

# Nucleophilic substitution reactions of cinnamoyl chlorides with anilines in acetonitrile and acetonitrile–methanol mixtures

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Kinetic studies on the solvolysis (in MeOH–MeCN mixtures) and aminolysis (with anilines in MeCN) of cinnamoyl chlorides have been carried out at 25.0 °C. The relatively large negative values of  $\rho_Y^+ = -0.9 \sim -1.5$  for the methanolysis are consistent with a dissociative  $S_N2$ -like mechanism. For the aminolysis, the  $\rho_Y$  values are positive ( $\rho_Y = 0.52 \sim 1.64$ ) and  $\rho_X$  values range from  $-1.68$  to  $-2.51$  in acetonitrile. The positive values of  $\beta_X = 0.6\text{--}0.9$  and  $\rho_{XY} = 0.88$  in acetonitrile, and isotope effect data suggest that the aminolysis proceeds by a stepwise mechanism with rate-limiting breakdown of the tetrahedral intermediate,  $T^\pm$ . It is noted that in the acyl-transfer reactions proceeding by rate-limiting departure of the leaving group from the tetrahedral intermediate the signs of both  $\rho_Y$  and  $\rho_{XY}$  are positive and the reactivity–selectivity principle (RSP) is valid in general.

## Introduction

Acyl-transfer reactions are believed to proceed either through a stepwise mechanism with a tetrahedral addition intermediate that has a significant lifetime,<sup>1</sup> or through a concerted, single step mechanism involving a tetrahedral transition state (TS) with no addition intermediate.<sup>2</sup>

For the solvolysis of acyl halides, a concerted displacement mechanism, which can be associative or dissociative in character, has often been proposed.<sup>3</sup> Recent mechanistic work on the solvolysis of acyl chlorides in alcohol–water mixtures indicated that the reactions proceed by competing mechanisms involving two broad channels:<sup>3,4</sup> electron donation by an aryl group favours a carbocation or an  $S_N2$ – $S_N1$  process whereas electron withdrawal favours a general base catalysed process having a lower sensitivity to changes in solvent ionizing power.

The aminolysis of acyl compounds is in general known to proceed by a stepwise mechanism in which a tetrahedral addition intermediate,  $T^\pm$ , is involved. The rate determining step can be either formation or breakdown of the intermediate. The aminolysis in aprotic solvents mostly involves rate-limiting decomposition of a zwitterionic tetrahedral intermediate,  $T^\pm$ .<sup>5–7</sup>

The aminolysis of substituted benzoyl halides has been extensively studied: Litvinenko and co-workers<sup>8</sup> reported on the reaction of benzoyl chlorides and bromides with anilines in organic solvents. Rogne<sup>9</sup> studied the reactions of benzoyl chlorides with anilines in water. Lee *et al.*,<sup>10a,11</sup> investigated the mechanism of the reactions of benzoyl fluorides and chlorides with anilines in methanol and acetonitrile. The results of all these works are reported to be consistent with a concerted displacement mechanism.

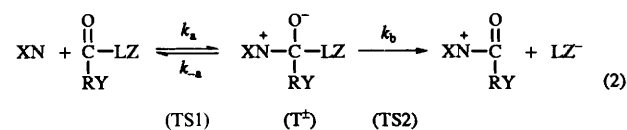
In contrast, Song and Jencks<sup>10b</sup> reported that the results of the reaction of benzoyl fluorides with primary amines in aqueous solution can be accommodated by an  $S_N2$ -like mechanism but a stepwise addition–elimination mechanism cannot be rigorously excluded. Satchell and co-workers<sup>5</sup> have studied the aminolysis of benzoyl fluorides in non-hydroxylic solvents and found different kinetic behaviour from that found for aqueous solutions. They interpreted their results in terms of a stepwise addition–elimination mechanism involving rate-limiting breakdown of a tetrahedral intermediate.

Structure–reactivity correlations have provided us with a very powerful tool for probing the structure of transition states (TSs). In recent years we have been developing the cross-interaction constants,<sup>12</sup>  $\rho_{ij}$  in eqn. (1) where  $i, j = X, Y$  or  $Z$ ,

$$\log(k_{ij}/k_{HH}) = \rho_i\sigma_i + \rho_j\sigma_j + \rho_{ij}\sigma_i\sigma_j \quad (1)$$

the substituent in the nucleophile, substrate or leaving group, respectively, as a mechanistic tool for organic reactions in solution.

