

Research Article

On the Importance of the Aromatic Ring Parameter in Studies of the Solvolyses of Cinnamyl and Cinnamoyl Halides

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In solvolysis studies using Grunwald-Winstein plots, dispersions were observed for substrates with aromatic rings at the α -carbon. Several examples for the unimolecular solvolysis of monoaryl benzylic derivatives and related diaryl- or naphthyl-substituted derivatives have now been reported, where the application of the aromatic ring parameter (I) removes this dispersion. A recent claim suggesting the presence of an appreciable nucleophilic component to the I scale has now been shown, in a review of the solvolysis of highly-hindered alkyl halides, to be unlikely to be correct. Attention is now focused on the application of the hI term for the solvolysis of compounds containing a double bond in the vicinity of any developing carbocation. Available specific rates of solvolysis (plus some new values) at 25°C of cinnamyl chloride, cinnamyl bromide, cinnamoyl chloride, *p*-chlorocinnamoyl chloride, and *p*-nitrocinnamoyl chloride are analyzed using the simple and extended (including the hI term) Grunwald-Winstein equations.

1. Introduction

To commemorate the 60th anniversary of the development of the simple Grunwald-Winstein equation [1], a review detailing its development and applications was recently published [2]. The linear free energy relationship (LFER) shown in (1) was developed in 1948 for the correlation of solvolysis reactions proceeding by an ionization ($S_N1 + E1$) pathway [1]. In (1), k and k_0 are the specific rates of solvolysis of the substrate under study in a given solvent and in the standard solvent, respectively; m is the sensitivity towards changes in the solvent ionizing power Y (initially set at unity for tert-butyl chloride solvolyses), and c is a constant (residual) term,

$$\log\left(\frac{k}{k_0}\right) = mY + c. \quad (1)$$

It was realized [3] that as the solvolyses of 1- and 2-adamantyl derivatives (Figure 1) cannot be subject to rearside nucleophilic participation and elimination, they could provide improved standard substrates for establishing

scales of solvent ionizing power [4, 5] and listings of Y_x values are available [6].

For bimolecular (S_N2 and/or $E2$) reactions, an additional term involving the sensitivity (l) to changes in solvent nucleophilicity (N) is added to (1) to give [7],

$$\log\left(\frac{k}{k_0}\right) = lN + mY + c. \quad (2)$$

The development of solvent nucleophilicity scales has been briefly reviewed [2, 8] and it has also been reviewed in considerable depth in a book chapter [9]. At the present time, the N_T scale [2, 8–10] with *S*-methylidibenzothiophenium ion (MeDBTh⁺) as the standard substrate has become the recommended standard [2] for considerations of solvent nucleophilicity.

Three approaches have been proposed to correct for dispersions observed in Grunwald-Winstein plots when aromatic rings are bonded to the carbon that is developing appreciable positive charge at the transition state or when substrates solvolyze with neighboring aryl group participation. Bentley et al. [11] favored the use of *p*-methoxybenzyl

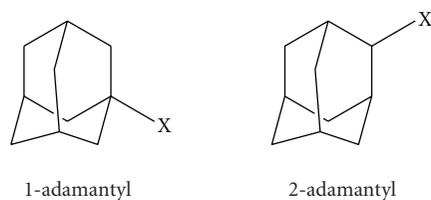


FIGURE 1: 1- and 2-adamantyl derivatives.

chloride as a similarity model to correlate the solvolyses of α -aryl halides. Liu and Sheu [12, 13] also using a similarity model approach developed Y_{BnX} scales for each leaving group X and $Y_{x\text{BnX}}$ scales [14] for x aromatic rings entering into conjugation with the reaction center. Early on, we pointed out [15] that only negligible to moderate improvements result from replacing the Y_x scale by a “specialized” scale and the considerable effort involved in developing the new scales is not justified. Fujio and co-workers proposed [16] a second approach for solvolyses that proceed via anchimeric assistance (k_{Δ}) and developed a scale (Y_{Δ}) derived from 2-methyl-2-(*p*-methoxyphenyl)propyl toluene-*p*-sulfonate solvolyses. We have favored a third, more general avenue by developing [17] an aromatic ring parameter (I), where an appropriate sensitivity h is added to Grunwald-Winstein equations (1) and (2) to give (3) and (4). This approach avoids the nontrivial task of choosing a closely related similarity model, furthermore, it can be used with multiple aromatic rings in conjugation with the developing carbocationic center, and to correlate solvolysis involving a 1,2-aryl shift [2],

$$\log\left(\frac{k}{k_0}\right) = mY_X + hI + c, \quad (3)$$

$$\log\left(\frac{k}{k_0}\right) = lN_T + mY_X + hI + c. \quad (4)$$

Recently, Martins and coworkers [18] applied (4) to the specific rates of solvolysis of five moderately-hindered tertiary alkyl halides (substrates mostly with the absence of π -electrons) and found the sensitivities (h) to changes in the aromatic-ring parameter (I) were sometimes positive and sometimes negative. They suggested that the negative h values arose because I was not a pure parameter and proposed that it included a solvent nucleophilicity component [18]. After a thorough analysis of the available specific rates of solvolyses of 30 highly-hindered tertiary alkyl derivatives, we concluded in a recent review [19] that it appears that the apparent utility of the hI term for substrates not having appropriately placed π -electrons is an artifact resulting from moderate multicollinearity that is present between the I values and a linear combination of N_T and Y_X values.

