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Kinetics and Mechanism of the Pyridinolysis of Phenyl Chloroformates in Acetonitrile

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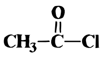
Kinetic studies on the reactions of Y-phenyl chloroformates with X-pyridines in acetonitrile are carried out at 25.0 °C. Both the Hammett and Brönsted plots are linear with enhanced substituent constants, σ_p^-, and basicities, pK_a^-, for strong para π-acceptor X-substituents, *p*-CN and *p*-CH_3CO. This indicates that the electron-rich formate (O−C−O) moiety overlaps with the pyridine ring π-system enabling, through conjugation with the para π-acceptors, the rate-limiting formation of a tetrahedral intermediate. The difference in the aminolysis mechanism between methyl, **II**, and phenyl chloroformate, **III**, is attributed to the much stronger electron-donating polarizability effect of C_6H_5 than of CH_3. The proposed mechanism is supported by a relatively small β_X ($\cong$0.3) and by the lower $\Delta H^\ddagger$ (6.7 kcal mol^{-1}) and $\Delta S^\ddagger$ (−44 eu) values for a stronger donor Y (Y = *p*-CH_3O) coupled with a stronger para π-acceptor (X = *p*-CN) in pyridine.

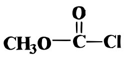
Introduction

The aminolysis rates of carbonyl compounds with good leaving groups usually exhibit a biphasic dependence on amine basicity. The Brönsted plots for these nucleophilic reactions show a change in slope from a large ($\beta_{nuc} \cong 0.8-1.0$) to a small ($\beta_{nuc} \cong 0.1-0.3$) value, which can be attributed to a change in the rate-determining step from breakdown to formation of a tetrahedral intermediate in the reaction path as the basicity of the amine nucleophile increases.[1] For acetyl chloride,[1g] **I**, and methyl chloroformate,[1d] **II**, such a change in the slope of the Bronsted plots were found to occur at relatively low amine basicity, p$K_a \cong 3.6$, in aqueous solution. In contrast, however, structurally similar phenyl chloroformate,[2] **III**, was found to react with aniline nucleophiles in acetonitrile by rate-limiting attack in the formation of a tetrahedral intermediate or by an associative S_N2 process. Since the aniline nucleophiles used there have a relatively narrow range of low basicity (five anilines of pK_a ranging from 4.60 to 1.00 in water at 20 °C), the evidence presented was considered not very convincing to decide whether the mechanism is stepwise (formation of a tetrahedral intermediate) or concerted (S_N2).



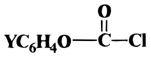
$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-Cl$

I



$CH_3O-\overset{\overset{\displaystyle O}{\|}}{C}-Cl$

II



$YC_6H_4O-\overset{\overset{\displaystyle O}{\|}}{C}-Cl$

III

In this paper, we report the kinetics of reaction of substituted pyridines with phenyl chloroformates, **III**, in acetonitrile at 25.0 °C, eq 1. The object of this work is to investigate the mechanism more closely, (i) confirm our previously proposed mechanism of the rate-limiting attack, and (ii) predict which of the two possibilities, a stepwise reaction with rate-limiting formation of a tetrahedral intermediate or a concerted process, are more likely. We chose 12 pyridines for this purpose including two strong π-acceptors, *p*-CH_3CO and *p*-CN. It turned out that these two pyridines with strong π-acceptors are crucial to substantiate the transition-state structure in the rate-limiting formation of the tetrahedral intermediate.

$$XC_5H_4N + YC_6H_4OCOCl \xrightarrow[25.0\ ^\circ C]{MeCN} XC_5H_4N^+OCOC_6H_4Y + Cl^- \qquad (1)$$

X = p-CH_3, m-CH_3, p-$CH_2C_6H_5$, m-$CH_2C_6H_5$, H, m-C_6H_5, m-$CONH_2$, m-CH_3CO, m-Cl, m-CH_3COO, m-CN or p-CN

