

## Solvolyses of *N*-Methyl-*N*-phenylcarbamoyl Chlorides with Electron Acceptor Substituents in Aqueous Binary Mixtures

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Solvolyses of *N*-methyl-*N*-phenylcarbamoyl chlorides in aqueous binary mixtures of acetone, ethanol, methanol and in water, D<sub>2</sub>O, and 50% D<sub>2</sub>O-CH<sub>3</sub>OD are investigated at 25.0 °C. The Grunwald-Winstein plots of first-order rate constants for *N*-methyl-*N*-phenylcarbamoyl chlorides with *Y*<sub>Cl</sub> (based on 2-adamantyl chloride) show a dispersion phenomenon. The ring parameter (*I*) has been shown to give considerable improvement when it is added as an *hI* term to the original Grunwald-Winstein and extended Grunwald-Winstein correlations for the solvolyses of *N*-methyl-*N*-phenylcarbamoyl chlorides. This study has shown that the magnitude of *l*, *m* and *h* values associated with a change of solvent composition is able to predict the dissociative S<sub>N</sub>2 transition state. The kinetic solvent isotope effects determined in deuterated water are consistent with the proposed mechanism of the general base catalyzed and/or a dissociative S<sub>N</sub>2 mechanism channel for *N*-methyl-*N*-phenylcarbamoyl chlorides solvolyses.

**Keywords :** Solvolyses, Ring parameter transition state, Isotope effect, Dissociative S<sub>N</sub>2 mechanism.

### Introduction

Nucleophilic substitution reactions of *N,N*-disubstituted carbamoyl chlorides have been studied extensively. Solvolysis of *N,N*-disubstituted carbamoyl chlorides proceeds primarily through an S<sub>N</sub>1 mechanism, which is favored by a strong electron delocalization from nitrogen.<sup>1-5</sup> However for some systems evidence in support of a weak nucleophilic participation by solvent has also been presented, and an S<sub>N</sub>2 (intermediate) mechanism has been proposed.<sup>6</sup> In contrast, several workers have often suggested an S<sub>N</sub>2 mechanism for the aminolysis reaction of *N,N*-disubstituted carbamoyl chlorides. Hall has suggested a bimolecular reaction mechanism for the reactions of *N,N*-dimethylcarbamoyl chloride with aliphatic amines.<sup>7</sup> Johnson *et al.*,<sup>3</sup> have shown that *N,N*-diphenylcarbamoyl chloride reacts directly with amines forming the corresponding *N,N*-diphenylurea derivatives. On the other hand, Kim *et al.*,<sup>8</sup> reported that nucleophilic substitution reactions of *N,N*-dimethylcarbamoyl chloride are bimolecular whereas those of *N,N*-diphenylcarbamoyl chloride are unimolecular. Aminolyses of *N*-arylcarbamates, ArNHCOOAr', are known to proceed by the overall second- and third-order processes in aprotic solvents.<sup>9</sup> Our recent work indicated that nucleophilic substitution reactions of *N*-methyl-*N*-phenylcarbamoyl chlorides with benzylamines in acetonitrile are direct displacement (S<sub>N</sub>2) mechanism based on the interpretation of inverse *k<sub>H</sub>/k<sub>D</sub>* values and negative ρ<sub>XY</sub> values.<sup>10</sup>

Dispersion into separate lines in the correlation of the specific rates of solvolysis of a substrate in various binary mixtures was documented<sup>11-15</sup> in early treatments using the Grunwald-Winstein eq. (1).<sup>6,16-17</sup>