Cinnamyl chloride is one of many chemicals that produce allergic contact dermatitis (ACD) in humans [20] and yet it is a common important chemical intermediate that has found use in a variety of pharmaceutical compositions, fragrance, and flavoring agents. The analysis of the substituent effects on carbocation reactivity using the Hammett plot for the chlorine exchange of substituted cinnamyl chlorides [21] and studies of the secondary deuterium isotope effect [22]

implied electron-donating conjugation through the double bond in a loose S_N1 transition state. Koo et al. have analyzed the solvolytic rate constants and product selectivities (S) of cinnamyl chloride [23] and cinnamyl bromide [24] in a number of binary mixtures of water with ethanol, methanol, acetone, and 2, 2, 2-trifluoroethanol (TFE). The close similarity of solvent kinetic isotope effects, rate-rate profiles of solvent effects on reactivity, and similar selectivity data to *p*-methoxybenzyl chloride [11, 25] made the authors conclude that the solvolyses of cinnamyl halides can be explained by product formation incorporating a general base-catalyzed nucleophilic attack on a contact ion pair [23, 24]. Cinnamyl bromide was subject to electrochemical reduction using cyclic voltammetry and controlled-potential electrolysis [26] where it was shown that the substrate could be reduced to a resonance-stabilized cinnamyl radical, which could further be reduced to a carbanion depending upon the selected potential.

Cinnamoyl derivatives are used to produce compounds that have shown promising antifungal, antibacterial [27], and anticancer [28] activity. Koo and coworkers also studied the solvolyses of substituted cinnamoyl chlorides [29] in aqueous binary mixtures of ethanol, methanol, acetone, and TFE, and in TFE-EtOH. Based on the examination of results obtained using their kinetic data in Hammett plot analysis and in exceedingly scattered Grunwald-Winstein plots, they proposed a dissociative S_N2 pathway for three *p*-substituted cinnamoyl chlorides [29].

2. Results and Discussion

In this study, we present specific rates of solvolysis of cinnamyl chloride (1) at 25.0°C in three aqueous ethanol (EtOH), three aqueous methanol (MeOH), one aqueous acetone, two aqueous TFE, and four TFE-EtOH mixtures. We reanalyze all available specific rates of solvolysis of cinnamyl chloride (1), cinnamyl bromide (2), cinnamoyl chloride (3), *p*-chlorocinnamoyl chloride (4), and *p*-nitrocinnamoyl chloride (5) (Figure 2), in terms of the simple and extended Grunwald-Winstein equations ((1) and (2)), and we also consider the extent to which these equations are improved on incorporation of the hI term ((3) and (4)).

In Table 1, we report specific rate constants at 25.0°C for the solvolyses of 1 in the aqueous binary mixtures of MeOH, EtOH, acetone, and TFE, and in TFE-EtOH. The specific rate constants for 1 in 97 and 90 TFE-H₂O (%w/w) were determined at 3 different temperatures and an Arrhenius treatment allowed estimation of the specific rate at the higher 25.0°C temperature also presented in Table 1. Our measurements at 25.0°C, when compared to those reported by Koo and coworkers [23] differ markedly (as shown in Table 1 and corresponding footnotes), by a factor of 5 in pure EtOH, by a factor of 3 in 90% EtOH (%v/v), and by a factor of 2 in 80%EtOH (%v/v). Furthermore, an acceptable 2% difference observed in the value of 80T-20E progressed to a much larger 30% difference in the 60T-40E value, then to a substantial 50% difference in the 40T-60E reported value, and culminated in a huge difference of 70% observed in the 20T-80E mixture. The observations of significant deviations