For acyl-transfer reactions involving amine nucleophiles, the effects of substituents in the nucleophile (X), substrate (Y) and leaving group (Z) on rate are important in understanding the nature of the rate-determining step and the question of whether these reactions are concerted or proceed through stepwise pathways involving metastable tetrahedral intermediates,  $T^\pm$ , reaction (2). Another facet of the acyl-transfer reaction that is



still incompletely understood is the effect of the remaining group, RY in reaction (2), on the mechanism. It has been shown that an electron-withdrawing RY group promotes the expulsion of weakly basic groups in the intermediate;<sup>13</sup> for example, the expulsion of a weakly basic amine (XN) is favoured by an electron-withdrawing RY over the expulsion of a higher  $pK_a$  phenolate group (LZ) in  $T^\pm$ . This indicates that the transition state corresponding to the first step, TS1, becomes looser with a lower degree of bond-making ( $\rho_X$  becomes less negative,  $\Delta\rho_X > 0$ ) for a stronger electron-acceptor Y ( $\Delta\sigma_Y > 0$ ) leading to a positive  $\rho_{XY}$ .<sup>13j,14</sup>

$$\rho_{XY} = \frac{\partial^2 \log k_{XY}}{\partial \sigma_X \times \partial \sigma_Y} = \frac{\partial \rho_X}{\partial \sigma_Y} = \frac{(+)}{(+)} > 0$$

Thus, for the stepwise mechanism with rate-limiting breakdown,  $k_b$ , of the intermediate,  $T^\pm$ , the sign of the cross-interaction constant  $\rho_{XY}$  ( $> 0$ ) is opposite to that of the concerted mechanism for which the intermediate,  $T^\pm$ , is absent or very short lived and the reaction proceeds through an  $S_N2$ -like transition state with negative  $\rho_{XY}$  ( $< 0$ ).<sup>14</sup> The  $\rho_{XY}$  values for  $S_N2$  reactions are reported to be always negative.<sup>12,14a</sup> The sign of  $\rho_{XZ}$  for the former mechanism is always positive but can be either positive or negative for the latter.<sup>12,14a</sup> Although the electronic effect of the remaining group (RY) is claimed to be of an inductive nature,<sup>13e,15</sup> there are conflicting results as to the

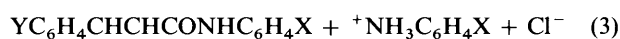
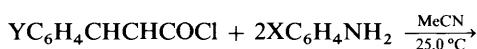
**Table 1** Pseudo-first-order rate constants,  $k_1/10^3 \text{ s}^{-1}$ , for the solvolyses of  $\text{YC}_6\text{H}_4\text{CHCHCOCl}$  in MeOH–MeCN mixtures at 25.0 °C

v/v% MeCN	$k_1/10^3 \text{ s}^{-1}$					$\rho_Y^{+a}$
	Y					
	<i>p</i> -Me	H	<i>p</i> -Cl	<i>p</i> -NO <sub>2</sub>		
100	174	63.7	37.3	21.9		-1.54
90	158	62.0	38.0	32.7		-1.49
80	137	53.3	34.2	26.3		-1.47
70	109	40.9	29.1	23.5		-1.35
50	59.7	24.8	17.0	14.4		-1.27
30	22.5	9.86	7.26	6.92		-1.15
10	3.06	1.65	1.28	1.21		-0.89

<sup>a</sup> Correlation coefficients are better than 0.992 in all cases.

nature of the electronic effects of the remaining group; thus, while the methoxy group (RY = MeO) behaved as an inductive electron-withdrawing substituent,<sup>16</sup> the effect of the ethoxy group (RY = EtO)† was interpreted as electron-donating.<sup>13h</sup>

In view of the importance of the remaining group (RY) in the mechanistic change-over from a concerted (for a strong electron donor RY) to a stepwise (for a strong electron acceptor RY) mechanism, we investigated the reactions of cinnamoyl chlorides with anilines in acetonitrile at 25.0 °C, reaction (3). We have also studied the methanolysis of cinnamoyl chlorides.



## Results and discussion

### Methanolysis

The pseudo-first-order rate constants,  $k_1/\text{s}^{-1}$ , for the methanolysis of substituted cinnamoyl chlorides in MeOH–MeCN mixtures at 25.0 °C are summarized in Table 1. The rates are seen to increase with the methanol content of the mixture and also with a more electron-donating (Y) substituent in the substrate. These trends indicate that the reaction proceeds with a TS in which bond cleavage is more advanced than bond making with positive charge development at the reaction centre carbonyl carbon, *i.e.* cinnamoyl chlorides solvolyse by a dissociative  $\text{S}_{\text{N}}2$  mechanism in MeOH–MeCN mixtures. The Hammett type plots with  $\sigma^+$  constants are curved for all solvent compositions; exclusion of Y = *p*-NO<sub>2</sub> however leads to good linear plots with the  $\rho_Y^+$  values (for three Y substituents, *p*-Me, H and *p*-Cl) ranging from -0.89 (10% MeOH) to -1.54 (100% MeOH) and correlation coefficients better than 0.992 in all cases. These  $\rho_Y^+$  values are of course not very reliable since only three points are used in the plots. Relatively large negative values of  $\rho_Y^+$  support the dissociative  $\text{S}_{\text{N}}2$  mechanism proposed. In view of the large negative values of  $\rho_Y^+$  for the reactions in methanol-rich media, an  $\text{S}_{\text{N}}1$ -like mechanism cannot be entirely excluded.<sup>3</sup> For Y = *p*-NO<sub>2</sub> the TS seems to become tighter and tends to react *via* a more associative type of  $\text{S}_{\text{N}}2$  mechanism, however the results could be due to a change of mechanism to addition–elimination, or possibly to a dual channel mechanism.<sup>4</sup> A comparison of the methanolysis rate