Y = p-CH_3O, p-CH_3, H, p-Cl or p-NO_2

Results

The pseudo-first-order rate constants observed (k_{obs}) for all the reactions obeyed eq 2 with negligible k_o (= 0) in acetonitrile. The second-order rate constants, k_2/dm^3 mol^{-1} s^{-1}, summarized in Table 1, were determined using eq 2 with at least five pyridine concentrations, [Py]. No third-order or higher-order terms were detected, and no complications were found in the determination of k_{obs} and also in the linear plots of eq 2. This suggests that there is no base-catalysis or noticeable side reactions, and the overall reaction follows the route given by eq 1. The Hammett ρ_X (ρ_{nuc}) and ρ_Y, (Figures 1 and 2), and the Brönsted β_X (β_{nuc}) values (Figure 3), are also shown in Table 1. For the two strong π-acceptors, *p*-CH_3CO and *p*-CN, enhanced substituent constants, σ_p^-, and basici-

$$k_{obs} = k_o + k_2[Py] \qquad (2)$$

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Table 1. Rate Constants, k_2 (M^{-1} s^{-1}), for the Reactions of Y-Phenyl Chloroformates with X-Pyridines in Acetonitrile at 25.0 °C

X or Y	pK_a[a]	p-CH_3O	p-CH_3	H	p-Cl	p-NO_2	ρ_Y[g]
p-CH_3	6.03	11.5	17.4	19.1	39.8	–	0.98 ± 0.04
m-CH_3	5.67	6.76	10.7	15.1	28.2	–	1.02 ± 0.05
p-$C_6H_5CH_2$	5.59	6.76	11.0	15.5	26.9	–	1.01 ± 0.04
m-$C_6H_5CH_2$	(5.62)[c]	6.46	10.2	15.1	26.3	–	1.01 ± 0.05
H	5.21	5.50	5.90	9.55	18.2	58.9	1.03 ± 0.05
m-C_6H_5	(4.87)[c]	2.63	4.37	6.03	12.9	43.7	1.17 ± 0.03
m-$CONH_2$	3.33[b]	1.09	1.78	2.51	5.13	20.0	1.18 ± 0.03
m-CH_3CO	(3.10)[c]	0.603	0.991	1.66	3.02	11.5	1.19 ± 0.05
m-Cl	2.81	0.589	0.989	1.58	2.82	10.7	1.16 ± 0.05
m-$CH_3C(O)O$	3.26[b]	0.575	0.871	1.55	2.69	10.2	1.18 ± 0.07
m-CN	1.35	0.159	0.263	0.339	1.01	3.89	1.33 ± 0.04
p-CH_3CO	(0.46)[d] 2.83	0.0575	0.0832	0.141	0.263	1.66	1.39 ± 0.03
p-CN	(−0.57)[d] 1.86	0.0201	0.0309	0.0537	0.0977	0.548	1.39 ± 0.03
ρ_X^- [e]		−2.35 ± 0.05 (0.996)	−2.28 ± 0.06 (0.996)	−2.25 ± 0.06 (0.996)	−2.23 ± 0.03 (0.999)	−2.50 ± 0.21 (0.976)	
β_X^- [f]		0.33 ± 0.01 (0.996)	0.33 ± 0.01 (0.995)	0.31 ± 0.01 (0.997)	0.31 ± 0.01 (0.994)	0.28 ± 0.02 (0.991)	

[a] pK_a values in water at 25.0 °C taken from ref 3. [b] Taken from Dean, J. A. *Handbook of Organic Chemistry*; McGraw-Hill: New York, 1987; Table 8. [c] Calculated values using eq 3. [d] Calculated values with σ_p^- constants. [e] The σ and σ_p^- values were taken from Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165. Correlation coefficients are shown in parenthesis. [f] Based on the pK_a values in acetonitrile at 25.0 °C calculated by eq 4. [g] The source of σ is the same as in e. Correlation coefficients are better than 0.990 in all cases.

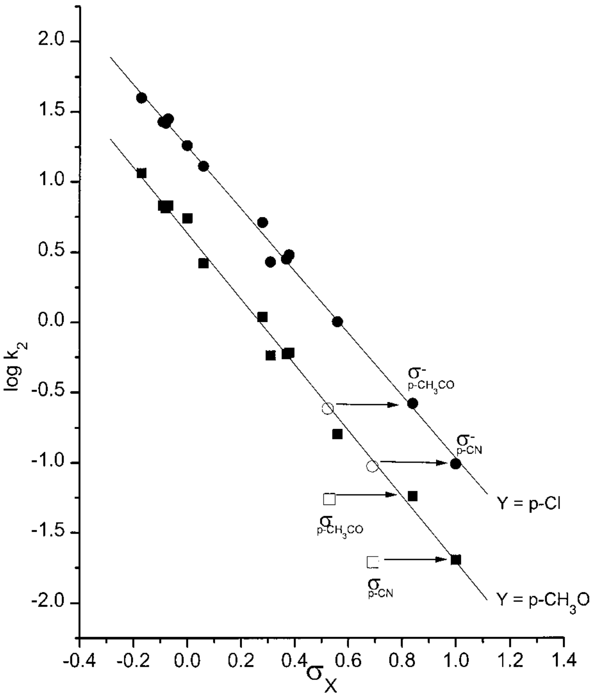

Figure 1. The Hammett plots (ρ_X^-) for the pyridinolysis of phenyl chloroformates (for Y = p-CH_3O and Y = p-Cl) in MeCN at 25.0 °C.