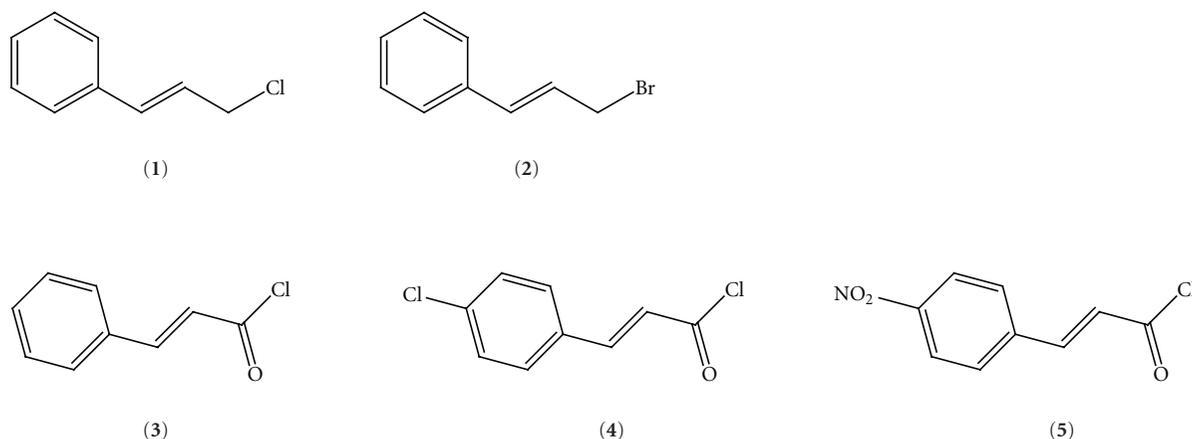


FIGURE 2: Molecular structures for cinnamyl chloride (1), cinnamyl bromide (2), cinnamoyl chloride (3), *p*-chlorocinnamoyl chloride (4), and *p*-nitrocinnamoyl chloride (5).

seen only in EtOH-rich mixtures indicated that the deviant behavior was a general characteristic (in this particular case) of that solvent. We minimized experimental error by designing mechanical mixing for uniform consistency, using ACS reagent grade solvents, repeating the titrimetric procedures using different batches of EtOH, and the key reactions were also repeated during different months to verify that the same trends persisted. The specific rates for the EtOH containing mixtures reported in Table 1 are the averages of at least four independent kinetic runs.

The specific rate constants for solvolyses of **1** in solvents other than EtOH are within an acceptable $\pm 7\%$ range of values reported by Koo and coworkers [23]. Hence, the new data in the thirteen solvents listed in Table 1 were combined with the nineteen reported values [23] in solvents other than ethanol. As reported in Table 2 for the 32 solvents, we obtained a fair linear correlation using (1), with $m = 0.76 \pm 0.03$, $c = -0.25 \pm 0.08$, 0.975 for the correlation coefficient, and 571 for the F -test value. Use of (2) leads to an essentially zero l value (0.09 ± 0.09) associated with a 0.29 probability that the $\ln T$ term is statistically insignificant. In contrast, use of (3) displays an m value of 0.79 ± 0.03 , an h value of 0.47 ± 0.20 (with a 0.03 probability of insignificance) and with a negligible improvement in the correlation coefficient (0.979) when compared to the solution obtained using (1). As observed in Table 2, analysis of the solvolysis of **1** is best carried out in terms of (4), with a considerably higher correlation coefficient of 0.987, a l value of 0.33 ± 0.08 , an m value of 0.91 ± 0.04 , an h value of 0.97 ± 0.21 , a c value of 0.20 ± 0.07 , and an F -test value of 340.

Excluding the data point for 100 EtOH, the solvent with highest nucleophilicity and lowest ionizing power (favoring bimolecular reaction); the correlation using equation (4) in the remaining 31 solvents has l , m , and h values similar to those obtained with 32 solvents, but with a considerably improved correlation coefficient of 0.992 and a significantly higher F -test value of 551. The l (0.33), m (0.95), and h (1.00) values obtained for **1** in 31 solvents (Table 2) are very similar to $l = 0.25 \pm 0.06$, $m = 0.92 \pm 0.03$, and $h = 0.88 \pm 0.13$, reported for *p*-methoxybenzyl chloride [30]; and $l =$

0.34 ± 0.15 (0.04 probability that the $\ln T$ term is statistically insignificant), $m = 0.89 \pm 0.04$, and $h = 0.92 \pm 0.15$ for 2,6-dimethylbenzoyl chloride [31], where we suggested that the nucleophilic solvation of the developing carbocation rather than a covalent involvement of the solvent molecule, is effective. This affirmation of appreciable nucleophilic solvation for **1** as indicated by the l value of 0.33 (in Table 2), is consistent with recent results showing that the *p*-methoxybenzyl carbocation is more stable than the cinnamyl carbocation but less stable than its *p*-methoxycinnamyl analog [32]. These results arose from a synthetic method involving a chlorosulfonyl isocyanate reaction with various alkyl allyl ethers to study carbocation stability in the solution phase, and using this newly developed procedure, the authors also showed that a cinnamyl carbocation is more stable than a benzylic carbocation and less stable than a 3° carbocation [32]. The h value reported in Table 2 of 1.00 ± 0.16 for **1** in 31 solvents is also consistent with one aromatic ring easily entering into conjugation [17] with the developing resonance stabilized transition state. This possibility of neighboring π -bond stabilization of the developing carbocation (phenacyl effect) is confirmed on visual inspection of the 3-D structure of cinnamyl chloride (**1'**), shown in Figure 3, due to the perfect planarity of the ring and the adjacent vinylic double bond.

