developing mesomeric cation by *N*-phenyl groups.

Taking the data obtained in aqueous-ethanol mixtures as a reference plot, inspection of Figure 1 suggests, in addition to a certain amount of curvature, a relatively modest dispersion of the general type commonly observed in Grunwald–Winstein plots for solvolyses of benzylic derivatives.[14a] These effects have been ascribed,[14a,34–37] for benzylic systems, to differences in the changes in solvation in going from the ground state to the transition state of the solvolysis reaction in the presence of aryl substituents relative to the corresponding changes in their absence, such as in the standard (reference) solvolyses of *tert*-butyl chloride or 1-adamantyl chloride.[10]

Table 5. Correlation of the Specific Rates of Solvolysis of 2[a] Using Either the Simple or Extended Grunwald–Winstein Equation (N_T and Y_{Cl} values) with or without the *hI* Term[b]

scales[c]	*l*[d]	*m*[d]	*h*[d]	*c*[d]	*R*[e]
Y_{Cl}		0.45 ± 0.03		0.01 ± 0.32	0.941
N_T, Y_{Cl}	0.20 ± 0.05	0.55 ± 0.03		0.07 ± 0.25	0.965
I, Y_{Cl}		0.45 ± 0.03	−0.23 ± 0.16[f]	0.04 ± 0.31	0.946
N_T, *I*, Y_{Cl}	0.38 ± 0.07	0.65 ± 0.04	0.58 ± 0.19	0.06 ± 0.22	0.975

[a] In 30 solvents at 62.5 °C (data from Table 1). [b] The *I* values are from ref 38. [c] Indicating the terms of eq 5 included in the analysis. [d] For definition see eqs 1 and 5 (with associated standard errors). [e] Correlation coefficient. [f] For this analysis, a 0.14 probability that the *hI* term is not statistically significant.

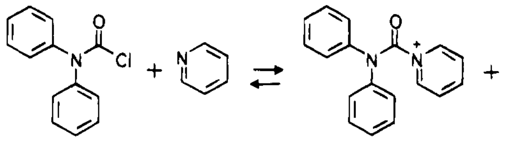
Since the kinetic influence of phenyl substituents in carbamoyl chlorides has been found to be very different from the influence in benzylic derivatives, it is quite possible that the recently developed[38] *I* scale, designed for removal of dispersion in Grunwald–Winstein plots of benzylic derivatives, will not be appropriate for removal of the dispersion in the corresponding plots for solvolyses of **2**. Analyses have been carried out in terms of eq 5, with use of either the full equation or with

$$\log (k/k_o) = lN + mY + hI + c \qquad (5)$$

omission of one or two terms. In eq 5, the symbols are as described for eq 1 but with addition of a sensitivity (*h*) to the aromatic ring parameter (*I*).[38] The data for solvolysis in 30 of the 36 solvents reported in Table 1 (no *I* values for 10% methanol, 10% ethanol, 10% acetone, and 30, 20, and 10% acetonitrile) have been analyzed, and the results are presented in Table 5.

Only a modest increase in correlation coefficient value accompanies inclusion of the *hI* term, together with the mY_{Cl} term, and the negative *h* value probably reflects an actual dependence on N_T value; it has been shown[38] that a very approximate (negative) relationship exists between the *I* and N_T scales. The best correlation is obtained with use of the full eq 5. However, the improvement in the correlation coefficient value (*R*), from 0.965 to 0.975, on inclusion of the *hI* term is only modest. Further, it has been shown[38] that *I* correlates moderately well ($R = 0.749$) with a linear combination of N_T and Y_{Cl} ($I = -0.33N_T - 0.13Y_{Cl} - 0.03$) and the fairly large value for *h*, accompanied by moderately large changes in *l* and *m* values, could be a consequence of this multicollinearity.

Effect of Additives upon the Kinetics of Solvolysis. Addition of pyridine to the ethanolysis of **2** leads to a pronounced acceleration (Table 2 and Figure 2). It has been shown previously that, in water as solvent, amines react directly with **2** to form the corresponding *N*,*N*-diphenylurea derivatives.[6] Similarly, Hall has proposed a bimolecular mechanism for the reactions of **1** with aliphatic amines.[2b] The increases in specific rate with increases in pyridine concentration are close to linear, and the specific rate of 3.35×10^{-3} s^{-1} with 0.08 M added pyridine is slightly higher than the corresponding[39] specific rate of ethanolysis of (*N*,*N*-diphenylcarbamoyl)pyridinium chloride (**3**) of 3.05×10^{-5} s^{-1}. If only nucleophilic catalysis was to operate (eq 6), the specific



(6)

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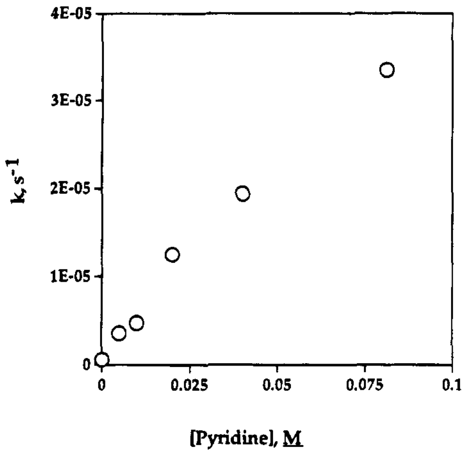