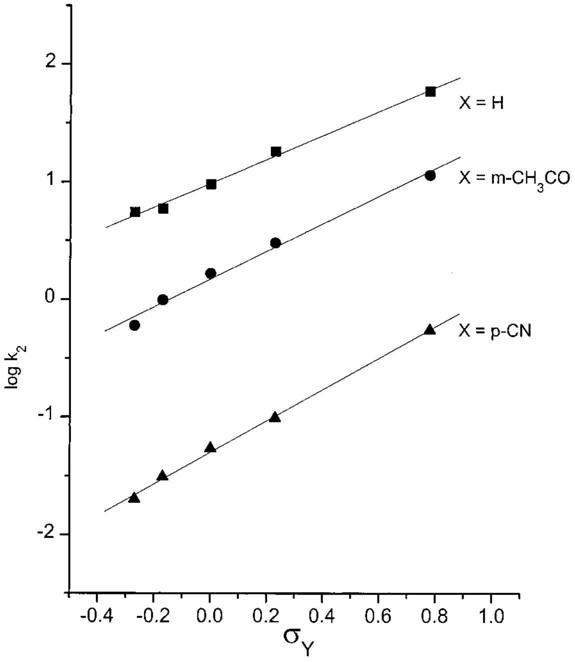

Figure 2. The Hammett plots (σ_Y) for the X-pyridinolysis of phenyl chloroformates (for X = H, m-CH_3CO and p-CN) in MeCN at 25.0 °C.

ties, pK_a^- (*vide infra*), were required for the linear plots, indicating operation of through-conjugation between the reaction site, the N atom of pyridine, and the strong π-acceptor substituents. The pK_a^- values for p-CH_3CO (σ_p^- = 0.82, pK_a^- = 0.46) and p-CN (σ_p^- = 1.00, pK_a^- = −0.57) were determined by extrapolation using σ_p^- values in eq 3, which was obtained with 30 pK_a values in water at 25 °C.[3]

$$\mathrm{p}K_a = -5.73(\pm 0.12)\sigma + 5.16(\pm 0.05) \qquad r = 0.994,\ n = 30 \tag{3}$$

Similar correlations between pK_a and σ were reported by Charton[4] (slope, intercept: −5.70, 5.39), Clark and Perrin[5] (−5.90, −5.25), and Leffek[6a] (−5.24, 5.34). These pK_a values for pyridinium ions in water can be converted to those in acetonitrile using a relationship given by eq 4.[6] The β_X values shown in Table 1 are those based on pK_a's in acetonitrile.

$$\mathrm{p}K_{a(\mathrm{acetonitrile})} = (1.23 \pm 0.03)\mathrm{p}K_{a(\mathrm{water})} + (6.2 \pm 0.2) \tag{4}$$

The activation parameters, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ (Table 2), were determined based on the k_2 values at three tem-

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(3) The 30 pK_a values used to derive this correlation were taken from Fisher, A.; Galloway, W. J.; Vaughan, J. *J. Chem. Soc.* **1964**, 3591.

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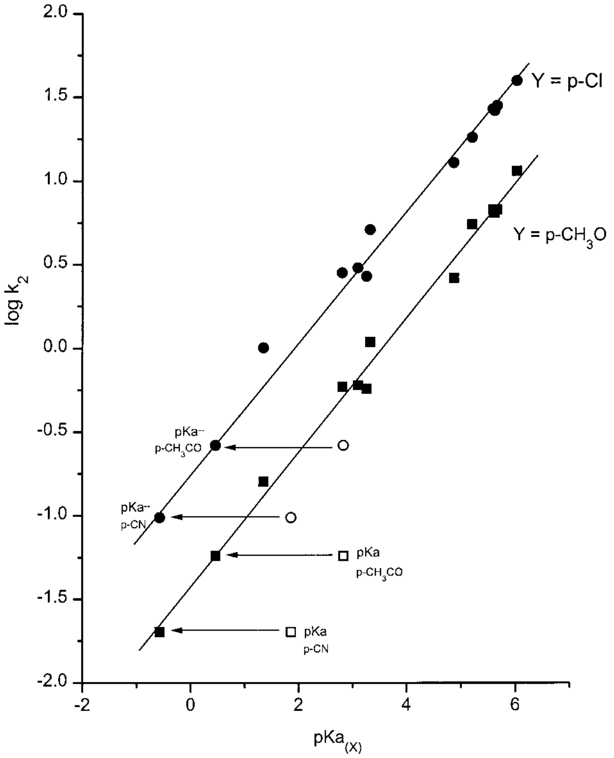