† The inductive and mesomeric substituent constants for the MeO group are  $\sigma_{\text{I}} = 0.27$  and  $\sigma_{\text{R}} = -0.43$  and the values for EtO group are  $\sigma_{\text{I}} = 0.26$  and  $\sigma_{\text{R}} = -0.44$ .<sup>17</sup>

**Table 2** Rate constants and kinetic solvent isotope effects for solvolyses of  $\text{YC}_6\text{H}_4\text{CHCHCOCl}$  in methanol at 25.0 °C

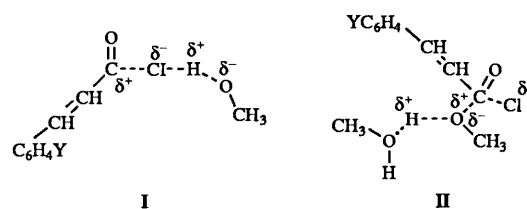
Y	$k_{\text{MeOH}}/10^2 \text{ s}^{-1}$	$k_{\text{MeOD}}/10^2 \text{ s}^{-1}$	$k_{\text{MeOH}}/k_{\text{MeOD}}$
<i>p</i> -Me	17.4 (± 0.2) <sup>a</sup>	14.0 (± 0.3)	1.24 ± 0.03 <sup>b</sup>
H	6.37 (± 0.05)	5.69 (± 0.02)	1.12 ± 0.01
<i>p</i> -Cl	3.73 (± 0.06)	3.45 (± 0.01)	1.08 ± 0.02
<i>p</i> -NO <sub>2</sub>	2.19 (± 0.02)	1.52 (± 0.04)	1.44 ± 0.04
$\rho_Y^{+c}$	-1.54	-1.40	$\Delta\rho_Y^+ = -0.14$

<sup>a</sup> Standard deviation. <sup>b</sup> Standard error<sup>14</sup> =  $1/k_{\text{D}} [(\Delta k_{\text{H}})^2 + (k_{\text{H}}/k_{\text{D}})^2 \times (\Delta k_{\text{D}})^2]$ . <sup>c</sup> Correlation coefficients are better than 0.990 in all cases.

constants at 25.0 °C shows that cinnamoyl ( $63.7 \times 10^{-3} \text{ s}^{-1}$ ) reacts much faster than benzoyl ( $4.33 \times 10^{-3} \text{ s}^{-1}$ )<sup>18</sup> chloride indicating that the cinnamyl group is acting as an electron donor; the  $\sigma_{\text{I}}$  value is smaller (0.07 *vs.* 0.11) but  $\sigma_{\text{R}}^{\ominus}$  is more negative for the cinnamyl group ( $\sigma_{\text{R}} = -0.15$  *vs.*  $-0.08$ ).<sup>17</sup>

We attempted the *mY* plots using  $Y_{1-\text{AdOTs}}$  values<sup>19</sup> for each Y substituent. Linearity of the plots is only fair ranging from  $r = 0.978$  to  $r = 0.992$  with decreasing slope, *m*, as the Y substituent becomes less electron-donating or more electron-withdrawing;  $m = 1.55, 1.44, 1.31$  and  $1.11$  for the substrates with Y = *p*-Me, H, *p*-Cl and *p*-NO<sub>2</sub>, respectively. The relatively large *m* values are again consistent with the dissociative type of mechanism proposed for the former three substituents.

Kinetic solvent isotope effects,  $k_{\text{MeOH}}/k_{\text{MeOD}}$ , determined for the methanolysis in pure methanol are collected in Table 2. It has been shown that the solvent isotope effect,  $k_{\text{SOH}}/k_{\text{SOD}}$ , is near unity (=1.1) for a dissociative type process whereas it is relatively large (=2.3) for a general-base catalysed solvolysis of acyl fluorides.<sup>3b</sup> Our results in Table 2 are in line with the dissociative mechanism for the three Y substituents, (Y = *p*-Me, H and *p*-Cl) and the increase in associative character for Y = *p*-NO<sub>2</sub> as Song and Jencks proposed.<sup>3b</sup> The values are smaller than those for the associative  $\text{S}_{\text{N}}2$  reactions of benzoyl chlorides with methanol at 25.0 °C ( $k_{\text{MeOH}}/k_{\text{MeOD}} = 1.19$ – $2.29$ ).<sup>18</sup> In the dissociative type of mechanism (for Y = *p*-Me, H, *p*-Cl) the electrophilic assistance of the methanol by hydrogen bonding to the cleaving chloride ion, **I**, will be important but in



