

Kinetics of Reaction of Phenacyl Bromide with 3- & 4-Substituted Pyridines & 4-Substituted 4-Styrylpyridines

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The rates of reaction of phenacyl bromide with 3- and 4-substituted pyridines and 4'-substituted 4-styrylpyridines have been measured in aq. acetone (90% v/v) at 30°, 35° and 40°C and the activation parameters have been evaluated. Satisfactory Hammett correlations are obtained for both pyridine and styrylpyridine series. The effectiveness of transmission of substituent effect in styrylpyridine system relative to pyridine system in this reaction is calculated to be 0.104. From the Bronsted relationship the coefficient (β_s) is found to be 0.48, indicating that the extent of bond formation in the transition state is moderate.

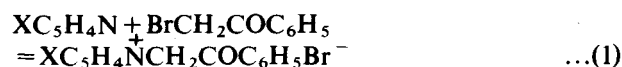
Kinetics of the reactions of phenacyl bromide with substituted anilines^{1,2}, benzoate^{3,4}, naphthoate⁵, cinnamate⁶ and phenoxyacetate⁷ ions have been studied. Forster and Laird⁸ have reported the rate constants for the reaction of phenacyl bromide with a few 3- and 4-substituted pyridines in methanol. The present work has been undertaken to extend the range of substituents and compare the reactivity of substituted pyridines with other nucleophiles under identical conditions.

All the chemicals used were of AR grade. The kinetic measurements were done in aq. acetone (90% v/v), using purified acetone and triply distilled water. Substituted pyridines were purified by distillation or recrystallisation. 4-Methylpyridine-3-carboxylate was prepared by esterifying nicotinic acid. 4'-Substituted 4-styrylpyridines were prepared by the condensation⁹ of 4-methylpyridine with appropriate benzaldehydes and their purity was checked by comparing their melting points with those reported in literature and by TLC.

The kinetics were followed titrimetrically using Volhard method as reported earlier⁶. Reactant solutions were always prepared afresh. The reaction was carried out under second order conditions. The concentration of phenacyl bromide was 0.02 mol dm⁻³ and the concentrations of pyridines and styrylpyridines ranged from 0.02 to 0.1 mol dm⁻³ depending on the reactivity of pyridines. The second order rate constants were calculated by the method of least squares from the slopes of $x/a(a-x)$ versus time plots for equal concentrations of the reactants and from the slopes of $\log [b(a-x)/(b-x)]$ versus time plots

for unequal concentrations of the reactants. The precision in k_2 values was calculated in terms of 95% confidence limit. Activation parameters were evaluated from the Arrhenius plots. The errors quoted in $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were calculated using the method of Petersen *et al.*¹⁰.

The reaction of phenacyl bromide with substituted pyridines and 4-styrylpyridines takes place quantitatively according to Eq. (1)



The substituent X is present either in 3- or 4-position of pyridine. In 4-styrylpyridines X is the substituent at position-4' in the aromatic nucleus.

The second order rate constants, given in Table I show that the reaction is accelerated by electron-releasing substituents and retarded by electron-withdrawing substituents in the pyridine ring or in the phenyl ring of the styrylpyridine. Correlation of the present rate data at 30°C with σ_p and σ_m substituent constants for pyridines and σ_p constants of Katritzky *et al.*¹¹ for styrylpyridines is satisfactory ($r=0.972$), as has been observed in the earlier studies on styrylpyridines^{12,13}. The substituents F, Br and OAc are not included in this correlation as the σ_p constants are not available for these substituents.

The procedure of Katritzky *et al.*¹¹ for obtaining σ_p values for the substituted styryl groups did not appear adequate as the effect of substituent was very small on their pK_a values. Therefore it was decided to correlate the rate data for 3- and 4-substituted pyridines and 4'-substituted 4-styrylpyridines separately with Hammett σ constants¹⁴. In both the cases the correlations are found to be satisfactory (Table 2). In the correlation of $\log k_2$ of styrylpyridines with the Hammett σ constants, the data point for OAc group shows deviation hence it is not used in the calculation.

Jaffé and Dock¹⁵ observed a value of $\rho = -5.71 \pm 0.30$ for protonation equilibrium of 3- and 4-substituted pyridines. The magnitude of ρ (-2.80) obtained in the present study shows that the effect of substituents is much less pronounced as compared to that of protonation equilibrium of 3- and 4-substituted pyridines and that only one-half of the positive charge carried by the pyridinium ion is developed in the transition state of the reaction of substituted pyridines with phenacyl bromide. The ρ -value (-0.29) obtained for the reaction of phenacyl bromide with styrylpyridines reflects not only the sensitivity of the reaction to the substituent but also the degree of

Table 1—Second Order Rate Constants and Activation Parameters for Reaction of Phenacyl Bromide with Substituted Pyridines and 4'-Substituted 4-Styrylpyridines in 90% Acetone- 10% Water (v/v) Mixture