Figure 3. Brönsted plots (β_X) for the pyridinolysis of phenyl chloroformates (for Y = *p*-CH_3O and *p*-Cl) in MeCN at 25.0 °C.

Table 2. Activation Parameters[a] for the Reactions of Y-Phenyl Chloroformates with X-Pyridines in Acetonitrile

X	Y	T/°C	k_2 (M^{-1} s^{-1})	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$-\Delta S^{\ddagger}$ (cal mol^{-1} K^{-1})
p-CH_3	*p*-CH_3O	5.0	4.55	7.1 ± 0.1	30 ± 1
		15.0	7.23		
		25.0	11.5		
p-CN	*p*-CH_3O	5.0	0.00837	6.7 ± 0.1	44 ± 2
		15.0	0.0130		
		25.0	0.0201		
H	*p*-CH_3O	5.0	2.23	6.9 ± 0.1	32 ± 1
		15.0	3.50		
		25.0	5.50		
H	*p*-NO_2	5.0	23.0	7.2 ± 0.1	26 ± 1
		15.0	36.8		
		25.0	58.9		

[a] Calculated by the Eyring equation. Errors shown are standard deviations.

peratures, 5.0, 15.0, and 25.0 °C. These are comparable to those corresponding values for the reactions of phenyl chloroformate with anilines in acetonitrile.[2] The second-order rate constants, k_2, for the pyridinolysis of methyl chloroformate in acetonitrile at 25.0 °C are summarized in Table 3.

Table 3. Rate Constants, k_2 (x10^3 M^{-1} s^{-1}), for the Reactions of Methyl Chloroformate with X-Pyridines in Acetonitrile at 25.0 °C

X	*p*-CH_3O[a]	*p*-CH_3	m-CH_3	H	m-$CONH_2$	m-Cl	*p*-CN	m-CN
k_2	309	280	244	158	31.5	11.8	2.67	1.23

[a] The pK_a value in water at 25.0 °C for X = *p*-CH_3O in 6.58.[3]

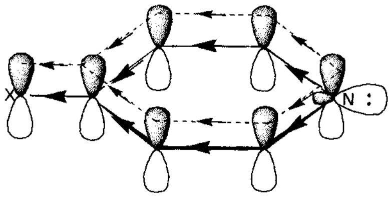
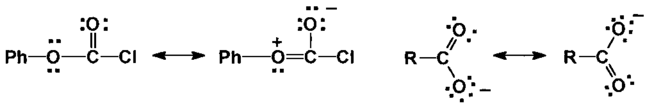


Figure 4. Lone pair and π-orbitals in pyridine with a π-acceptor para substituent, X.

Discussion

Comparison of k_2 under the same reaction conditions, in MeCN at 25.0 °C, shows that the two nucleophiles, aniline[2] (pK_a = 4.60, k_2 = 6.37) and pyridine (pK_a = 5.17, k_2 = 9.55 dm^3 mol^{-1} s^{-1}) react with phenyl chloroformate at approximately the same rate. This rate is, however, lower (ca. $^1/_2$) than those for the corresponding reactions of benzoyl[7] and cinnamoyl chlorides.[8] Although there is no directly comparable rate data available for the reaction of acetyl chloride,[1g] **I**, the rate of phenyl chloroformate, **III**, is much lower than that of **I**. This lower rate is attributed to initial-state stabilization by π-electron resonance **IVa**, which is smaller than that of carboxylate anion, **IVb**,[9] due to charge separation. The negative charge delocalization over the two oxygen atoms forms nevertheless a π-electron-rich O−C−O moiety in **IVa** as well as in **IVb**.