the associative type for Y = *p*-NO<sub>2</sub> general base catalysis by the second methanol molecule, **II**, will become more important; thus, in both cases, the  $k_{\text{MeOH}}/k_{\text{MeOD}}$  value will be greater than unity but the values do not change in a continuous manner, *i.e.* there is a discontinuity between the values for variation in  $\sigma_Y$  for the two types of mechanism as can be seen in Table 2.

### Aminolysis

The rate follows the clean second-order kinetics given by eqn. (4) with  $k_1 = 0$  in acetonitrile. The  $k_2$  values were determined

$$k_{\text{obs}} = k_1 + k_2[\text{Nu}] \quad (4)$$

under pseudo first-order kinetic conditions using at least four nucleophile (aniline) concentrations up to *ca.* 100 times the substrate concentration. We found no third-order term at this range of [Nu]. The  $k_2$  values determined are summarized in

**Table 3** Second-order rate constants,  $k_2/\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$ , for the reactions between  $\text{YC}_6\text{H}_4\text{CHCHCOCl}$  and  $\text{XC}_6\text{H}_4\text{NH}_2$  in acetonitrile at 25.0 °C

X	$k_2/\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$				$\rho_Y^a$
	Y				
	<i>p</i> -Me	H	<i>p</i> -Cl	<i>p</i> -NO <sub>2</sub>	
H	10.0	13.3	16.8	32.1	0.52
<i>p</i> -Cl	2.94	4.23	5.70	16.9	0.79
<i>m</i> -Cl	1.03	1.47	2.72	9.54	1.03
<i>m</i> -NO <sub>2</sub>	0.133	0.249	0.458	2.74	1.37
<i>p</i> -NO <sub>2</sub>	0.006 84	0.0133	0.0251	0.250	1.64
$\rho_X^{-b}$	-2.51	-2.37	-2.24	-1.68	
$\beta_X^c$	0.88	0.83	0.78	0.59	

<sup>a</sup> Correlation coefficients are better than 0.994 in all cases. <sup>b</sup> Correlation coefficients are better than 0.990 in all cases. <sup>c</sup> Correlation coefficients are better than 0.994 in all cases. <sup>d</sup>  $\rho_{XY} = 0.88$ .

Table 3. Comparison of the  $k_2$  values in MeCN at 25.0 °C shows that cinnamoyl (13.3  $\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$ ) has a similar reactivity to benzoyl (14.0  $\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$ ) chloride.<sup>11</sup> This is in contrast to the greater reactivity found in the methanolysis and suggests that in the aminolysis the cinnamoyl chloride reacts by a different mechanism from that in the methanolysis.

In Table 3  $\rho_Y$ ,  $\rho_X^-$  and  $\beta_X$  values are also shown; for the Hammett plots with substituent changes in the nucleophile (X), only the  $\sigma^-$  value<sup>20</sup> gave good linearity ( $> 0.990$ ) with negative  $\rho_X^-$  values. The cross-interaction constant  $\rho_{XY}$  determined by subjecting the  $k_2$  values to multiple regression analysis using eqn. (1)<sup>12</sup> (with  $i, j = X, Y$ ) is positive and relatively large ( $\rho_{XY} = 0.88$ ). However, if a fall-off factor of *ca.* 2.5 is applied to account for the intervening ethylene group in between the reaction centre carbon and the ring,<sup>21</sup> then the  $\rho_{XY}$  value increases to *ca.* 2.2. The  $\beta_X$  ( $\beta_{\text{nuc}}$ ) values range from 0.59 to 0.88, which are large considering that the solvent is an aprotic one with a moderate relative permittivity ( $\epsilon$  37.5). The magnitude of  $\beta_X$  is similar ( $\beta_X = 0.4\text{--}0.7$ ) to those found for the reactions of phenyl benzoates with anilines in acetonitrile,<sup>14c</sup> for which the stepwise mechanism with rate-limiting breakdown of the tetrahedral intermediate,  $\text{T}^\pm$ , has been predicted. The observed  $\beta_X$  values are, however, not much different from those for the aminolysis of benzoyl fluorides in aqueous solution, for which a concerted mechanism is proposed.<sup>10b</sup>