The previously reported specific rates of solvolysis at 25°C for cinnamyl bromide (**2**) [24] are analyzed using (1)–(4). These results are reported in Table 3 for all 37 solvents and results are also tabulated for those obtained without the pure EtOH value (36 solvents). The slight improvements (for both **1** and **2**) seen in the R and the F -test values on exclusion of the specific rates in 100 EtOH, and the similarities in trends observed in the numerical values for l , m , and h , (reported in Tables 2 and 3) for **1** and **2** in thirty identical solvents are substantiated by the linear plot shown in Figure 4 of the $\log(k/k_0)$ values for **1** against those for **2**, with an excellent correlation coefficient of 0.989, F -test value of 1201, slope of 0.99 ± 0.03 , and intercept of -0.02 ± 0.05 . We can thus conclude that both, cinnamyl chloride and cinnamyl bromide solvolyze with nucleophilic solvation of the developing resonance-stabilized S_N1 transition state.

TABLE 1: Specific rates of solvolysis (k)^a of **1**, in several binary solvents at 25.0°C and literature values for (N_T) and (Y_{Cl}).

Solvent (%) ^b	1@25.0°C; $10^5 k$, s ⁻¹	N_T^l	Y_{Cl}^m
100% MeOH	0.905	0.17	-1.2
90% MeOH	4.87	-0.01	-0.20
80% MeOH	21.5	-0.06	0.67
100% EtOH	0.416 ^c	0.37	-2.50
90% EtOH	2.28 ^d	0.16	-0.90
80% EtOH	8.05 ^e	0.00	0.00
90% Acetone	0.00731	-0.35	-2.39
97% TFE (w/w)	488 ^f	-3.30	2.83
90% TFE (w/w)	626 ^g	-2.55	2.85
80T-20E	83.5 ^h	-1.76	1.89
60T-40E	14.5 ⁱ	-0.94	0.63
40T-60E	3.52 ^j	-0.34	-0.48
20T-80E	1.12 ^k	0.08	-1.42

^aDetermined titrimetrically; typical error \pm 4%. ^bSubstrate concentration of ca. 0.0052 M; binary solvents on a volume-volume basis at 25.0°C, except for TFE-H₂O solvents which are on a weight-weight basis. T-E are TFE-ethanol mixtures. ^cValue reported in Table 1 is the average obtained using $10^5 k$ (s⁻¹) values at 25.0°C of 0.409, 0.420, 0.418, and 0.417 from four independent runs. A value of $0.0839 \times 10^{-5} \text{s}^{-1}$ is reported in the literature [23]. ^dValue reported in Table 1 is the average obtained using $10^5 k$ (s⁻¹) values at 25.0°C of 2.26, 2.27, 2.30, and 2.30 from four independent runs. A value of $0.970 \times 10^{-5} \text{s}^{-1}$ is reported in the literature [23]. ^eValue reported in Table 1 is the average obtained using $10^5 k$ (s⁻¹) values at 25.0°C of 8.03, 8.03, 8.03, and 8.11 from four independent runs. A value of $4.73 \times 10^{-5} \text{s}^{-1}$ has been reported in the literature [23]. ^fCalculated from Arrhenius plots using $10^5 k$ (s⁻¹) values at 0.0°, -5.0°, and -10.0°C of 17.8, 8.9, and 4.0. ^gCalculated from Arrhenius plots using $10^5 k$ (s⁻¹) values at 0.0°, -5.0°, and -10.0°C of 23.9, 10.2, and 5.4. ^hValue reported in Table 1 is the average obtained using $10^5 k$ (s⁻¹) values at 25.0°C of 82.7, 83.1, 83.8, and 84.2 from four independent runs. A value of 84.8×10^{-5} is reported in the literature [23]. ⁱValue reported in Table 1 is the average obtained using $10^5 k$ (s⁻¹) values at 25.0°C of 14.1, 14.6, 14.6, and 14.7 from four independent runs. A value of 10.4×10^{-5} is reported in the literature [23]. ^jValue reported in Table 1 is the average obtained using $10^5 k$ (s⁻¹) values at 25.0°C of 3.48, 3.50, 3.55, and 3.56 from four independent runs. A value of 1.91×10^{-5} is reported in the literature [23]. ^kValue reported in Table 1 is the average obtained using $10^5 k$ (s⁻¹) values at 25.0°C of 1.09, 1.10, 1.13, and 1.14 from four independent runs. A value of 0.353×10^{-5} is reported in the literature [23]. ^lRefs. [9, 10]. ^mRefs. [5, 6].

Koo's claim [24, 33] of the presence of a through conjugation of the ring π system with the reaction center in phenyl chlorothionoformate (PhOCSCl) was invalidated [34] lately as no evidence was found requiring inclusion of the h parameter for ionization reactions with only one aromatic ring on the nitrogen of carbamoyl chlorides, or for the solvolyses of the chloroformate, or chlorothionoformate proceeding by an addition-elimination (association-dissociation) mechanism.