IVa **IVb**

The magnitudes of ρ_X^- (−2.23− −2.50) and ρ_Y (0.98−1.39) for the reactions with pyridines are quite similar again with those corresponding reactions with anilines (ρ_X^- = −2.21− −2.30, ρ_Y = 1.16−1.26).[2] For the strong π-acceptor para substituents, *p*-NO_2 in aniline[2] and *p*-CH_3CO and *p*-CN in pyridine, the enhanced para substituent constants of σ_p^- are required for linear correlations, Figure 1. This suggests that the π-acceptor para substituents interact directly through the ring π-system with the reaction site, the N atom on the pyridine, in the rate-determining step. This state of affairs is, however, rather surprising in view of the fact that the σ-lone pair on N is orthogonal to the ring π-system, Figure 4; the reaction, no doubt, takes place with the σ-lone pair while the interaction with the π-acceptor para substituent occurs through the ring π-system, and the two are orthogonal so that the two, reaction site (σ-lone pair) and ring π-system, are completely independent and do not mix together. In this respect, the linear correlation with σ_p^- for *p*-NO_2 in aniline is quite normal.[2] In aniline the reaction site is again the lone pair on the amino nitrogen, which is, however, nearly a π-type, Figure 5. The nucleophilic reaction takes place at the lone-pair on N which, unlike the σ-lone pair on the N atom of pyridine, can interact directly through the ring π-system with a π-acceptor para substituent.

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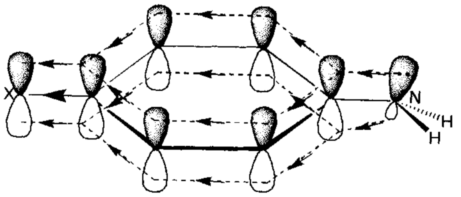

Figure 5. Lone pair and π-orbitals in aniline with a π-acceptor para substituent, X.

The similiarity and difference between the role of the lone pair on N in the nucleophilic reactions of aniline and that of pyridine are quite intriguing and in fact provide a useful mechanistic criterion. Although the linear Hammett plots for the aminolysis of phenyl chloroformate in acetonitrile required the enhanced constants, σ_p^-, for the π-acceptor para substituents in both aniline (p-NO_2)[2] and pyridine nucleophiles (p-CH_3CO and p-CN), the Brönsted plots using the experimental pK_a values (pK_a for p-NO_2 = 1.00) were linear for anilines but were nonlinear for pyridines (e.g., pK_a value for p-CN = 1.86 in H_2O at 25 °C) and required enhanced pK_a values (an extrapolated pK_a of −0.57 for p-CN) corresponding to σ_p^- (say pK_a^-) to obtain linear correlations. Rationalization of this dichotomy is as follows.

The protonation/deprotonation of aniline in water involves the lone pair on the amino nitrogen, which can overlap with the ring π-system, i.e., the lone pair on N in aniline is practically a π-lone pair, Figure 5. Thus a strong π-electron acceptor para substituent can interact directly through the ring π-system with the lone pair in aniline. For such substituents, the Hammett correlation requires σ_p^- constants. On the other hand, the pK_a values of anilines represent protonation/deprotonation at the lone-pair so that the experimentally determined pK_a values correspond to basicities under through-conjugative condition, e.g., for p-NO_2 in aniline, $\sigma^- = 1.24$ and pK_a = 1.00 in water at 25 °C represent the same substituent effect.

In contrast for pyridine, the protonation/deprotonation takes place at the σ lone pair on N which is orthogonal to the ring π-system (Figure 4) so that the protonation/deprotonation (pK_a measurement) does not disturb the ring π-system, but the positive charge center in the conjugate acid, of course, attracts π-electrons inductively and there is no through-conjugation between the σ-lone pair and the π-acceptor para substituent. Thus the experimental pK_a value represents the inductive effect only and corresponds to the basicity of the normal σ constant (for p-NO_2, $\sigma_p = 0.78$), not σ_p^- (for p-NO_2, $\sigma_p^- = 1.24$). This is evident from a comparison of the effects of a substituent in meta and para positions on the pyridine basicities. Normally a stronger inductive acceptor ($\delta\sigma > 0$), meta substituent, leads to a weaker basicity ($\delta pK_a < 0$) than does a weaker inductive acceptor, para substituent, as expected from a consideration of inductive electron depletion of the N atom of pyridine. Thus the pK_a and σ are inversely correlated, $\delta pK_a/\delta\sigma = (pK_a(\text{meta}) - pK_a(\text{para}))/\sigma_m - \sigma_p) < 0$. However, for substituents which have strong para π-acceptor ability, e.g., CN, NO_2, etc., the sign reverses to $\delta pK_a/\delta\sigma > 0$. For example, the ratios for substituents CH_3, CH_3O, Br, and Cl are ca. −4, −5, −6, and −7[3] respectively, whereas for NO_2 and CN they are ca. +3 and +5,[3] respectively. This simply shows that the experimental values of pyridine reflect the weak π-electron-donating effects under a cationic charge on N in the pK_a measurements so that the para π-acceptors exhibit abnormally higher pK_a values in contrast to the substituent constants, σ_p, which represent the inductive and π-electron-withdrawing effects only.

