The Pyridine-catalysed Acylation of Phenols by Carboxylic Acid Anhydrides in Carbon Tetrachloride: Hammett, Brønsted, and Taft Relationships as Evidence for General Base Catalysis

By **Trevor G. Bonner** * and **Kenneth Hillier,** Department of Chemistry, Royal Holloway College (University of London), Englefield Green, Surrey

Rate constants for the pyridine-catalysed acylation of eight phenols by acetic anhydride in carbon tetrachloride closely follow the Hammett ρσ relationship with a positive ρ value indicating general base catalysis. Examination of additional kinetic data by means of the Brønsted and Taft relationships using different pyridines for the former and different carboxylic anhydrides for the latter confirm this mechanism.

NUCLEOPHILIC catalysis has been demonstrated for the aqueous hydrolysis of acetic anhydride,[1] and the acylpyridinium ion has been observed and firmly established [2] as a reaction intermediate in this system. This ion has not been detected in non-polar solvents and pyridine is more likely here to act as a general base catalyst. To test this view we have studied the acylation of phenols with carboxylic acid anhydrides in carbon tetrachloride in the presence of pyridine and other bases. Relating the reaction constants such as Brønsted [3] β and the Hammett [4] ρ values of reactions of known mechanism to reactions under investigation has been usefully applied in related studies on the hydrolysis of acyl α-chymotryspin [5] and of esters,[6] and we have used this method here.

It has been found in many reactions that 2-picoline and 2,6-lutidine have negligible catalytic activity or one which is much lower than their pK values would suggest [7] and steric overcrowding at the nitrogen atom is assumed to cause this reduced reactivity. At low concentrations of these bases in carbon tetrachloride there is no catalysis with either 2-picoline or 2,6-lutidine but at higher concentrations we find that there is a very fast acylation.

RESULTS AND DISCUSSION

The acylation of a phenol (PhOH) by acetic anhydride (A) in the presence of pyridine (Py) is represented as proceeding by nucleophilic catalysis in reaction (1) and by general base catalysis in reaction (2). In (1) if

$$\mathrm{Py} + \mathrm{A} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{AcPy}^+ + \mathrm{AcO}^- \xrightarrow[\mathrm{PhOH}]{k_n} \mathrm{Products} \quad (1)$$

$$\text{Rate} = k_nK_n[\mathrm{Py}][\mathrm{A}][\mathrm{PhOH}] \text{ where } K_n = k_1/k_2$$

$$\mathrm{Py} + \mathrm{PhOH} \overset{K_\mathrm{b}}{\rightleftharpoons} \mathrm{Ph]OH,Py} \xrightarrow[\mathrm{A}]{k_\mathrm{b}} \mathrm{Products} \quad (2)$$

$$\text{Rate} = k_\mathrm{b}K_\mathrm{b}[\mathrm{Py}][\mathrm{PhOH}][\mathrm{A}]$$

the rate of formation of the acetylpyridinium ion (AcPy^+) is slow and the acetylation fast then the kinetic order in phenol should be zero, *i.e.* rate =

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[1] A. R. Butler and V. Gold, *J. Chem. Soc.*, 1961, 4362.

[2] W. P. Jencks and A. R. Fersht, *J. Amer. Chem. Soc.*, 1970, 5432.

[3] J. N. Brønsted, *Chem. Rev.*, 1928, **5**, 231.

[4] L. P. Hammett, 'Physical Organic Chemistry,' McGraw-Hill, New York, 1940.

[5] T. H. Fife, *J. Amer. Chem. Soc.*, 1965, **87**, 4957.

[6] W. P. Jencks and J. Carriuolo, *J. Amer. Chem. Soc.*, 1961, **83**, 1743.