The 3-D views for cinnamoyl chloride (**3'**) and *p*-nitrocinnamoyl chloride (**5'**) are shown in Figure 3 incorporating prior results [35] for the position of the halogen in the ground-state structure of acid chlorides. The 3-D images of **3'** and **5'** clearly attest to the planar conformation between the aromatic ring, the vinylic double bond, and the carbonyl group. Studies have shown that when cinnamoyl-based structures were synthesized and characterized by a *syn*

disposition of the carbonyl group with the vinylic double bond, they specifically inhibited the enzymatic reactions associated with HIV-1 integrase (IN) [36].

The specific rate order reported [29] for the three *p*-substituted cinnamoyl chlorides is $k(\mathbf{3}) > k(\mathbf{4}) > k(\mathbf{5})$ in the pure and binary aqueous mixtures of EtOH, MeOH, and acetone, and a broader rate order of $k(\mathbf{3}) > k(\mathbf{4}) \gg k(\mathbf{5})$ is reported in the aqueous TFE and the TFE-EtOH mixtures. The substantial rate decrease (of over a factor of 100) from **3** to **5** in TFE, 97 TFE, and 90 TFE is attributed to the powerful inductive destabilizing ability of the *p*-nitro group when positive charge is developing at the reaction center, due to the coplanarity observed between the ring, the vinylic double bond, and the reaction center in the 3-D view of **5** (**5'** in Figure 3).

For a meaningful comparison of the application of (1)–(4) to the specific rates of solvolysis of **3**, **4**, and **5** [29], it is important that the comparisons are made in identical solvents. A close examination of the data presented in Table 4 shows that for the three substrates in 24 common solvents, applications of (1) and (3) (without the lN_T term) gave exceedingly poor correlation coefficients (R) and F -test values. This indicates that the correlations are very sensitive to solvent nucleophilicity, with a possibility for the further need of nucleophilic solvation [2, 17, 30, 31, 34, 37, 38] of the developing transition state.

For compound **3** in the 24 solvents studied, use of (2) gives rise to an l value of 0.19 ± 0.06 with a probability of 0.01 that the lN term is statistically insignificant; an m value of 0.49 ± 0.05 ; -0.12 ± 0.06 for c ; a correlation coefficient of 0.940 and an F -test of 80. On application of (4) to the 24 solvents studied for **3**, there is a slight improvement in the value of R to 0.956, $l = 0.31 \pm 0.07$, $m = 0.56 \pm 0.05$, $h = 0.48 \pm 0.19$ with a 0.02 probability that the hl term is statistically insignificant, $c = -0.12 \pm 0.06$, and a F -test value of 70. With compound **4**, use of (2) in the identical 24 solvents used in the calculations for **3**, yields $l = 0.33 \pm 0.05$, $m = 0.59 \pm 0.04$, $c = -0.04 \pm 0.06$, $R = 0.961$, and F -test = 128. Essentially no improvements are observed with the use of (4) (for **3**), where $l = 0.36 \pm 0.07$, $m = 0.60 \pm 0.05$, $h = 0.12 \pm 0.19$, $c = -0.04 \pm 0.06$, $R = 0.962$, and F -test = 83. Use of (2) or (4) does not improve the immense scatter seen in the Grunwald-Winstein plots with the use of (1) or (3) for **5**. Employing equation (2) for the same 24 solvents studied with **5** produces an l value of 0.55 ± 0.08 , $m = 0.51 \pm 0.06$, $c = 0.02 \pm 0.08$, $R = 0.894$, and F -test = 42. Application of (4) to the 24 solvents used with **5** shows no change in the scatter with $l = 0.63 \pm 0.11$, $m = 0.57 \pm 0.04$, $h = -0.08 \pm 0.29$, $c = -0.02 \pm 0.08$, $R = 0.961$, and F -test = 128.

There has been considerable discussion regarding the reactivity-selectivity trends in aqueous TFE and TFE-EtOH [39–41]. Additionally, for a number of substrates [2, 34, 42–48], there have been several instances where removal of the TFE-EtOH points has led to a considerable improvement of the goodness-of-fit parameters in Grunwald-Winstein linear free energy plots. Also presented in Table 4 are our correlation analysis results for **3**, **4**, and **5**, with the exclusion of the data points in TFE-EtOH. This was done in order to evaluate the phenomena of dispersion commonly seen

TABLE 2: Correlation of the specific rates of reaction of 1, at 25.0°C using equations (1)-(4).