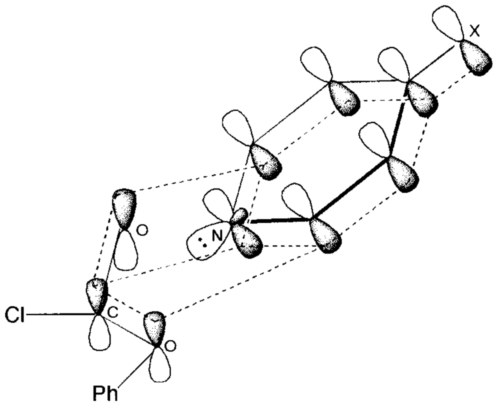

Figure 6. The proposed transition-state structure.

However, whenever an anionic center or an electron-rich moiety, such as **IVa** and **IVb**, overlaps with the π-orbital on the N atom of pyridine and hence with the ring π-system, through-conjugation with the π-acceptor para substituent becomes viable and an elevated para constant, σ_p^-, is required to correlate the effect of the anionic center as evidenced by the Hammett plots, Figure 1. This causes, however, a nonlinear Brönsted plot if the experimentally determined pK_a value is used to correlate the effect. In such cases an elevated pK_a value (pK_a^-) corresponding to σ_p^- is required. Experimental determination of such an elevated basicity, pK_a^-, is, however, impossible, since experimentally protonation/deprotonation (pK_a measurement) involves a σ lone pair on the pyridine nitrogen atom which is orthogonal to the ring π-system. A linear correlation between the pK_a and σ_m, eq 3, can be used to extrapolate the pK_a^- value corresponding to the σ_p^- value. For example, p-CN has $\sigma_p = 0.66$ and $\sigma_p^- = 1.00$ so that substitution of $\sigma_p^- = 1.00$ into eq 3 leads to pK_a^- = −0.57, which is much more negative than the experimentally determined pK_a = 1.86 corresponding to σ_p (= 0.66).

The Brönsted plots in Figure 3 clearly show that the two strong π-acceptor para substituents require enhanced basicities (pK_a^- values) which give excellent linear correlations (correlation coefficients > 0.992; standard deviations of the slopes < 0.03). The β_X (β_{nuc}) values in Table 1 range from 0.28 to 0.33, which agree with the similar range of values for the aminolysis of acyl compounds when nucleophilic attack is rate limiting.[1] The linear correlation over the whole range of pK_a values (pK_a = −0.45−+6.03) with low β_X ($\cong$0.3) and and the requirement of the pK_a^- values for the strong π-acceptor para substituents in the Brönsted plots strongly support that the aminolysis (with pyridines as well as with anilines) of phenyl chloroformates in acetonitrile at 25.0 °C proceeds by a rate-limiting attack of the nucleophile.

The transition state (TS) structure can be envisaged as shown in Figure 6, where the through-conjugative π-overlap is explicitly shown. A similar TS structure can be constructed for the reactions with anilines. The requirement of pK_a^-, i.e., the possibility of through-conjugation between N and π-acceptors, in the linear Brönsted plots for the reactions of phenyl chloroformate with pyridines (and also with anilines) rules out a