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

In general, dispersion effects in unimolecular solvolyses<sup>18,19</sup> make smaller contribution to the overall linear free energy relationship (LFER) than solvent nucleophilicity effects in bimolecular solvolysis. It was suggested that a second term which is governed by the sensitivity *l* to solvent nucleophilicity *N*, should be added to eq. (1) for bimolecular solvolysis.<sup>20</sup> The resulting eq. (2) is often referred to as the extended Grunwald-Winstein equation.<sup>20</sup>

$$\log(k/k_0) = mY + lN \quad (2)$$

Kevill *et al.*, recently suggested<sup>21-24</sup> that, since the dispersion seems to follow a consistent pattern, it should be possible to develop an aromatic ring parameter (*I*), which, as qualified by the appropriate sensitivity (*h*), can be added to eq. (1) or (2) to give eq. (3) or (4), respectively.<sup>25,26</sup>

$$\log(k/k_0) = mY + hI + c \quad (3)$$

$$\log(k/k_0) = mY + lN + hI + c \quad (4)$$

In this work, we determined rate constants for solvolyses of *N*-methyl-*N*-phenylcarbamoyl chlorides in aqueous binary mixtures of acetone, ethanol, methanol and in pure water and D<sub>2</sub>O at 25.0 °C, and transition states variation are discussed by applying the Grunwald-Winstein equation, extended Grunwald-Winstein equation, aromatic ring parameter equation and kinetic solvent isotope effect.

### Result and Discussion

Rate constants for solvolyses of *N*-methyl-*N*-phenylcarbamoyl chlorides in aqueous binary mixtures of acetone,

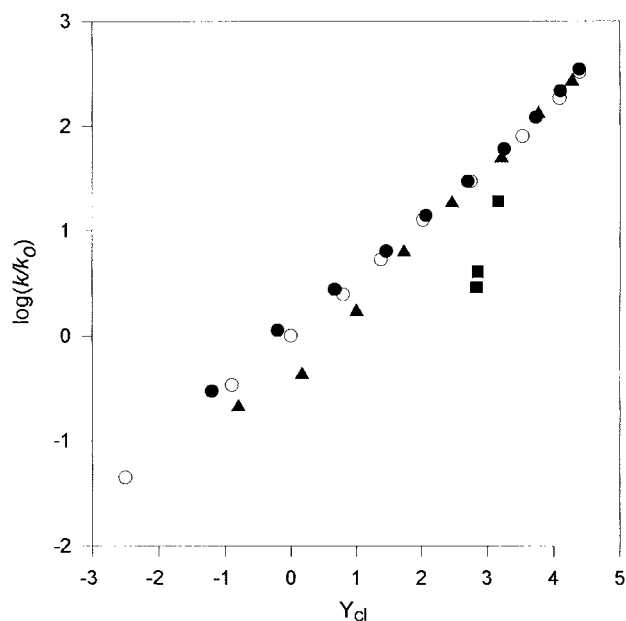
**Table 1.** Rate constants ( $k \times 10^5$ ,  $\text{sec}^{-1}$ ) for solvolyses of *p*-substituted *N*-methyl-*N*-phenylcarbamoyl chlorides in aqueous binary mixtures at 25 °C

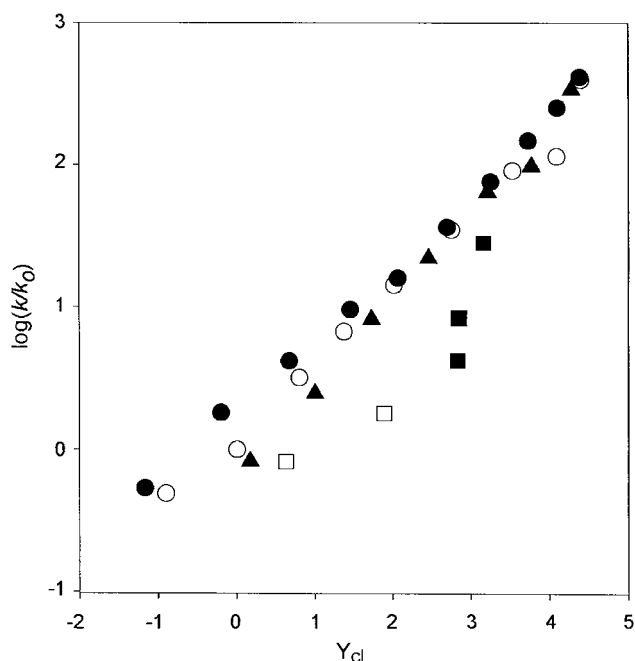
Solvent	$v/v$ %	$k \times 10^5 \text{ sec}^{-1}$		
		H	<i>p</i> -Cl	<i>p</i> -NO <sub>2</sub>
MeOH	100	0.0965	0.182	
	90	0.367	0.617	
	80	0.891	1.42	
	70	2.06	3.25	0.174
	60	4.53	5.45	0.341
	50	9.67	12.4	0.538
	40	19.6	25.6	0.877
	30	39.4	49.9	2.05
	20	69.8	85.2	2.63
	10	113	143	4.71
	H <sub>2</sub> O	173	217	7.40
D <sub>2</sub> O	127	160	5.16	
EtOH	100	0.0146		
	90	0.110	0.166	
	80	0.327	0.341	
	70	0.800	1.09	
	60	1.71	2.28	0.0541
	50	4.09	4.84	0.200
	40	9.67	11.7	0.453
	30	25.7	31.2	1.04
	20	60.0	38.9	1.58
	10	105	135	4.61
	Acetone	80	0.0685	0.280
70		0.140	0.840	
60		0.550	0.840	
50		2.03	2.76	0.278
40		5.91	7.54	0.372
30		16.1	22.0	0.802
20		41.8	33.4	1.79
10	86.8	115	3.66	