Substrate	Sn^a	l^b	m^b	h^b	c^c	R^d	F^e	
1; 25.0°C	32 ^f		0.76 ± 0.03		-0.25 ± 0.08	0.975	571	
		0.09 ± 0.09 (0.29) ^g	0.79 ± 0.04		-0.21 ± 0.09	0.976	288	
			0.79 ± 0.03	0.47 ± 0.20 (0.03) ^g	-0.30 ± 0.08	0.979	331	
	31 ^h		0.33 ± 0.08	0.91 ± 0.04	0.97 ± 0.21	-0.20 ± 0.07	0.987	340
				0.79 ± 0.03		-0.33 ± 0.08	0.979	664
		0.09 ± 0.08 (0.26) ^g	0.82 ± 0.04		-0.29 ± 0.09	0.980	337	
	30 ⁱ			0.82 ± 0.03	0.49 ± 0.17	-0.38 ± 0.07	0.984	416
			0.33 ± 0.06	0.95 ± 0.03	1.00 ± 0.16	-0.29 ± 0.06	0.992	551
				0.73 ± 0.03		-0.15 ± 0.08	0.977	594
		0.06 ± 0.10 (0.53) ^g	0.74 ± 0.04		-0.13 ± 0.09	0.978	291	
				0.75 ± 0.03	0.37 ± 0.19 (0.07) ^g	-0.21 ± 0.08	0.980	327
		0.36 ± 0.11	0.90 ± 0.05	0.88 ± 0.23	-0.15 ± 0.07	0.986	295	

^aUsing data at 25.0°C from Table 1; N_T values from refs. [9, 10]; Y_{Cl} values from refs.[5, 6]; the 70-0% MeOH, 80-10% Acetone, 100TFE, 70TFE(w/w), 50TFE(w/w) values are from reference [23]; n is the number of solvents. ^bWith associated standard error. ^cAccompanied by standard error of the estimate. ^dCorrelation coefficient. ^e F -test value. ^fAll solvents. ^gProbability that the contribution to the linear free energy relationship is insignificant. ^hExcluding 100EtOH. ⁱIn exactly the same solvents as 2.

TABLE 3: Correlation of the specific rates of reaction of 2, at 25.0°C using equations (1)-(4).

Substrate	n^a	l^b	m^b	h^b	c^c	R^d	F^e	
2; 25.0°C	37 ^f		0.76 ± 0.03		-0.15 ± 0.08	0.973	616	
		0.14 ± 0.10 (0.17) ^g	0.79 ± 0.04		-0.11 ± 0.08	0.974	317	
			0.79 ± 0.04	0.33 ± 0.21 (0.12) ^g	-0.20 ± 0.08	0.975	323	
	36 ^h		0.51 ± 0.11	1.01 ± 0.05	1.13 ± 0.24	-0.13 ± 0.06	0.985	354
				0.78 ± 0.03		-0.20 ± 0.08	0.972	577
		0.13 ± 0.09 (0.17) ^g	0.81 ± 0.04		-0.16 ± 0.09	0.973	298	
	30 ⁱ			0.81 ± 0.03	0.37 ± 0.20 (0.08) ^g	-0.26 ± 0.08	0.974	311
			0.54 ± 0.10	1.05 ± 0.05	1.23 ± 0.21	-0.20 ± 0.06	0.987	403
				0.75 ± 0.04		-0.17 ± 0.09	0.970	440
		0.11 ± 0.11 (0.30) ^g	0.78 ± 0.05		-0.12 ± 0.10	0.971	222	
				0.78 ± 0.04	0.40 ± 0.23 (0.09) ^g	-0.23 ± 0.09	0.973	238
		0.49 ± 0.12	1.00 ± 0.06	1.14 ± 0.26	-0.15 ± 0.07	0.983	255	

^aUsing data at 25.0°C from [24]; N_T values from [9, 10]; Y_{Br} values from [6]; n is the number of solvents. ^bWith associated standard error. ^cAccompanied by standard error of the estimate. ^dCorrelation coefficient. ^e F -test value. ^fAll solvents. ^gProbability that the contribution to the linear free energy relationship is insignificant. ^hExcluding 100 EtOH. ⁱIn exactly the same solvents as 1.

for the TFE-EtOH solvents [39–41] and this observation is probably due to the bulky nature of this solvent (when compared to aqueous TFE) [43]. In the case of the solvolysis of 3, omission of the two TFE-EtOH solvents (22 solvents), and use of (2) yield $l = 0.17 \pm 0.06$ associated with a 0.01

probability of statistical insignificance, $m = 0.49 \pm 0.05$, $c = -0.10 \pm 0.06$, $R = 0.945$, and F -test = 80. There is considerable improvement of the goodness-of-fit parameters on application of (4) to the specific rates of solvolysis of 3 in 22 solvents. The significant improvement of $R = 0.982$, and