[7] J. A. Feather and V. Gold, *J. Chem. Soc.*, 1965, 1752 and refs. 4—8 therein.

k_1[Py][A]. In the less likely case of the acetylation being rate limiting in reaction (1) or in the more probable event of the acetylation of the complex PhOH,Py being the rate-limiting step in reaction (2) the reaction should be first order in phenol and if a is the initial concentration of phenol and $a - x$ its total concentration at time t a plot of log $[a/(a - x)]$ against t should be a straight line if [A] is in sufficiently large excess of [PhOH].

TABLE 1

Calculated R values for acetylation of *p*-chlorophenol (0·01M) by acetic anhydride (0·05M) in the presence of pyridine (0·02M)

Reaction (%)	20	30	40	50	60	70	80
R	0·606	0·606	0·606	0·601	0·599	0·597	0·598
			Mean R 0·602				

Association constant values used were 112·8 l mol^{-1} for pyridine and *p*-chlorophenol (ref. 11) and 220 l mol^{-1} for pyridine and acetic acid (ref. 12).

At a fixed initial concentration of the phenol (0·01M) and with the acetic anhydride in a five-fold or greater excess the kinetic data fit a pseudo-first-order rate equation which points to reaction (2) with the second step rate limiting. This dependence can only occur if, in the two step process postulated, the ratio R, of the concentration terms [PhOH,Py] and $(a - x)$ remains constant throughout the reaction. Table 1 shows the calculated values of R for a typical kinetic run on the assumption that throughout the reaction pyridine associates in a 1 : 1 hydrogen-bonded complex with both residual *p*-chlorophenol and the acetic acid liberated in the acylation, the position of the equilibrium in both cases being governed by the association constant for the complex formation. The constancy of R is evident. Results of typical experiments in which the relative initial concentrations of substituted phenol and pyridine base have been varied, thus giving rise to different R values, are shown in Table 2. There is reasonable constancy in all cases of the ratio $k_e : R$ where k_e is the experimentally determined rate constant obtained from the straight line plots of log $[a/(a - x)]$ against t. It implies that this ratio is k_b[A] where k_b is the true rate constant of reaction (2) for the acetylation of the hydrogen-bonded form of the phenol. It corresponds to the rate coefficient which would be found experimentally if sufficient base was present to convert the whole of the phenol substrate into its hydrogen-bonded form. This interpretation is supported by the data in Table 2(i) which are represented graphically in Figure 1 and show that the rate constant approaches a limiting value as the base concentration is increased.

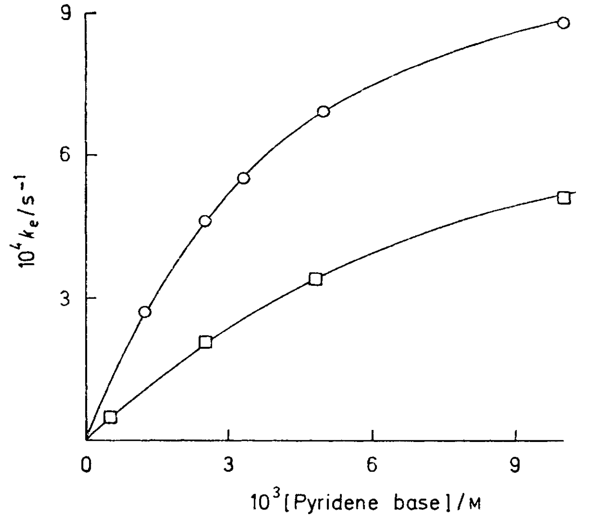

FIGURE 1 Variation of rate coefficient with increasing concentration of pyridine base: ○ 4-picoline; □ 3-picoline

TABLE 2

Reaction in carbon tetrachloride at 25°

(i) *m*-Nitrophenol (0·005M) and acetic anhydride (0·05M)

[3-Picoline]/M	10^4k_e/s^{-1}	R	$10^4k_eR^{-1}$/s^{-1}	[4-Picoline]/M	10^4k_e/s^{-1}	R	$10^4k_eR^{-1}$/s^{-1}
0·0005	0·56	0·077	7·27	0·00125	2·72	0·192	14·17
0·0025	2·09	0·315	6·63	0·00250	4·66	0·338	13·79
0·0050	3·40	0·501	6·79	0·00315	5·48	0·398	13·77
0·0100	5·10	0·690	7·39	0·00500	6·97	0·532	13·10