ethanol, methanol and in pure water and D<sub>2</sub>O at 25.0 °C are reported at Table 1. Rate constants increase in the order of acetone-H<sub>2</sub>O < ethanol-H<sub>2</sub>O < methanol-H<sub>2</sub>O and the rate increases fast as the water content of the mixtures increase. First-order rate constants for solvolysis of *N*-methyl-*N*-phenylcarbamoyl chlorides vary over ten thousand-fold range in alcohol-water mixtures, whereas the observed first-order rate constants for phenyl chloroformates vary only over twenty-fold range<sup>27</sup> which is known to react *via* an S<sub>N</sub>2 like S<sub>A</sub>N or carbonyl addition-elimination reaction mechanism. These results indicate that the rate determining step is not the bond formation step which was found in the reaction of phenyl chloroformates but the bond breaking step for the reaction of *N*-methyl-*N*-phenylcarbamoyl chlorides where transition state is sensitive to solvent ionizing power. These results are very similar to those of solvolytic reactions of benzyl chloride,<sup>28,29</sup> *p*-methoxybenzoyl chloride<sup>12,28</sup> and thenoyl chloride,<sup>30</sup> but they are different from the results of solvolytic reactions of *p*-nitrobenzoyl chloride,<sup>13,31</sup> *p*-nitrobenzenesulfonyl chloride<sup>11,32</sup> and furoyl chloride.<sup>30</sup>

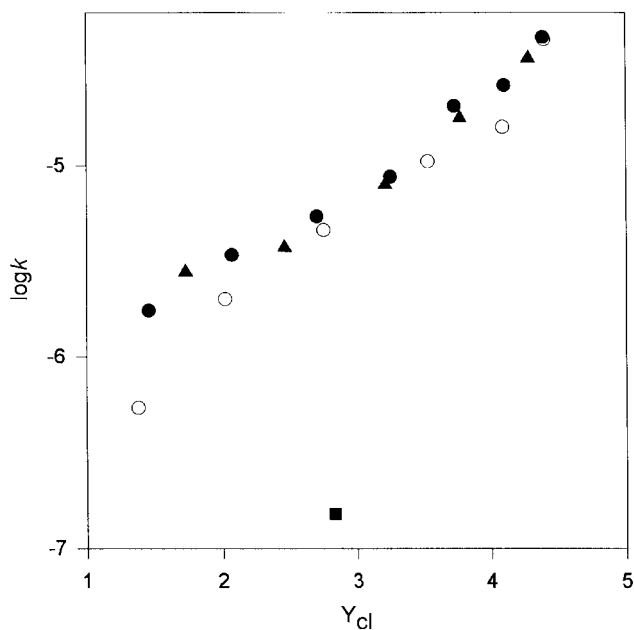
Reference to Table 1 reveals that the rate constants increase in the order of *p*-NO<sub>2</sub> < *p*-H < *p*-Cl which is not the order of electron donating or withdrawing ability. The rates slightly increase for the weakly electron withdrawing substituent, *p*-Cl, however the rate decrease is large for the strong electron withdrawing substituent, *p*-NO<sub>2</sub>. Therefore, the positive charge of the carbonyl cation is stabilized by the resonance effect of neighbouring nitrogen atom. This result implies that the positive charge of the carbonyl cation is stabilized by the  $\pi$ -electron donation of *p*-Cl and the positive charge of the carbonyl cation is destabilized by the strong  $\sigma$ -electron withdrawal of *p*-NO<sub>2</sub>. These results are consistent with S<sub>N</sub>1 like S<sub>N</sub>2 mechanism where bond-breaking is more important than bond-formation in the rate determining step.