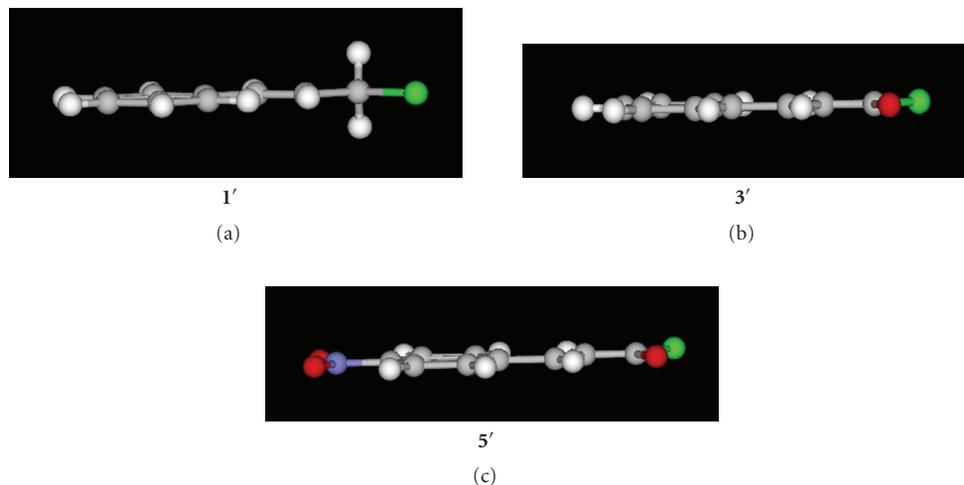


FIGURE 3: 3-D views of cinnamyl chloride ($1'$), cinnamoyl chloride ($3'$), and *p*-nitrocinnamoyl chloride ($5'$), computed using the KnowItAll platform.

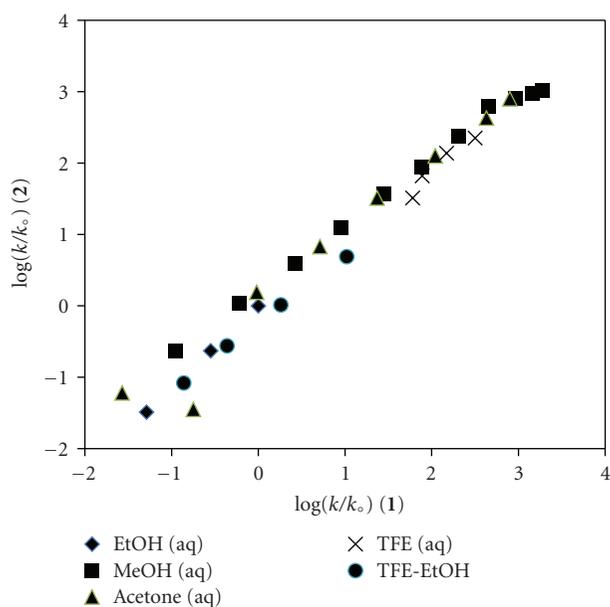


FIGURE 4: A plot of $\log(k/k_0)$ for cinnamyl bromide (2) against $\log(k/k_0)$ for cinnamyl chloride (1) in pure and binary solvents at 25°C. This plot has a correlation coefficient of 0.989, *F*-test value of 1201, slope of 0.99 ± 0.03 , and intercept of -0.02 ± 0.05 .

F-test = 163, suggests that there is a need for nucleophilic solvation of the developing resonance stabilized carbocation with $l = 0.37 \pm 0.05$, $m = 0.60 \pm 0.03$, $h = 0.89 \pm 0.15$, and $c = -0.08 \pm 0.04$. The similarities of the *l*, *m*, and *h* values (Tables 2 and 4) between cinnamyl (1) and cinnamoyl (3) chloride further suggest that the presence of a carbonyl oxygen has no major impact on either the amount of nucleophilic solvation needed to stabilize the developing carbocation or the amount of charge delocalized into the ring.

Analysis using (2) for the identical 22 solvents in solvolyses of 4 produces $l = 0.30 \pm 0.04$, $m = 0.58 \pm 0.03$, $c = -0.02 \pm 0.05$, $R = 0.975$, and *F*-test = 187. Use of (4) improves the correlation coefficient significantly to 0.987 and

the *F*-test is raised to 221. The values of $l = 0.43 \pm 0.04$, $m = 0.64 \pm 0.03$, $h = 0.53 \pm 0.14$, and $c = -0.01 \pm 0.04$, observed for 4 in the 22 solvents indicate a slightly higher need for nucleophilic solvation (when compared to 3) due to the destabilizing effect caused by the presence of a chlorine atom in the *para* position. This destabilization also impacts the amount of charge delocalization into the ring resulting in a lower *h* value. The destabilizing effect is amplified in 5 due to the existence of a more powerful inductive effect due to the presence of the electron-withdrawing nitro group at the *para* position. The efficiency of transmission of the destabilizing electronic effects in 5 is made possible due to the complete coplanarity (as shown in the 3-D image, 5') between the nitro group, the aromatic ring, the vinylic double bond, and the carbonyl group. At the other end of the spectrum, it was shown [49] that the observed specific rate order of $k_{p\text{-nitrophenyl chloroformate}} > k_{p\text{-nitrobenzyl chloroformate}}$ is due in part to the *p*-nitrobenzyl group twisting out of the plane with its ether oxygen and therefore being able to exert only a fraction of its inductive ability.