(ii) *p*-Chlorophenol (0·01M)

[4-Picoline]/M [a]	10^4k_e/s^{-1}	R	$10^4k_eR^{-1}$/s^{-1}	10[Acetic anhydride]/M [b]	10^4k_e/s^{-1}	10^4k_e[A]/l mol^{-1} s^{-1}
0·005	1·62	0·331	4·89	0·523	6·30	12·05
0·010	2·54	0·520	4·88	1·046	12·7	12·14
0·015	2·91	0·630	4·58	1·569	18·1	11·54
0·020	3·47	0·709	4·89	2·092	27·4	13·10
				2·615	33·5	12·81
						Mean 12·33 (= k_bR)

[a] 0·05M-Acetic anhydride. [b] 0·02M-Pyridine.

R Values in each case were calculated using the association constants K_{ass} (l mol^{-1}) of 148 for 4-picoline and *p*-chlorophenol, 269 for *m*-$NO_2C_6H_4OH$ and 3-picoline, and 309 for *m*-$NO_2C_6H_4OH$ and 4-picoline (all our values). From Tables 1 and 2 for pyridine at 0·02M and acetic anhydride at 0·0523—0·2615M, k_b has the value 2·05 × 10^{-3} l mol^{-1} s^{-1} (*cf.* 1·97 × 10^{-3} from data in Table 3).

The Hammett Equation.—In the equation log $k/k_0 = \rho\sigma$, the reaction constant ρ gives an indication of the extent to which the transition state is stabilised by the donation or withdrawal of electrons. Experimentally a large positive value is obtained suggesting, in accordance with the previous work, that general base catalysis is occurring. Table 3 gives rate constants for eight phenols substituted in the *meta*- and *para*-positions. A plot of log k_e against σ^0, where k_e is the pseudo-first-order rate constant and σ^0 the substituent constant, gives ρ 1·52 (Figure 2). This result clearly is not in accord with simple nucleophilic catalysis but does not thereby prove general base catalysis. Although the hydroxy-oxygen atom in *p*-cresol is more nucleophilic than in *p*-chlorophenol, it is found by competitive experiments that in the presence of pyridine the more acidic phenols are more reactive. To illustrate this point further the rate constant k_e can be replaced by k_b to allow for the differing degrees of hydrogen bonding for each phenol. log k_b Plotted against σ gives also a satisfactory straight line correlation having a slope, ρ, of 0·99. The positive slope is consistent with a reaction in which the pyridine–phenol hydrogen bonded complex is involved in the rate-determining step.

TABLE 3

Reaction in carbon tetrachloride at 25° of phenols with acetic anhydride (0·05M) in the presence of pyridine (0·02M)

0·01M-Phenol	10^5k_e/s^{-1}	δ^0 [a]	K_{ass}/l mol^{-1} [b]	R	10^5k_b[A]/s^{-1}
p-Cresol	1·16	−0·15	33·8	0·328	3·54
Phenol	1·98	0·00	46·3	0·398	4·98
p-Fluoro-	3·45	+0·17	69·1	0·488	7·07
p-Chloro-	5·92	+0·27	112·8	0·602	9·83
p-Bromo-	4·86	+0·26	110·0	0·594	8·19
m-Chloro-	6·86	+0·37	98·9	0·570	12·0
m-Bromo-	7·10	+0·38	124·0	0·621	11·4
m-Nitro- [c]	17·50	+0·70	217·7		

[a] Ref. 14. [b] Ref. 11. [c] 0·005M.