Substituent	$10^4 k_2$ (dm ³ mol ⁻¹ s ⁻¹)			$\Delta H^\ddagger$ (kJ mol ⁻¹) at 35°C	$-\Delta S^\ddagger$ (JK ⁻¹ mol ⁻¹) at 35°C
	30°	35°	40°		
Pyridine series					
3-Me	36.95 ± 1.64	44.76 ± 1.84	50.50 ± 0.80	26.1 ± 1.6	204.2 ± 17.5
4-Me	30.62 ± 1.11	44.11 ± 1.78	64.1 ± 1.92	56.0 ± 5.6	108.3 ± 18.8
H	15.67 ± 1.30	25.03 ± 0.62	30.94 ± 1.10	57.6 ± 7.4	127.2 ± 24.8
3-COOH	2.76 ± 0.13	3.68 ± 0.07	5.13 ± 0.14	46.5 ± 5.1	159.3 ± 17.0
COMe	2.71 ± 0.14	3.12 ± 0.18	4.54 ± 0.10	38.1 ± 6.9	188.3 ± 23.2
3-COOMe	1.70 ± 0.05	2.80 ± 0.15	3.38 ± 0.05	52.2 ± 5.2	143.4 ± 17.6
3-CN	0.216 ± 0.009	0.280 ± 0.021	0.343 ± 0.011	34.1 ± 7.9	221.3 ± 26.5
4-CH =CH.C ₆ H ₅	31.43 ± 1.25	37.90 ± 0.70	51.70 ± 1.22	36.8 ± 1.3	184.2 ± 4.2
$10^3 k_2$ (dm ³ mol ⁻¹ s ⁻¹)					
4'-Substituted 4-styrylpyridines					
OMe	3.94 ± 0.07	5.48 ± 0.06	7.45 ± 0.07	47.7 ± 2.0	133.1 ± 6.6
OAc	4.19 ± 0.08	5.30 ± 0.10	6.14 ± 0.26	45.1 ± 6.1	145.0 ± 20.4
Me	3.22 ± 0.17	4.26 ± 0.11	6.00 ± 0.23	46.6 ± 7.8	137.6 ± 23.7
F	3.24 ± 0.20	4.91 ± 0.22	6.02 ± 0.17	44.2 ± 6.9	147.1 ± 23.2
Cl	2.59 ± 0.09	4.02 ± 0.19	4.88 ± 0.24	40.0 ± 2.6	160.7 ± 8.7
Br	2.80 ± 0.07	4.05 ± 0.01	4.77 ± 0.11	67.0 ± 4.6	74.1 ± 15.3
NO ₂	1.86 ± 0.05	3.59 ± 0.09	4.17 ± 0.15	44.7 ± 4.3	143.4 ± 14.5

Table 2—Linear Correlation for Reaction of Phenacyl Bromide with Substituted Pyridines and 4-Styrylpyridines

Parameter	ρ	r	s	n
Pyridines and styrylpyridines				
Katritzky σ_m/σ_p	-2.74 ± 0.48	0.972	0.177	12 ^a
Pyridines				
Hammett σ	-2.80 ± 0.75	0.970	0.220	8
Styrylpyridines				
Hammett σ	-0.290 ± 0.079	0.973	0.026	7 ^b

r = correlation coefficient; s = standard deviation; and n = number of points.

(a) The substituents F, Br and OAc are not included.

(b) The substituent OAc is excluded.

transmission of the substituent effect through the styryl group to the reaction centre. From the basicities of 4-styrylpyridines¹¹ the value of ρ is found to be -0.85. The effectiveness of transmission of substituent effect via styryl system in the protonation equilibrium¹¹ has been calculated to be ~0.15. The ratio obtained in the present reaction series (-0.29/-2.80) compares satisfactorily with the above value. This value is also in close agreement with the result obtained for the charge-transfer complex formation with iodine¹⁶.

The Bronsted correlation involving $\log k_2$ at 30°C and the pK_a values of corresponding conjugate acids of substituted pyridines and styrylpyridines is found to be good ($\beta_N = 0.48 \pm 0.04$; $r = 0.995$; $s = 0.074$; $n = 10$), indicating that the reaction rate depends on the basicity of the nucleophile. The pK_a values of substituted pyridines used in correlation are those given by Jaffe and Dock¹⁵ and of 4'-substituted 4-styrylpyridines are those given by Katritzky *et al.*¹¹. The positive sign of β_N points out that the rate increases with increasing basicity of the nucleophile. The value of β_N , a measure of the extent of bond making in the transition state, is higher than that observed for the reaction of phenacyl bromide with *trans*-cinnamate ions⁶ ($\beta_N = 0.404$) and lower than that observed for the reaction of phenacyl bromide with anilines² ($\beta_N = 0.768$). The present value of $\beta_N = 0.48$ indicates that the extent of bond formation in the transition state is moderate^{17,18}.

Activation parameters for the reaction of phenacyl bromide with pyridines and styrylpyridines are given in Table 1. The enthalpies of activation for the reaction of pyridines are slightly lower than those reported for benzoate and cinnamate ions^{3,6} and comparable to those reported for anilines². The entropies of activation are all negative in line with the expectation for S_N2 processes. Since there is charge development in the transition state, the entropies of activation are more negative than those of the carboxylate nucleophiles^{3,4,6}. Exner plot of $\log k_2$ at 313K versus $\log k_2$ at 303K is linear ($r = 0.990$). Existence of good

correlation shows that in the reaction series all the pyridines and styrylpyridines follow the same mechanism.

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