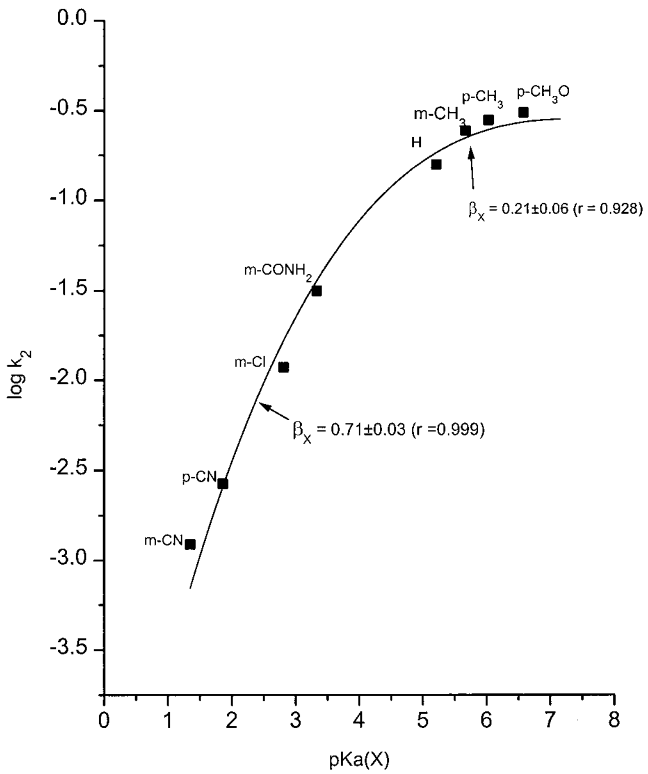

Figure 7. Bronsted plot (β_X) for the pyridinolysis of methyl chloroformate in MeCN at 25.0 °C.

stepwise mechanism with rate-limiting breakdown of a tetrahedral intermediate; in the tetrahedral intermediate, and/or in the TS for rate-limiting expulsion of the leaving group, Cl^-, the π-orbital in the formate moiety is orthogonal to, and hence cannot overlap with, the ring π-system, precluding the possibility of through-conjugation. If the reactions were proceeding by rate-limiting breakdown of the intermediate, the normal pK_a values for *p*-CN ($pK_a = 1.86$) would have been required in a more steeper linear Brönsted plot ($\beta_X \cong 0.8-0.9$), as has been reported for the pyridinolysis of methyl chloroformate in water.[1d,g] This provides a novel way of distinguishing between the two rate-limiting steps, formation and breakdown of the intermediate, $T^{\pm}$. That this mechanistic difference of the pyridinolysis between methyl (biphasic Brönsted plots in water)[1d] and phenyl chloroformate (monophasic Brönsted plots with rate-limiting attack in acetonitrile) is not due to the solvent effect has been tested by conducting the pyridinolysis of methyl chloroformate in acetonitrile (Table 3). The results show that the same biphasic Brönsted plot with a break at $pK_a \cong 3.6$[1d] is also applicable in acetonitrile, Figure 7. The Hammett plot is also biphasic with a lower slope ($\rho_X = -0.48 \pm 0.02$) for electron-donating X-substituents and a greater slope ($\rho_X = -3.10 \pm 0.25$) for electron acceptor X-substituents, clearly indicating a mechanistic changeover at $\sim\sigma_X = 0.0$. This mechanistic change from biphasic for methyl, **II**, to monophasic with rate-limiting formation of the intermediate for phenyl, **III**, may be attributed to the strong electron-donating polarizability effect of C_6H_5, which has a much greater negative polarizability substituent constant ($\sigma_\alpha = -0.81$) than CH_3 ($\sigma_\alpha = -0.35$).[10] The resonance electron-donating ability expressed by the σ_R^+ scale is also much larger for phenyl ($\sigma_R^+ = -0.22$) than for the methyl group ($\sigma_R^+ = -0.03$).[10] Thus in the charge-separated resonance form of the phenyl chloroformate, **IVa**, the positive charge on the ester oxygen can be much more stabilized by strong electron donation from the phenyl group in **III** than by the relatively weak electron donation from CH_3 in **II**. As a result, the formate moiety becomes strongly electron-rich in **III**, and direct conjugation with the para π-acceptor substituents is possible in the rate-limiting attack; for **II** this is not possible due to insufficient electron supply from the CH_3 group to provide an electron-rich formate moiety. Therefore, the key to the mechanistic changeover to rate-limiting formation of the intermediate for **III** is the sufficiently strong electron supply from the C_6H_5 group to provide the electron-rich O−C−O moiety which can donate π-electrons through the ring π-system to a para acceptor in pyridine.

Since electrons will be partially depleted from the formate moiety by the leaving group, Cl^-, in a concerted (S_N2) mechanism, through-conjugation will not be viable, and hence the enhanced basicity (pK_a^-) will not be required for the linear Brönsted correlation. We therefore conclude that the aminolysis of phenyl chloroformate with pyridines as well as with anilines proceeds by a stepwise mechanism in which the formation of a tetrahedral intermediate is rate limiting. Our recent results are in line with the proposed mechanism. (i) In the pyridinolysis of benzenesulfonyl chlorides in methanol, log *k* vs pK_a plots were normal but log *k* vs σ plots showed positive deviations for the para π-acceptors, *p*-CN and *p*-CH_3CO, indicating positive charge development on N of pyridines in the TS as required from an S_N2 mechanism. (ii) In the correlation of solvolysis rate constants of phenyl chloroformate, incorporation of aromatic-ring parameter, hI, gave excellent linearity in contract to scattered plots without the hI term. This indicates that in the solvolysis of phenyl chloroformate, the phenyl ring participates to stabilize the TS as proposed in the present work.