The Grunwald-Winstein plots (equation 1) of the rates in Table 1 and 2 are presented in Figure 1, 2, and 3 using the solvent ionizing power scale  $Y_{\text{Cl}}$ , based on 2-adamantyl chloride.<sup>33</sup> Examination of Figure 1, 2, and 3 shows that the plots for the three aqueous mixtures exhibit dispersions into three separate line. The plots for all binary solvents show a very large  $m$  value,  $m = 0.56$  ( $r = 0.986$ ) for H,  $m = 0.53$  ( $r = 0.946$ ) for *p*-Cl, and  $m = 0.51$  ( $r = 0.941$ ) for *p*-NO<sub>2</sub> respectively and show a similar reactivity for TFE-H<sub>2</sub>O and TFE-EtOH. The similar reactivity of TFE solvent mixtures shows a small deviation from the correlation of Grunwald-Winstein plots for aqueous alcohol and acetone. Rate ratios in solvents of the same  $Y_{\text{Cl}}$  value and different nucleophilicity provide measures of the minimum extent of nucleophilic solvent assistance (e.g.,  $[k_{40\text{EW}}/k_{97\text{TFE}}]_{\text{Y}} = 10.3$  for H,  $[k_{40\text{EW}}/k_{97\text{TFE}}]_{\text{Y}} = 8.18$  for *p*-Cl,  $[k_{40\text{EW}}/k_{97\text{TFE}}]_{\text{Y}} = 30.2$  for *p*-NO<sub>2</sub> and, EW = ethanol-water).<sup>34</sup> The low nucleophilicity and high ionizing power of the fluorinated alcohol, CF<sub>3</sub>CH<sub>2</sub>OH, show small deviation from Figure 1, 2, and 3.

**Figure 1.** Plots of  $\log(k/k_0)$  versus  $Y_{\text{Cl}}$  for solvolyses of *N*-methyl-*N*-phenylcarbamoyl chloride at 25 °C (solvent codes: ●; methanol, ○; ethanol, ▲; acetone, ■; TFE).



**Figure 2.** Plots of  $\log(k/k_0)$  versus  $Y_{Cl}$  for solvolyses of *p*-chloro-*N*-methyl-*N*-phenylcarbamoyl chloride at 25 °C (solvent codes: ●; methanol, ○; ethanol, ▲; acetone ■; TFE, □; TFE-Ethanol).



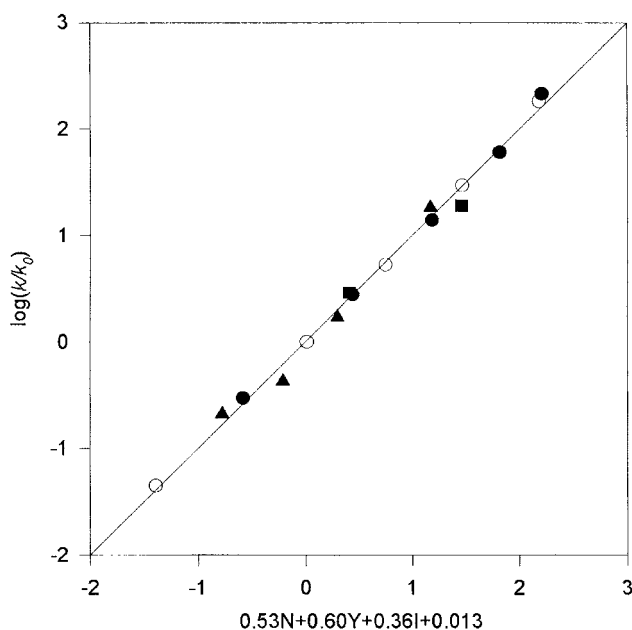
**Figure 3.** Plots of  $\log k$  versus  $Y_{Cl}$  for solvolyses of *p*-nitro-*N*-methyl-*N*-phenylcarbamoyl chloride at 25 °C (solvent codes: ●; methanol, ○; ethanol, ▲; acetone, ■; TFE).