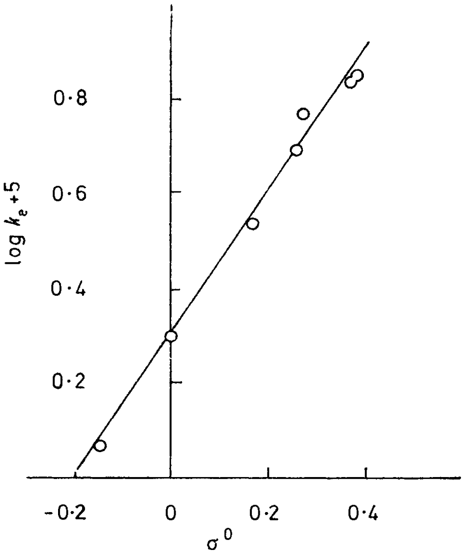

FIGURE 2 Hammet plot of log k_e against σ^0 for the reaction of *para*-substituted phenols with acetic anhydride (Table 3)

The Brønsted Equation.—General base and nucleophilic catalysis show marked differences in β values and hence it should be possible to differentiate between these two mechanisms. In our work, alkyl-substituted pyridine bases only have been investigated which restricts the pK_a range. This was unavoidable as the reactions with *m*-chloro, *m*- and *p*-cyanopyridines, and quinoline were found to be slow and to give non-reproducible results. Association constants between most of the phenols and pyridines listed in Table 4 are not available. Slopes obtained by plotting log k_e against the pyridine base pK_a value for the reaction of acetic anhydride with *p*-chlorophenol, *p*-cresol, and *m*-nitrophenol are 0·93, 0·85, and *ca.* 0·96, respectively; the reaction between isobutyric anhydride and *m*-nitrophenol gave a value of 0·87 (Figure 3). The values are high for general base catalysis and fall nearer the accepted range for nucleophilic catalysis 0·7—0·8.[8] However our work deals with a molecule other than water as a proton donor in general base catalysis and the value of β will undoubtedly reflect the acidity of the attacking nucleophile, *i.e.* the increase in β values from *p*-cresol to *m*-nitrophenol may be a result of an increasingly greater degree of proton release in the transition state. Other systems which could be compared with ours are difficult to discover.

TABLE 4

Reaction in carbon tetrachloride at 25° of phenols with carboxylic acid anhydrides (0·05M)

		Acetic anhydride +			Isobutyric anhydride +
		0·01M-*p*-ClC$_6$H$_4$OH	0·01M-*p*-Cresol	0·005M-*m*-NO$_2$C$_6$H$_4$OH	0·005M-*m*-NO$_2$C$_6$H$_4$OH
0·02M-Base	pK_a [a]	10^5k_e/s^{-1}	10^5k_e/s^{-1}	10^5k_e/s^{-1}	10^5k_e/s^{-1}
Pyridine	5·20	5·93	1·16	17·5 [b]	0·60
2-Picoline	5·96	0	0	0	0
3-Picoline	5·65	17·10	3·54	3·40 [c]	1·37
4-Picoline	6·00	34·70	6·83	6·97 [c]	2·79
3-Ethylpyridine	5·65	21·80			1·48
4-Ethylpyridine	6·00	39·70	7·16		3·29
3,4-Lutidine	6·46	99·60	15·20		7·47
3,5-Lutidine	6·15				2·89
2,6-Lutidine	6·73	0	0	0	0

[a] Ref. 7. [b] Pyridine concentration 0·01M. [c] Base concentration 0·005M.

Although acetylpyridinium ion formation in carbon tetrachloride is highly improbable, it is apparent that in the general base catalysis mechanism association between pyridine and a carbonyl carbon atom could

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[8] J. M. Knoblich, J. M. Sugihara, and T. Yamazaki, *J. Org. Chem.*, 1971, **36**, 3407.

help in stabilising the transition state, as shown in the possible configuration (I). Such an interaction is more probable if the electronegativity of the nitrogen atom is enhanced due to its involvement in a hydrogen bond.[9]