Figure 2. The effect of added pyridine upon the specific rate of ethanolysis of *N,N*-diphenylcarbamoyl chloride (**2**) at 62.5 °C.

rate of 3.05×10^{-5} s^{-1} would be expected as a limiting value. The observation of higher values suggests that general-base catalysis must also be a factor; general-base catalysis has been observed for solvolyses of **3** in the presence of pyridine.[39]

A corresponding addition of pyridine to solvolysis in TFE leads to only a very small rate increase. One would expect the nucleophilicity of pyridine toward additives to be reduced upon transfer from ethanol to the more acidic TFE. With 0.01 M pyridine the fall off in specific rate with extent of reaction is reduced and it is essentially absent during the first 20% of reaction in the presence of 0.02 M pyridine; these observations suggest that an acid-promoted loss of acid is being suppressed. It is known that, at elevated temperatures, hydrogen chloride does react with alcohols at an appreciable reaction rate.[40]

The absence of any acid catalysis after the addition of up to 3×10^{-3} M perchloric acid to the solvolysis of **2** in 50% TFE (Table 2) is to be expected. For hydrolyses of **2** in pure water, even concentrations as high as 0.2 M in added perchloric acid or 1 M in added hydrochloric acid have a negligible effect upon the specific rates of solvolysis.[6]

For the solvolysis of **1**, a rate depression upon adding chloride ion-containing salts has been reported for some,[7,26] but not all,[7] solvents. We find that additions of up to 0.02 M tetraethylammonium chloride to solvolyses of **2** in ethanol at 62.5 °C do not lead to any appreciable depression of the initial rate of acid formation. The additions do lead to a decrease in each individual run of the apparent integrated first-order rate coefficient with extent of reaction. This effect has not been studied in detail but it can be rationalized in terms of a chloride ion-induced increase in the rate of the reaction removing previously formed acid, as expressed by eq 7.

$$\mathrm{EtO^{+}H_2 + Cl^{-} \rightarrow EtCl + H_2O} \qquad (7)$$

Mechanistic Evidence from Product Partitioning. The selectivity values, calculated using eq 3 and presented in Table 3, for approximately constant partitioning between ether and alcohol products in ethanol–water (average *S* of 0.90) and methanol–water (average *S* of 1.4) are very similar to those previously observed[21] for the corresponding solvolyses of *p*-methoxybenzoyl chloride (average *S* of 0.70 in ethanol–water and of 1.31 in methanol–water). These comparisons provide evidence in favor of a similarity of mechanism, and since *p*-methoxybenzoyl chloride has been considered to solvolyze by a mechanism close to S_N1 but with evidence for a weak nucleophilic solvent assistance,[21,41] the product studies complement nicely the kinetic studies. Indeed, an analysis using eq 1 of the solvolysis of *p*-methoxybenzoyl chloride in 32 solvents, consisting of binary mixtures of water with methanol, ethanol, TFE, acetonitrile, acetone, and dioxane, led to values of 0.33 ± 0.07 for *l*, 0.81 ± 0.02 for *m*, and 0.11 ± 0.21 for *c* (correlation coefficient of 0.990).[39] The *l* value is comparable to the value of 0.23 ± 0.04 for solvolyses of **2** in similar solvents (Table 4). The *m* value being higher for solvolysis of *p*-methoxybenzoyl chloride than the 0.58 ± 0.03 for solvolysis of **2** can be considered to reflect the pronounced mesomeric assistance present in the solvolyses of **2**. The observation of inverse and constant selectivities in ethanol–water mixtures for both **2** and *p*-methoxybenzoyl chloride[21] suggests, from the similar behavior to solvolyses of adamantyl derivatives,[20,23] that products are being formed primarily by reaction of the carbocation with solvent at the solvent-separated ion-pair stage.

The trends in *S* values for TFE–water and TFE–ethanol mixtures (Table 3) are more difficult to rationalize by comparisons with published data. Adamantyl solvolyses show[19] a surprising increase in *S* value as water is added to TFE, whereas **2** shows a constant *S* value. Also, in TFE–ethanol mixtures the *S* values (k_{EtOH}/k_{TFE}) are usually < 1,[19] whereas the cation derived from **2** shows a considerable preference for reaction with the ethanol component (*S* = 11). This may reflect differences in selectivity between ion pairs derived from adamantyl substrates and from **2**, possibly because **2** is also susceptible to rearside attack. Also, the presence within the solvolysis medium of TFE, a solvent of only weak nucleophilicity but of high ionizing power, may lead to an increased probability for progression to the fully dissociated ions and to appreciable amounts of product formation from the free cation.