Such a large  $m$  value and small value of  $k_{40EW}/k_{97TFE}$  imply that the solvolysis of *N*-methyl-*N*-phenylcarbamoyl chlorides in the binary mixtures proceeds by a dissociative  $S_N2$  or  $S_N1$  mechanism channel rather than by an  $S_{AN}$  channel.<sup>34</sup>

In order to examine the cause of this dispersion phenomenon, we correlated the rate data in Table 1 and 2 using equation (4). The plots showed good correlations ( $r = 0.994$  for H, and  $r = 0.989$  for *p*-Cl) for the solvolysis of *N*-methyl-

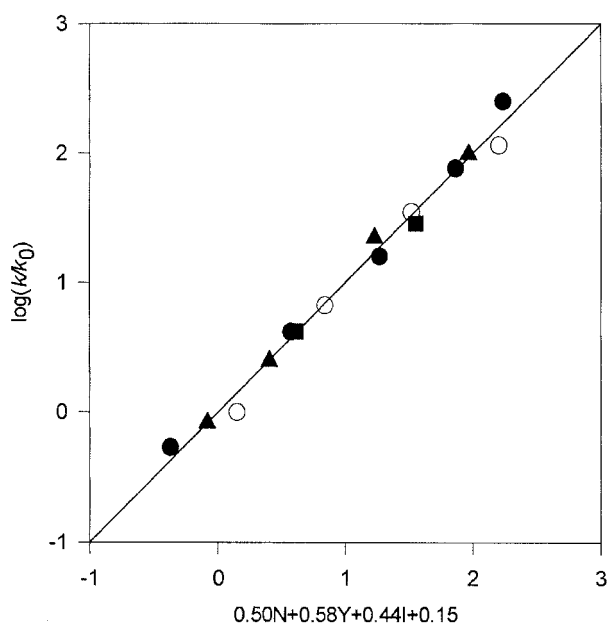
**Table 2.** Rate constants ( $k \times 10^5$ ,  $\text{sec}^{-1}$ ) for solvolyses of *p*-substituted *N*-methyl-*N*-phenylcarbamoyl chlorides in TFE binary mixtures at 25 °C

	$v/v$ %	$k \times 10^5 \text{sec}^{-1}$
H	97TFE-3H <sub>2</sub> O	0.941
	90TFE-10H <sub>2</sub> O	1.32
	50TFE-50H <sub>2</sub> O	6.22
<i>p</i> -Cl	97TFE-3H <sub>2</sub> O	1.43
	90TFE-10H <sub>2</sub> O	2.83
	50TFE-50H <sub>2</sub> O	9.58
	80TFE-20EtOH	0.280
	60TFE-40EtOH	0.615
<i>p</i> -NO <sub>2</sub>	97TFE-3H <sub>2</sub> O	0.0150



**Figure 4.** Plots of  $\log(k/k_0)$  for *N*-methyl-*N*-phenylcarbamoyl chloride against  $(0.53N + 0.60Y + 0.36I + 0.013)$ ,  $r = 0.999$  (solvent codes: ●; methanol, ○; ethanol, ▲; acetone, ■; TFE).