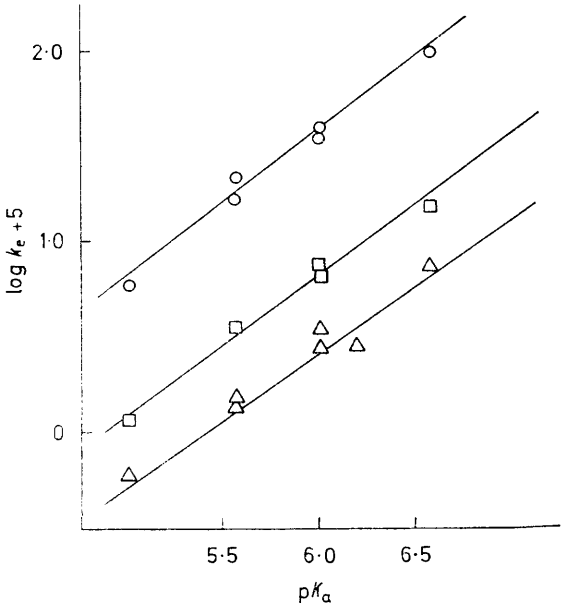
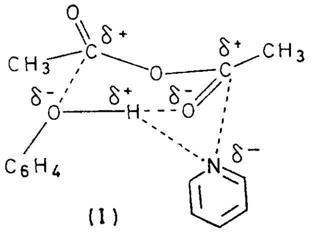


FIGURE 3 Brønsted plot of log k_e against pK_a (Table 4): ○ *p*-chlorophenol + acetic anhydride; □ *p*-cresol + acetic anhydride; △ *m*-nitrophenol + isobutyric anhydride

In a related acylation study, Koskikallio found that when ethanol is acetylated by acetic anhydride in cyclohexane an increase in alcohol concentration led to a decrease in the second-order rate constant.[10] This behaviour was ascribed to the alcohol forming a non-reactive hydrogen-bonded species in which a hydrogen bond had to be broken before reaction could proceed. In the transition state (I) however as the hydrogen bond to pyridine is being broken a stronger hydrogen bond to acetic acid is being produced (K_{ass} phenol–pyridine[11] 46·3 l mol^{-1}, K_{ass} acetic acid–pyridine[12] 220·1 l mol^{-1}).



(I)

Experiments with 4-dimethylaminopyridine (4-DMAP) are also in accord with a general base catalysis mechanism (Table 5). This pyridine is by far the most reactive encountered and in order to follow this reaction kinetically only very small base concentrations could be employed (2×10^{-5}M). It was therefore possible to observe changes in rate constant without the levelling-off effect found for the other pyridine bases presumably because the whole of this added base is associated with the phenol. A plot of log k_e against log [DMAP] is linear for phenol with a slope of 0·97 (Table 5). K_{ass} for 4-DMAP–phenol was calculated as 160·1 l mol^{-1} from the data of Rubin and Panson[13] by extrapolation of a σ *vs.* pK_{ass} diagram using a σ value for the *p*-dimethylamino-group[14] of −0·44. The unit slope indicates an order of one for this base and general base catalysis is indicated from the constancy of the values of k_b. There was no evidence for the resonance stabilised *N*-acetyl-4-dimethylaminopyridinium ion, which would be the reaction intermediate in nucleophilic catalysis.

TABLE 5

Reaction in carbon tetrachloride at 25° of acetic anhydride (0·05M) with phenol in the presence of 4-dimethylaminopyridine (4-DMAP)

	0·01M-Phenol					
10^5[4-DMAP]/M	0·412	0·824	1·236	1·648	2·060	2·47
10^5k_e/s^{-1}	4·00	9·80	13·9	19·0	23·6	28·2
10^4R	4·38	8·12	10·6	14·4	18·8	21·0
10^2k_b[A]/s^{-1}	9·15	12·07	13·1	13·2	12·6	13·4