The activation parameters in Table 2 are also consistent with the proposed mechanism. Since a bond is being formed and there is no bond cleavage in the TS, the energy requirement will be small, a low $\Delta H^{\ddagger}$, and the entropy loss will be large, a large negative $\Delta S^{\ddagger}$. Albeit the differences in activation parameters are small and may not warrant a close examination, there is a correct trend of the lowest $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values for X = *p*-CN with Y = *p*-CH_3O; a π-donor on the phenyl ring will increase the electron density of the formate moiety and should lead to a strongest through-conjugation with a strongest π-acceptor, *p*-CN, rendering the TS the greatest degree of bond formation, i.e., the lowest activation enthalpy coupled with the largest negative entropy of activation.

Finally the 63 rate constants ($k_2 = k_{XY}$) in Table 1 are subjected to multiple regression analysis using eq 5, and the result is presented in eq 6.[14] We note that the correlation is quite satisfactory with the cross-interaction

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$$\log(k_{XY}/k_{HH}) = \rho_X\sigma_X + \rho_Y\sigma_Y + \rho_{XY}\sigma_X\sigma_Y \qquad (5)$$

$$\log(k_{XY}/k_{HH}) = (-2.25 \pm 0.02)\sigma_X + (1.07 \pm 0.03)\sigma_Y + (0.31 \pm 0.06)\sigma_X\sigma_Y$$
$$r = 0.998,\ n = 63 \qquad (6)$$

constant, ρ_{XY}, of +0.3. Previously we have shown that in the S_N2 process or in the rate-limiting formation of an intermediate the ρ_{XY} is negative, but in a stepwise mechanism with a rate-limiting breakdown of the tetrahedral intermediate it is large positive.[12] In the present work, a small positive ρ_{XY} value is obtained and this does not conform to any of the two mechanisms, a negative ρ_{XY} for S_N2[15a] and a large positive ρ_{XY} for rate-limiting breakdown.[12c] The small positive ρ_{XY} obtained in this work[15d] and the small negative ρ_{XY} obtained in the reactions with aniline nucleophiles ($\rho_{XY} = -0.04$)[2] thus appear to be in line with rate-limiting formation of the intermediate for the aminolysis of phenyl chloroformate in acetonitrile.

Experimental Section

Materials. Merck GR acetonitrile was used after three distillations. The pyridine nucleophiles, Aldrich GR, were used without further purification. Aldrich Y-phenyl chloroformates were used after identification by GC-MS and TLC analysis without further purification. Since they are corrosive and moisture sensitive, they were treated in a glove box filled with N_2 gas.

Rate Constants. Rates were measured conductimetrically at 25.0 ± 0.05 °C. The conductivity bridge used in this work was a self-made computer automatic A/D converter conductivity bridge. Pseudo-first-order rate constants, k_{obs}, were determined by the Guggenheim method[13] with a large excess of pyridine; [phenyl chloroformate] $\cong 1 \times 10^{-4}$ M and [Py] = 0.002−0.025 M. Second-order rate constants, k_2, were obtained from the slope of a plot of k_{obs} vs [Py] with more than five concentrations of pyridine, eq 2. The k_2 values in Table 1 are the averages of more than three runs and were reproducible to within ±3%.

Product Analysis. *p*-Chlorophenyl chloroformate was reacted with an excess of *p*-methylpyridine with stirring for more than 15 half-lives at 25.0 °C in acetonitrile, and the products were isolated by evaporating the solvent under reduced pressure. The product mixture was treated with column chromatography (silica gel, 20% ethyl acetate/n-hexane). Analysis of the product gave the following results. *p*-$ClC_6H_4OC(=O)N^+C_5H_4$-*p*-CH_3. Mp 131−133 °C. δ_H, NMR (250 MHz, $CDCl_3$), 2.18 (3H, s, CH_3), 7.19−7.48 (8H, m, C_5H_4N, C_6H_4), ν_{max} (KBr), 2900 (CH, aromatic), 1720 (C=O); mass, m/z 248 (M^+) Anal. Calcd for $C_{13}H_{11}NO_2$: C, 62.9; H, 4.44. Found: C, 63.0; H, 4.43.

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