The positive sign of  $\rho_{XY}$  as well as  $\rho_Y$  together with the relatively large magnitude of  $\beta_X$  (and  $\rho_{XY}$ )<sup>14</sup> supports a stepwise mechanism in which the rate determining step is breakdown of  $\text{T}^\pm$  [ $k_b$  in eqn. (2)] for the aminolysis of cinnamoyl chlorides. However, since any kinetic mechanistic criterion cannot be sufficient but provides only a necessary condition,<sup>6,22,23</sup> rate-limiting formation of  $\text{T}^\pm$  or concerted process cannot be vigorously precluded. There is an example of a concerted acyl transfer reaction in the literature corresponding to a positive  $\rho_{XY}$ .<sup>23</sup> We were unable to observe a break in the plots of  $\log k_2$  versus  $\text{p}K_a$ , at which the mechanistic change-over takes place from rate-limiting breakdown to formation of  $\text{T}^\pm$  as the basicity of the nucleophile is increased. Most probably the point lies beyond the range of  $\text{p}K_a$  used in this experiment due to the narrow range of  $\text{p}K_a$  for the aniline nucleophiles ( $\text{p}K_a = 1.00\text{--}4.60$ ). Unfortunately the use of the higher basicity aniline nucleophiles was limited due to much faster reaction rates.

For the mechanism proposed, the macroscopic rate constant,  $k_2$ , is a complex quantity. By applying a steady-state treatment to  $\text{T}^\pm$ , we arrive at eqn. (5) with an approximation of  $k_{-a} \gg k_b$ ,

$$k_2 = Kk_b, \text{ where } K = k_a/k_{-a} \quad (5)$$

The decrease in  $\beta_X$  (or similarly the decrease in  $-\rho_X^-$ ) with a more electron withdrawing group in the ring ( $\Delta\sigma_Y > 0$ ) can be rationalized as follows. Partial differentiation of  $k_2$  with respect to  $\text{p}K_a(\text{X})$  leads to eqn. (6).

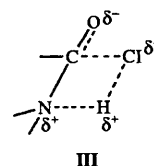
$$\frac{\partial \log k_2}{\partial \text{p}K_a(\text{X})} = \frac{\partial \log k_a}{\partial \text{p}K_a(\text{X})} - \frac{\partial \log k_{-a}}{\partial \text{p}K_a(\text{X})} + \frac{\partial \log k_b}{\partial \text{p}K_a(\text{X})} \quad (6)$$

Consideration of rate changes with respect to  $\text{p}K_a(\text{X})$  gives signs for each component term as shown in eqn. (7). This

$$\frac{\partial \log k_2}{\partial \text{p}K_a(\text{X})} = (+) - (-) + (+) \quad (7)$$

indicates that the observed  $\beta_X$  ( $\beta_{\text{nuc}}$ ) value should be large for the rate-limiting breakdown, as has been advocated as a mechanistic criterion,<sup>13,15,16</sup> since the three terms contribute additively even though the third term is likely to be small. If however, Y is an electron withdrawing group, then amine expulsion is favoured over leaving group ( $\text{Cl}^-$ ) expulsion and as a result  $k_b$  decreases much with little change in  $k_{-a}$ .<sup>13e,15c</sup> This will result in a decrease in the third term with little change in the second term in eqn. (6) leading to a lower value of  $\beta_X$  observed.

The relatively smaller positive values of  $\rho_Y$  in general observed for the stepwise mechanism with rate-limiting breakdown of the tetrahedral intermediate can be understood in a similar way as considered above for the large  $\beta_X$  observed.

**III**

In this case the terms corresponding to the first and third in eqn. (6) [or eqn. (7)] have different signs and partially cancel each other out thereby reducing the observed  $\rho_Y$  values. A similar argument predicts a large magnitude for  $\rho_Z$  and/or  $-\beta_Z$  ( $-\beta_{1g}$ ) as indeed observed experimentally.<sup>14c</sup> We note in Table 3 that faster rates are invariably accompanied by smaller selectivity parameters,  $\rho_X$  ( $\beta_X$ ) and  $\rho_Y$ , *i.e.* the reactivity-selectivity principle (RSP)<sup>24</sup> is valid.

Now we have to explain why the use of  $\sigma^-$  instead of  $\sigma$  for substituent Y gave a better Hammett plot. In this respect we must note that in this work the aniline nucleophiles used are all of the low basicity type and the solvent is aprotic with low polarity. Since charge dispersion in the TS is favourable for the reactions in a low polarity medium and the solvent cannot assist leaving group departure by hydrogen bonding in an aprotic solvent, the TS is likely to be of a form, III, in which one of the two hydrogen atoms on N helps chloride ion departure. As a proton shift occurs in the TS, a large negative charge accumulates on N which can be directly conjugated to the X substituent leading to a better representation of the electronic effect by  $\sigma^-$  rather than  $\sigma$ .