Steric Retardation.—In contrast to 4-DMAP, 2-dimethylaminopyridine (2-DMAP) is a weak catalyst for the acetylation of *p*-chlorophenol by acetic anhydride with only *ca.* 4% reaction occurring after one day. This suggests that the high reactivity of 4-DMAP is due to the ring nitrogen atom and that the low reactivity of 2-DMAP is the result of steric interference at this atom by the α-dimethylamino-group. The number of bases which could be investigated was restricted by solubility factors and in the case of the strongest nitrogen bases, by marked reactivity with carbon tetrachloride[15] but a similar contrast of catalytic activity was evident with triethylenediamine and 1,8-bis(dimethylamino)naphthalene. The low reactivity found for the latter base, in spite of its very high pK_a of 12·34,[16] must be due to steric hindrance of the methyl groups on the tertiary nitrogen atoms; triethylenediamine as expected gave a very fast reaction. The importance of the steric effect is shown also by the fact that imidazole gave a measurable reaction whereas 2-methylimidazole showed virtually no reaction. Dimethyl sulphoxide is known to be a strong hydrogen bond acceptor although it is only a weak base (*p*K_a − 2·6),[17] and the fact that it is a poor catalyst for this reaction can be explained by the internally associated

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[9] (*a*) P. A. Kollman and L. C. Allen, *J. Amer. Chem. Soc.*, 1970, **92**, 753; 1971, **93**, 4991; (*b*) A. S. N. Murthy, K. G. Rao, and C. N. R. Rao, *ibid.*, 1970, **92**, 3544.

[10] J. Koskikallio and K. Koivala, *Suomen Kem.*, 1967, **40**, 138.

[11] A. M. Dierks, P. Huyskens, and T. Zeegers-Huyskens, *J. Chim. phys.*, 1965, **62**, 336.

[12] J. Barrow, *J. Amer. Chem. Soc.*, 1956, **78**, 5802.

[13] J. Rubin and G. S. Panson, *J. Phys. Chem.*, 1965, **69**, 3089.

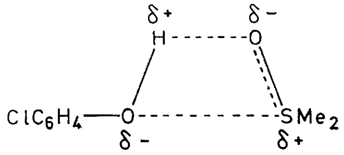
[14] R. W. Taft, jun., *J. Amer. Chem. Soc.*, 1960, **64**, 1805.

[15] T. G. Bonner and R. A. Hancock, *Chem. and Ind.*, 1965, 267.

[16] R. W. Alder, P. S. Bowman, W. R. S. Steele, and D. R. Winterman, *Chem. Comm.*, 1968, 723.

[17] D. Gurka and R. W. Taft, *J. Amer. Chem. Soc.*, 1969, **91**, 4794.

complex (II) which it has been postulated is formed with the phenol.[17]



(II)

The Taft Equation.—Increasing the steric bulk of the acyl group in the anhydride should markedly inhibit nucleophilic catalysed acylation, whereas a general base catalysed mechanism should not experience such a severe constraint.[3] Table 6 gives results found for the reaction of *m*-nitrophenol with acetic, propionic, isobutyric, and pivalic anhydrides in the presence of 3- and 4-picolines. With 4-picoline a plot of log k/k_0 against E_s (where k_0 is the pseudo-first-order rate constant for acetic anhydrides and E_s is the corresponding Taft steric effect constant) gives a slope of 0·77 with a standard deviation of 0·08; Taft[18] proposed the linear free energy relationship (3) for evaluating the steric effect of a group here since the polar term $\sigma^*\rho^*$ is small and does not vary sufficiently while the resonance term E_r is negligible.