Conclusions

Solvolyses of *N,N*-diphenylcarbamoyl chloride (**2**) proceed with a very weak nucleophilic solvent assistance (*l* = 0.2, Table 4). Product studies in ethanol–water and methanol–water mixtures suggest that product formation occurs at the solvent-separated ion-pair stage (*S* ~ 1 in these solvent mixtures). Because positive charge is delocalized from the developing acylium ion to the adjacent nitrogen, the transition state is stabilized and a relatively low sensitivity to changes in solvent ionizing power is observed (*m* = 0.58). The solvolyses have kinetic and product-partitioning characteristics very similar to those previously observed for *p*-methoxybenzoyl chloride, except for the higher *m* value (0.81) for the solvolyses of the acyl chloride.

Solvolyses of **2** in ethanol are accelerated by pyridine, believed to be acting primarily as a nucleophilic catalyst,

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consistent with the bimolecular nature of the aminolyses of **2**[5,6] and further illustrating the sensitivity to nucleophilic attack. Pyridine also suppresses a side reaction, between an alcohol-rich solvent and the developing HCl,[40] a reaction which could be confused with common-ion rate depression.

Experimental Section

Materials. *N,N*-diphenylcarbamoyl chloride (Aldrich, 98%) was used directly for kinetic studies; samples for product studies were recrystallized from petroleum ether and were shown to be >99% pure by HPLC of the product from solvolysis in pure methanol. Diphenylamine was ACS reagent grade (Aldrich, >99%). Other standards for product studies were obtained as follows: Ethyl *N,N*-diphenylcarbamate (Aldrich, 99%) was recrystallized from petroleum ether: mp 70–72 °C (lit.[42] mp 72 °C). Methyl *N,N*-diphenylcarbamate was prepared from the chloride by standard methods and was recrystallized from petroleum ether: mp 86–87 °C (lit.[42] mp 86 °C).

Solvents for kinetics were commercially available and were further purified before use. Ethanol and methanol were distilled from the corresponding magnesium alkoxides, and 2,2,2-trifluoroethanol (TFE) was dried by refluxing over phosphorus pentoxide and was then distilled; Karl Fischer titration showed that 0.03–0.04 wt % water was present in the TFE. Solvents for HPLC were AR grade methanol (Fisons) and HPLC grade acetonitrile (Fisons).

2,2,2-Trifluoroethyl *N,N*-Diphenylcarbamate. *N,N*-diphenylcarbamoyl chloride was heated under reflux with 2,2,2-trifluoroethanol for 48 h, and after a standard workup procedure, a solid was obtained in 60% yield. Recrystallization from petroleum ether gave a white crystalline solid: mp 63–64 °C; IR (KBr) 1150, 1280, 1320, 1770 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.46 (q, 2H), 7.2 (m, 10H); ^{13}C NMR ($CDCl_3$, proton decoupled) δ 61.48 (q, CCF splitting), 125.49 (q, CF splitting), 126.69, 129.04, 129.29, 141.79, 152.95; MS *m/z* 295 (M^+). Anal. Calcd for $C_{15}H_{12}NO_2F_3$: C, 61.02; H, 4.09; N, 4.74. Found: C, 61.27; H, 4.04; N, 4.90.

Kinetic Methods. Concentrations of **2** of 0.003–0.007 M were allowed to solvolyze in the solvent under consideration at the required temperature. At appropriate time intervals, 5-mL portions were removed and added to 20 mL of acetone containing resorcinol blue (Lacmoid), cooled to −78 °C. For runs in HFIP-containing solvents, the procedure was modified and 1-mL portions were removed from 10 mL of solution and added to 10 mL of acetone. The acid developed was titrated against a standardized solution of sodium methoxide in methanol. The infinity titer was taken after 10 half-lives, except that for very slow runs the 5-mL portion was added to 5 mL of water, followed by addition of 20 mL of acetone after the completion of the now considerably reduced time to 10 half-lives; this technique also avoided the perturbation of the V_∞ value in alcohol-rich solvents due to loss of HCl (eq 7). All runs were performed, at least, in duplicate. The calculations of the first-order solvolysis rate coefficients were as previously described.[43]

Product Studies. *N,N*-diphenylcarbamoyl chloride was dissolved in dry acetonitrile to give 5% or 1% solutions; 20 μL aliquots of these solutions were then added to 5.00 mL of solvolysis medium and heated at 62.5 °C for about 10 half-lives. Products were then analyzed by reversed-phase HPLC by direct injection of 10 μL aliquots: column (15 cm × 1/4 in. Spherisorb ODS2); eluents (50% acetonitrile/water for Et ester, methanol/water for Me and CH_2CF_3 esters); absorbance range 0.2 at $\lambda = 250$ nm. Responses were calibrated by injecting standard 10^{-3} M solutions of pure products (duplicate injections of duplicate solutions; responses for the alkyl (R) esters varied in the order R = Et > Me > CH_2CF_3).

Equipment for HPLC was an LDC Milton-Roy Constametric 3000 solvent delivery system, a Spectromonitor 3100 variable wavelength UV detector, and a CI4100 integrator, operating with a Promis autosampler or manually with a Rheodyne 7125 injection valve.

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