In the 22 solvents for the solvolyses of 5, application of (2) yield, $l = 0.61 \pm 0.06$, $m = 0.49 \pm 0.04$, $c = 0.07 \pm 0.06$, $R = 0.941$, and *F*-test = 73, and application of (4) leads to $l = 0.74 \pm 0.07$, $m = 0.56 \pm 0.04$, $h = 0.56 \pm 0.20$ (0.01 probability of statistical insignificance), $c = -0.08 \pm 0.05$, $R = 0.959$, and *F*-test = 68. Such large *l* values have been observed in the unimolecular solvolysis of other structurally diverse acid chlorides [2, 48] and are indicative of the need for appreciable solvation of the developing carbocation plus a more facile approach of the solvent to an initially sp^2 -carbon than to an initially sp^3 -carbon.

3. Conclusions

In the present study we demonstrate that dispersions observed in Grunwald-Winstein correlations of the unimolecular solvolyses of substrates containing an adjacent π -electrons can be very well corrected by addition of an *hI* term. For the cinnamyl and cinnamoyl halides studied,

TABLE 4: Correlation of the specific rates of reaction of 3, 4, and 5, at 25.0°C using equations (1)–(4).

Substrate	n^a	l^b	m^b	h^b	c^c	R^d	F^e
3; 25.0°C	24 ^f		0.39 ± 0.04		-0.17 ± 0.07	0.913	110
		0.19 ± 0.06 (0.01) ^g	0.49 ± 0.05		-0.12 ± 0.06	0.940	80
			0.40 ± 0.04	-0.05 ± 0.19 (0.80) ^g	-0.17 ± 0.07	0.913	53
		0.31 ± 0.07	0.56 ± 0.05	0.48 ± 0.19 (0.02) ^g	-0.12 ± 0.06	0.956	70
4; 25.0°C	24 ^f		0.41 ± 0.05		-0.14 ± 0.09	0.885	79
		0.33 ± 0.05	0.59 ± 0.04		-0.04 ± 0.06	0.961	128
			0.41 ± 0.04	-0.51 ± 0.21 (0.02) ^g	-0.09 ± 0.08	0.911	52
5; 25.0°C	24 ^f		0.18 ± 0.08		-0.16 ± 0.16	0.411	5
		0.55 ± 0.08	0.51 ± 0.06		0.02 ± 0.08	0.894	42
			0.17 ± 0.07 (0.02) ^g	-1.17 ± 0.34	-0.07 ± 0.13	0.683	9
3; 25.0°C	22 ^h		0.40 ± 0.04		-0.14 ± 0.07	0.922	114
		0.17 ± 0.06 (0.01) ^g	0.49 ± 0.05		-0.10 ± 0.06	0.945	80
			0.40 ± 0.04	0.14 ± 0.22 (0.53) ^g	-0.15 ± 0.07	0.924	56
4; 25.0°C	22 ^h	0.37 ± 0.05	0.60 ± 0.03	0.89 ± 0.15	-0.08 ± 0.04	0.982	163
		0.30 ± 0.04	0.42 ± 0.04		-0.09 ± 0.08	0.911	97
			0.58 ± 0.03		-0.02 ± 0.05	0.975	187
5; 25.0°C	22 ^h		0.41 ± 0.04	-0.34 ± 0.24 (0.17) ^g	-0.08 ± 0.08	0.920	52
		0.43 ± 0.04	0.64 ± 0.03	0.53 ± 0.14	-0.01 ± 0.04	0.987	221
		0.61 ± 0.06	0.18 ± 0.08		-0.07 ± 0.15	0.470	6
			0.49 ± 0.04		0.07 ± 0.06	0.941	73
5; 25.0°C	22 ^h		0.17 ± 0.07 (0.02) ^g	-0.91 ± 0.40	-0.05 ± 0.13	0.627	6
		0.73 ± 0.07	0.56 ± 0.04	0.56 ± 0.20 (0.01) ^g	0.08 ± 0.05	0.959	68

^{a-c,g}See footnotes in Table 1; ^fData from [29], no 40E, 40M values for 5; ^hNo T-E mixtures.

a stepwise ionization mechanism is proposed to be operating with the need for nucleophilic solvation of a resonance-stabilized carbocation. The h values of ~ 1.00 in cinnamyl chloride (1), cinnamyl bromide (2), and cinnamoyl chloride (3) are also consistent with one aromatic ring easily entering into conjugation with the developing resonance stabilized transition state. In cinnamoyl chlorides, electron withdrawing inductive effects (p -chloro and p -nitro substituents) decrease the charge delocalized into the ring (lower h value) and increase the need for nucleophilic solvation of the carbocation (higher l value).

4. Experimental Section

The cinnamyl chloride was purchased from the Sigma-Aldrich chemical company and was used as received. Solvents were purified and the kinetic runs carried out as described previously [42]. A substrate concentration of approximately 0.005 M in a variety of solvents was employed. The specific rates and associated standard deviations, as presented in Table 1, are obtained by averaging all of the values from, at least, duplicate runs. Multiple regression analyses were carried out using the Excel 2007 package from the Microsoft

Corporation, and the 3D-views presented in Figure 3 for three of the five molecules used in this study were computed using the KnowItAll Informatics System, ADME/Tox Edition, from Bio-Rad Laboratories, Philadelphia, PA.

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