TABLE 6

Reaction of *m*-nitrophenol (0·005M) with carboxylic acid anhydride (0·05M) in the presence of pyridine bases in carbon tetrachloride at 25°

Anhydride	E_s	E_s^c	0·005M-4-Picoline $10^4k_b[A]/s^{-1}$	0·005M-3-Picoline $10^4k_b[A]/s^{-1}$
Acetic	0·00	0·00	13·15	6·79
Propionic	−0·07	−0·38	8·30	3·41
Isobutyric	−0·47	−1·08	5·26	2·74
Pivalic	−1·54	−2·46	1·02	0·23

$$\log (k/k_0) = \sigma^*\rho^* + E_r + \delta E_s \qquad (3)$$

Replacing 4-picoline with 3-picoline gave a value of δ of 0·88 with a standard deviation of 0·10. Very few examples have been reported which could serve for comparison with this system. General base catalysed hydrolyses of *N*-acetylserinamide ester[19] and nucleophilically catalysed hydrolyses of *p*-nitrophenyl esters[20] give δ 0·47—0·49 and 1·4 respectively. An attacking phenol molecule will be more sterically hindered approaching the reaction centre than an hydroxide ion in hydrolysis and hence values for δ of *ca.* 0·80—1·0 are not unreasonable for a general base catalysed acylation mechanism.

The importance of hyperconjugation in these reactions is uncertain. A revised steric constant[21] E_s^c has been used related to E_s by equation (4) where *h* is a reaction

$$E_s^c = E_s - h(n - 3) \qquad (4)$$

constant for hyperconjugation and *n* is the number of α-hydrogen atoms. Our results show better correlation with these E_s^c values giving δ 0·44 (standard deviation 0·05) for the 4-picoline reaction but not for 3-picoline [δ 0·58 (standard deviation 0·13)] (Figure 4). The advantage of using E_s^c values has been discussed by Shorter.[22]

The Rapid Acetylation Reaction with Sterically Hindered Bases.—Acylation of phenols by anhydrides is not normally catalysed by α-methyl-substituted pyridine bases at concentrations of the same order as the substrate, and this is the case with our system. However, at higher base concentrations a very fast reaction was found to take place and the extent to which it occurred increased with the concentration of added base. This reaction may be due to the presence of phenolate ions which are known to be highly reactive in this system;[23] evidence for these ions has been reported recently using n.m.r. spectroscopy[24] although we have not been able to detect this species in our system using the same method.

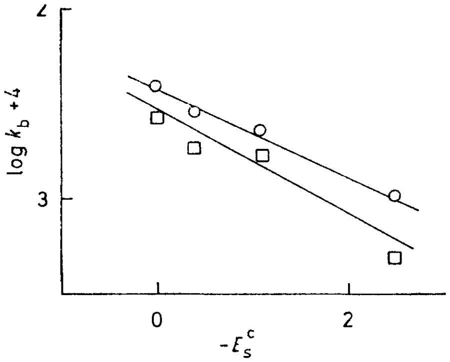


FIGURE 4 Taft plot of log k_b against E_s^c for the acylation of *m*-$NO_2C_6H_4OH$ by different carboxylic anhydrides (Table 6): ○ 4-picline; □ 3-picoline

The explanation for this unusual reactivity may be due to the fact that pyridine bases can exist as dimers,[25] which may not be reactive as nucleophilic catalysts but could be highly reactive as general bases.

The reaction of *m*-nitrophenol with acetic anhydride in the presence of 2,6-lutidine has been studied by varying the base concentration and also by addition of acetic acid. The variation of the initial fast acetate production with the 2,6-lutidine concentration is shown in Table 7. The rapid portion of the acetylation is complete in <1 min and the extent of ester formation in this time depends on the concentration of base. Assuming that the greatly enhanced catalytic effect is due to dimer formation it appears that this dependence can be very closely predicted up to 60% reaction if the dimerisation is assigned an association constant K_D of

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[18] R. W. Taft, jun., 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, New York, 1956.

[19] T. H. Fife and J. B. Milstein, *J. Amer. Chem. Soc.*, 1968, **90**, 2164.

[20] T. H. Fife and J. B. Milstein, *Biochemistry*, 1967, **6**, 2901.

[21] C. K. Hancock, E. A. Meyers, and B. J. Yager, *J. Amer. Chem. Soc.*, 1961, **83**, 4311.

[22] J. Shorter, *Quart. Rev.*, 1970, **24**, 433.