The  $k_2$  values in 10% MeOH-MeCN mixtures are given in Table 4. The rates are in general faster than those in MeCN, but the trends of changes in  $\rho_X^-$ ,  $\beta_X$ ,  $\rho_Y$  are the same as those in Table 1, except that the magnitudes are smaller. The lower selectivity parameters observed are again consistent with those expected from the RSP,<sup>24</sup> since the higher rates (in 10% MeOH-MeCN) are accompanied by the lower selectivities in Table 4. The faster rate should be a result of the help provided by the methanol for the leaving group departure, which will also lower

the susceptibility of N on the variation of  $\sigma_X$  as well as that of the carbonyl carbon on the variation of  $\sigma_Y$ . The smaller value of  $\rho_{XY}$ , however, predicts a lower degree of bond strength between the N and C $_{\alpha}$ <sup>14a</sup> in the mixed solvent. This could be due to weak hydrogen bonds available on N<sup>+</sup> and O<sup>-</sup> in T $^{\pm}$  from the methanol molecules.

Finally we have determined the kinetic isotope effects for deuteriated aniline nucleophiles (Table 5). The  $k_H/k_D$  values are all greater than unity and are in the range of values observed for the rate-limiting breakdown mechanism.<sup>6,14b,c</sup> Menger *et al.*,<sup>6</sup> reported  $k_H/k_D$  values of greater than one for the reaction of *p*-nitrophenyl acetate with amines deuteriated on the nitrogen. The only case where a  $k_H/k_D$  value of less than one observed was for the reaction with an added tertiary amine, triethylenediamine, which is known to catalyse the aminolysis of esters in aprotic solvents. For the aminolysis of *S*-phenyl dithiobenzoates in acetonitrile, which is believed to proceed by a stepwise mechanism with rate-limiting breakdown of T $^{\pm}$ , the  $k_H/k_D$  values with deuteriated anilines were all greater than one.<sup>14b</sup>

The magnitude of  $k_H/k_D$  tends to be greater with a more electron-donating Y substituent and a more electron-withdrawing X substituent. These types of trends are also observed in other similar reactions proceeding with a stepwise mechanism with rate-limiting breakdown of the tetrahedral intermediate.<sup>14b,c</sup>

For a one step, concerted acyl transfer reaction, an inverse  $\alpha$ -deuterium secondary kinetic isotope effect ( $k_H/k_D < 1.0$ ) is expected and experimentally observed.<sup>25,26</sup> Quite an interesting aspect of the  $k_H/k_D$  values shown in Table 5 is that here also the RSP is valid: a faster rate combination of X and Y shows a lower  $k_H/k_D$  (selectivity) value.

We conclude that the data for methanolysis of cinnamoyl chlorides suggests an S<sub>N</sub>2-like mechanism, while the aminolysis in acetonitrile is best accommodated by a stepwise mechanism in which departure of the leaving group is the rate determining step, although a mechanism involving rate-limiting nucleophilic

attack on the carbonyl carbon cannot be vigorously dismissed. We wish to point out that in nucleophilic reactions of carbonyl compounds proceeding by rate-limiting breakdown of a tetrahedral intermediate, the sign of  $\rho_Y$  and  $\rho_{XY}$  are positive and in general the RSP holds.<sup>24</sup>

## Experimental

### Materials

Acetonitrile and methanol were Merck HPLC grade. Deuteriated aniline was obtained as described previously,<sup>27</sup> and deuteriated methanol (CH<sub>3</sub>OD) was from Aldrich Chemical Company. The nucleophiles, aniline, were Aldrich G.R. grade, and were redistilled or recrystallized before use.<sup>10a</sup> The cinnamoyl chlorides were prepared by treating cinnamic acid with thionyl chloride in 60–70% yield. The spectral data for the compounds are given below.

**Cinnamic acid.**<sup>28a</sup> Mp 133–135 °C;  $\delta_H$ (250 MHz; CDCl<sub>3</sub>) 6.50 (CH, 1 H, d), 7.68 (CH, 1 H, d), 7.10–7.49 (C<sub>6</sub>H<sub>5</sub>, 5 H, m), 10.59 (OH, 1 H, s);  $\nu_{\max}$ (KBr)/cm<sup>-1</sup> 3200 (OH), 2900 (C–H aromatic), 1680 (C=O), 1620 (C=C).

***p*-Methylcinnamic acid.**<sup>28a</sup> Mp 196–198 °C;  $\delta_H$ (250 MHz; CDCl<sub>3</sub>) 2.35 (CH<sub>3</sub>, 3 H, s), 6.40 (CH, 1 H, d), 7.75 (CH, 1 H, d), 7.05–7.50 (C<sub>6</sub>H<sub>4</sub>, 4 H, m), 10.05 (OH, 1 H, s);  $\nu_{\max}$ (KBr)/cm<sup>-1</sup> 3300 (OH), 2900 (C–H aromatic), 1680 (C=O), 1620 (C=C).