*N*-phenylcarbamoyl chlorides (Figure 4 and 5). The nucleophilicity parameter ( $N$ ) and aromatic ring parameter ( $I$ ) have been shown to give considerable improvement when an  $IN$  term and  $hI$  term are added to the original Grunwald-Winstein [eqn. (1)] correlations of the solvolysis reaction of *N*-methyl-*N*-phenylcarbamoyl chlorides. Therefore, this shows an importance of aromatic ring parameter and solvent nucleophilicity parameter for solvolysis of *N*-methyl-*N*-phenylcarbamoyl chlorides. Therefore such phenomenon can be explained as dispersion effect caused by solvent nucleophilicity and delocalization into the aromatic ring. The dispersions in the Grunwald-Winstein correlations in the present studies are caused by the conjugation between the reaction center and aromatic ring through the nitrogen atom leading the medium value of sensitivity of  $I$  ( $h = 0.36$  for H,  $h = 0.44$  for *p*-Cl) in the full equation (4). The through conjugation of the ring  $\pi$  system with the nucleophile (solvent in this case) has also been found in the solvolysis of



**Figure 5.** Plots of  $\log(k/k_0)$  for *p*-chloro-*N*-methyl-*N*-phenylcarbamoyl chloride against  $(0.50N + 0.58Y + 0.44I + 0.15)$ ,  $r = 0.989$  (solvent codes: ●; methanol, ○; ethanol, ▲; acetone, ■; TFE).

**Table 3.** Rate constants ( $k \times 10^5, \text{sec}^{-1}$ ) and kinetic solvent isotope effects (KSIE) for solvolyses of *N*-methyl-*N*-phenylcarbamoyl chlorides in water at 25 °C

	<i>v/v</i> %	$k \times 10^5 \text{sec}^{-1}$		KSIE
		$k_{\text{SOH}}$	$k_{\text{SOD}}$	
H	H <sub>2</sub> O	173	126	1.37
	50H <sub>2</sub> O-50MeOH	9.67	6.68	1.45
<i>p</i> -Cl	H <sub>2</sub> O	217	160	1.36
	50H <sub>2</sub> O-50MeOH	12.4	8.76	1.42
<i>p</i> -NO <sub>2</sub>	H <sub>2</sub> O	7.40	5.16	1.43

phenyl chlorothionoformate<sup>35</sup> and pyridinolysis of phenyl chloroformates.<sup>36</sup> In these studies it has been interpreted to indicate the overlap of the reaction center and aromatic ring  $\pi$  system through lone pair electron of nitrogen atom in the rate-limiting step. With use of the full equation (4), the *l* and *m* values are similar to the values of 0.53 and 0.60 for H, 0.50 and 0.58 for *p*-Cl respectively for the solvolysis of *N*-methyl-*N*-phenylcarbamoyl chlorides. This study has shown that the magnitude of *l* and *m* values associated with a change of solvent composition is able to predict the dissociative  $S_N2$  transition state.<sup>21-24,39</sup>

We have determined the kinetic solvent isotope effect (KSIE),  $k_{\text{SOH}}/k_{\text{SOD}}$ , for the substrate using deuterated water (D<sub>2</sub>O) and 50% D<sub>2</sub>O-CH<sub>3</sub>OD, and the results are presented in Table 3. Previous works indicated that the KSIE values are relatively large,  $\geq 1.7$ , for a general base catalyzed reaction but is small, 1.2-1.5, for  $S_N2$  reaction.<sup>37</sup> For *N*-methyl-*N*-phenylcarbamoyl chlorides, the KSIEs are 1.37 for H, and 1.36 for *p*-Cl in water. These results are again in good agreement with our proposed reaction channels in

aqueous alcohol *N*-methyl-*N*-phenylcarbamoyl chlorides solvolyses through a general base catalyzed and/or a dissociative  $S_N2$  mechanism channel.

### Experimental Section

Methanol, ethanol, and acetone were Merck GR grade (< 0.1% H<sub>2</sub>O), and D<sub>2</sub>O and CH<sub>3</sub>OD were from Aldrich (99.9% D). Distilled water was redistilled with Buchi Fontavapor 210 and treated using ELGA UHQ PS to obtain specific conductivity of less than  $1 \times 10^{-6}$  mhos/cm. Preparation of substituted *N*-methyl-*N*-phenylcarbamoyl chlorides were as described previously.<sup>10</sup>

The rates were measured conductometrically at 25 ( $\pm 0.03$ ) °C at least in duplicate as described previously,<sup>11,27,38</sup> with concentrations of substrate *ca.*  $10^{-3}$  M.

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