[23] T. G. Bonner and E. G. Gabb, *J. Chem. Soc.*, 1966, 747.

[24] V. P. Lezina, V. F. Bystrov, L. D. Smirnov, and K. M. Dyumaev, *Teor. i. eskp. Khim.*, 1968, **4**, 379.

[25] (*a*) J. N. Murrell and V. M. S. Gil, *Trans. Faraday Soc.*, 1965, **61**, 402; (*b*) J. V. Hatton and R. E. Richards, *Mol. Phys.*, 1962, **5**, 153.

20 l mol^{-1} (Table 7). By adding acetic acid to the reaction mixture the extent of formation of the ester in the rapid stage is decreased as shown in Table 8. This result makes it clear that the rapid stage does not proceed to completion because the acetic acid released in the esterification nullifies the high catalytic activity of the base. This could occur through preferential association with the dimer or monomer.

Table 7

The acetylation of *m*-nitrophenol (0·005M) by acetic anhydride (0·05M) in the presence of 2,6-lutidine in carbon tetrachloride at 25°

10^2[2,6-Lutidine]/M	0·4	0·8	1·2	1·6	2·0
10^3[*m*-Nitrophenyl acetate]/M *	0·35	1·15	2·00	2·95	3·75
10^3[Dimer]/M (assuming K_D 20 l mol^{-1})	0·28	1·00	2·00	3·25	4·68

* Conc. of ester formed at the end of the rapid stage.

Table 8

Reaction of *m*-nitrophenol (0·005M) with acetic anhydride (0·05M) in the presence of 2,6-lutidine (0·02M) and acetic acid at 25°

10^3[Acetic acid]/M*	10^3[$CH_3CO_2C_6H_4NO_2$-*m*]/M	10^3[Acetic acid]/M	10^3[$CH_3CO_2C_6H_4NO_2$-*m*]/M	10^3[Acetic acid]/M	10^3[$CH_3CO_2C_6H_4NO_2$-*m*]/M
3·25	3·25	4·90	2·90	11·25	1·25
3·35	3·35	5·70	2·70	11·20	1·20
3·40	3·40	7·05	2·05	15·55	0·55
3·55	3·55	7·25	2·25	20·30	0·30
4·15	3·15	8·00	2·00		

* Total acetic acid, *i.e.* added acid plus acid formed in rapid acetylation. † Ester formed at the end of the rapid stage.

EXPERIMENTAL

The solvent and reagents other than those described below were purified as reported previously.[26,27] Pyridine bases were distilled from potassium hydroxide or recrystallised from ligroin. The carboxylic acid anhydrides and phenols were distilled, except *m*-nitrophenol which was recrystallised from chloroform. Imidazole was recrystallised twice from carbon tetrachloride and 1,8-bis-(dimethylamino)naphthalene was recrystallised from this same solvent immediately prior to reaction. 2-Dimethylaminopyridine, triethylenediamine, and 2-methylimidazole were used without further purification. M.p.s and b.p.s agreed with literature values.

Kinetic Measurements.—Reactions were carried out at 25 ± 0·05°. Those reactions involving acetic anhydride were followed by an i.r. technique as described previously.[28] The other carboxylic acid anhydrides could not be removed from the carbon tetrachloride phase by shaking with a saturated aqueous solution of potassium hydrogen carbonate. The ester carbonyl absorption could not then be observed by i.r. analysis. To avoid this, *m*-nitrophenol was used in these cases since it could be extracted with water from the carbon tetrachloride and the *m*-nitrophenolate ion estimated by u.v. spectroscopy. Aliquot portions (1 cm^3) of the reaction mixture were removed at intervals and shaken with water. The aqueous phase was separated and potassium hydrogen carbonate solution added, and the absorbance at 390 nm was measured with a Perkin-Elmer 137 u.v. spectrophotometer. The concentration of changed *m*-nitrophenol was found from a previously obtained calibration curve.

Further details of experimental techniques and results are available.[29]

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