***p*-Chlorocinnamic acid.**<sup>28a</sup> Mp 248–250 °C;  $\delta_H$ (250 MHz; CDCl<sub>3</sub>) 2.55 (OH, 1 H, s), 6.40 (CH, 1 H, d), 7.85 (CH, 1 H, d), 7.30–7.65 (C<sub>6</sub>H<sub>4</sub>, 4 H, m);  $\nu_{\max}$ (KBr)/cm<sup>-1</sup> 3300 (OH), 2900 (C–H aromatic), 1680 (C=O), 1620 (C=C).

***p*-Nitrocinnamic acid.**<sup>28a</sup> Mp 289 °C;  $\delta_H$ (250 MHz; CDCl<sub>3</sub>) 2.65 (OH, 1 H, s), 6.80 (CH, 1 H, d), 8.40 (CH, 1 H, d), 7.71–8.19 (C<sub>6</sub>H<sub>4</sub>, 4 H, m);  $\nu_{\max}$ (KBr)/cm<sup>-1</sup> 3300 (OH), 2900 (C–H aromatic), 1680 (C=O), 1620 (C=C).

**Cinnamoyl chloride.**<sup>28b</sup> Mp 35–37 °C, bp 121–122 °C/16 mmHg;  $\delta_H$ (250 MHz; CDCl<sub>3</sub>) 6.50 (CH, 1 H, d), 7.68 (CH, 1 H, d), 7.10–7.49 (C<sub>6</sub>H<sub>5</sub>, 5 H, m);  $\nu_{\max}$ (KBr)/cm<sup>-1</sup> 3000 (C–H aromatic), 1720 (C=O), 1670 (C=C), 800 (C–Cl); *m/z* 167 (M<sup>+</sup>).

***p*-Chlorocinnamoyl chloride.** Mp 72–74 °C, bp 134–136 °C/10 mmHg;  $\delta_H$ (250 MHz; CDCl<sub>3</sub>) 6.51 (CH, 1 H, d), 7.70 (CH, 1 H, d), 7.20–7.43 (C<sub>6</sub>H<sub>4</sub>, 4 H, m);  $\nu_{\max}$ (KBr)/cm<sup>-1</sup> 2900 (C–H aromatic), 1730 (C=O), 1600 (C=C), 700 (C–Cl) (Found: C, 54.4; H, 3.1. Calc. for C<sub>9</sub>H<sub>6</sub>Cl<sub>2</sub>O: C, 53.77; H, 3.01%); *m/z* 201 (M<sup>+</sup>).

***p*-Methylcinnamoyl chloride.** Mp 82–85 °C, bp 40–42 °C/10 mmHg;  $\delta_H$ (250 MHz; CDCl<sub>3</sub>) 2.45 (CH<sub>3</sub>, 3 H, s), 6.50 (CH, 1 H, d), 7.75 (CH, 1 H, d), 7.10–7.50 (C<sub>6</sub>H<sub>4</sub>, 4 H, m);  $\nu_{\max}$ (KBr)/cm<sup>-1</sup> 2800 (C–H aromatic), 1720 (C=O), 1590 (C=C), 700 (C–Cl) (Found: C, 66.0; H, 4.95. Calc. for C<sub>10</sub>H<sub>9</sub>ClO: C, 66.51; H, 5.01%); *m/z* 181 (M<sup>+</sup>).

***p*-Nitrocinnamoyl chloride.**<sup>28c</sup> Mp 148–151 °C, bp 42–44 °C/10 mmHg;  $\delta_H$ (250 MHz; CDCl<sub>3</sub>) 6.71 (CH, 1 H, d), 8.29 (CH, 1 H, d), 7.52–8.05 (C<sub>6</sub>H<sub>4</sub>, 4 H, m);  $\nu_{\max}$ (KBr)/cm<sup>-1</sup> 2800 (C–H aromatic), 1710 (C=O), 1600 (C=C), 600 (C–Cl); *m/z* 212 (M<sup>+</sup>).

**Table 4** Second-order rate constants,  $k_2/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ , for the reaction between YC<sub>6</sub>H<sub>4</sub>CHCHCOCl and XC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> in 10% MeOH–MeCN at 25.0 °C

X	$k_2/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$			$\rho_Y^a$
	Y			
	<i>p</i> -Me	H	<i>p</i> -Cl	
H	15.4	17.4	20.5	0.31
<i>p</i> -Cl	4.21	5.71	7.50	0.62
<i>m</i> -Cl	1.98	2.74	4.00	0.76
<i>m</i> -NO <sub>2</sub>	0.305	0.456	0.770	1.00
<i>p</i> -NO <sub>2</sub>	0.0118	0.0211	0.0420	1.37
$\rho_X^{-b}$	-2.45	-2.31	-2.13	
$\beta_X^c$	0.85	0.82	0.74	

<sup>a</sup> Correlation coefficients are better than 0.992 in all cases. <sup>b</sup> Correlation coefficients are better than 0.990 in all cases. <sup>c</sup> Correlation coefficients are better than 0.993 in all cases.

**Table 5** Kinetic isotope effects for the reactions of YC<sub>6</sub>H<sub>4</sub>CHCHCOCl with XC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>(D<sub>2</sub>) in acetonitrile at 25.0 °C

X	Y	$k_H/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	$k_D/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	$k_H/k_D$
H	<i>p</i> -Me	10.0 (±0.1) <sup>a</sup>	9.44 (±0.09)	1.06 ± 0.02 <sup>b</sup>
H	H	13.3 (±0.1)	12.9 (±0.1)	1.03 ± 0.01
H	<i>p</i> -Cl	16.8 (±0.3)	16.4 (±0.1)	1.02 ± 0.02
<i>m</i> -NO <sub>2</sub>	<i>p</i> -Me	13.3 (±0.1) × 10 <sup>-2</sup>	12.2 (±0.1) × 10 <sup>-2</sup>	1.09 ± 0.01
<i>m</i> -NO <sub>2</sub>	H	24.9 (±0.2) × 10 <sup>-2</sup>	23.1 (±0.1) × 10 <sup>-2</sup>	1.08 ± 0.01
<i>m</i> -NO <sub>2</sub>	<i>p</i> -Cl	45.8 (±0.5) × 10 <sup>-2</sup>	42.8 (±0.4) × 10 <sup>-2</sup>	1.07 ± 0.02

<sup>a</sup> Standard deviation. <sup>b</sup> Standard error<sup>14</sup> =  $1/k_D [(\Delta k_H)^2 + (k_H/k_D)^2 \times (\Delta k_D)^2]^{\frac{1}{2}}$ .

**Kinetic procedure**

Rates were measured conductimetrically at  $25.0 \pm 0.05$  °C in acetonitrile and acetonitrile–methanol mixtures. The  $k_2$  values were obtained as reported previously under pseudo-first-order conditions<sup>14b,c</sup> with [cinnamoyl chloride]  $\approx 10^{-4}$  mol dm<sup>-3</sup> and [aniline]  $\geq 10^{-2}$  mol dm<sup>-3</sup>. The  $k_2$  values were reproducible to within  $\pm 3\%$ .

**Product analysis**

Products formed in the aminolysis were obtained under the same reaction conditions as for the kinetic measurements with product yields of 90%. The spectral data are given below.

***N*-Phenylcinnamamide.**  $\delta_{\text{H}}$ (250 MHz; CDCl<sub>3</sub>) 6.50 (CH, 1 H, d), 7.78 (CH, 1 H, d), 7.15–7.70 (C<sub>6</sub>H<sub>5</sub>, 10 H, m), 10.20 (NH, 1 H, s);  $\nu_{\text{max}}$ (KBr), 3300 (NH), 2900 (C–H aromatic), 1710 (C=O), 1660 (C=C).

***p*-Methyl-*N*-phenylcinnamamide.**  $\delta_{\text{H}}$ (250 MHz; CDCl<sub>3</sub>) 2.45 (CH<sub>3</sub>, 3 H, s), 6.49 (CH, 1 H, d), 7.70 (CH, 1 H, d), 7.05–7.60 (C<sub>6</sub>H<sub>5</sub>, C<sub>6</sub>H<sub>4</sub>, 9 H, m), 9.92 (NH, 1 H, s);  $\nu_{\text{max}}$ (KBr)/cm<sup>-1</sup> 3400 (NH), 2900 (C–H aromatic), 1710 (C=O), 1680 (C=C).

***p*-Chloro-*N*-phenylcinnamamide.**  $\delta_{\text{H}}$ (250 MHz; CDCl<sub>3</sub>) 6.44 (CH, 1 H, d), 7.76 (CH, 1 H, d), 6.90–7.56 (C<sub>6</sub>H<sub>5</sub>, C<sub>6</sub>H<sub>4</sub>, 9 H, m), 10.13 (NH, 1 H, s);  $\nu_{\text{max}}$ (KBr) 3200 (NH), 2850 (C–H aromatic), 1680 (C=O), 1650 (C=C).

***p*-Nitro-*N*-phenylcinnamamide.**  $\delta_{\text{H}}$ (250 MHz; CDCl<sub>3</sub>) 6.70 (CH, 1 H, d), 8.15 (CH, 1 H, d), 7.50–8.05 (C<sub>6</sub>H<sub>5</sub>, C<sub>6</sub>H<sub>4</sub>, 9 H, m), 10.44 (NH, 1 H, s);  $\nu_{\text{max}}$ (KBr)/cm<sup>-1</sup> 3200 (NH), 2900 (C–H aromatic), 1685 (C=O), 1660 (C=C).

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