Structure-Reactivity Relationships in Nucleophilic Substitution Reactions of Phenacyl Bromide with Aliphatic Carboxylate Ions

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The second order rate constants for the reactions of phenacyl bromide with various substituted aliphatic carboxylate ions (XCOO⁻: X = H, Me, Pr, Et, ClCH₂, BrCH₂, HOOCCH₂, Ph, PhCH₂, PhCH=CH, PhSCH₂, PhOCH₂ and PhSO₂CH₂) have been measured in 90% acetone-10% water (v/v) mixture at 30°, 35° and 40°C. The rate constants have been analysed in terms of electronic and steric effects using various single and multi-parameter equations.

Kinetics of the reactions of phenacyl bromide with various aromatic nucleophiles have been reported[1-8]. Similar studies involving the aliphatic nucleophiles are not many since the analysis of the results is somewhat difficult because of possible interaction of the substituent with the reaction site through electronic and steric effects, hydrogen bonding etc. In the present note, we report the S_N2 reaction of a few aliphatic carboxylate ions with phenacyl bromide in aq. acetone. The rate data have been correlated with different single-parameter and the extended Hammett equations in order to investigate the effect of structure on reactivity and to separate the polar and steric effects in the above reactions.

Various aliphatic acids were either commercial samples or prepared by literature methods.

The solvent used in all the kinetic measurements was 90% acetone-10% water (v/v) mixture. The kinetics were followed by estimating the liberated bromide ion by the Volhard method as reported previously[1-3]. The product under the kinetic conditions was identified to be $CH_3COOCH_2COC_6H_5$ in the reaction of acetate ion with phenacyl bromide. The second order rate constants were calculated by least squares method and the precision of rate constants is given in terms of 95% confidence limit. The precision of the activation parameters was calculated using the method of Petersen *et al*[9].

The reaction between phenacyl bromide and aliphatic carboxylate ions follows second order kinetics and can be represented by the general Eq.(1)

$$XCOO^- + BrCH_2COC_6H_5 = XCOOCH_2COC_6H_5 + Br^- \qquad \ldots (1)$$

The second order rate constants measured at 30°, 35° and 40°C and activation parameters at 35° are given in Table 1.

The rate data were analysed in terms of Taft's linear free energy-polar energy and linear free energy-steric energy relationships[10] to know whether the reactivity of aliphatic series is compatible either with Taft's polar substituent parameter (σ^*) or size of the substituent (E_s). The results of the analyses may be expressed by Eqs (2) and (3):

$$\log k_{35°} = -0.562\,\sigma^* - 1.880$$
$$r = 0.520; \ s = 0.453; \ n = 12 \qquad \ldots (2)$$
$$\log k_{35°} = -0.043\,E_s - 2.169$$
$$r = 0.079; \ s = 0.528; \ n = 12 \qquad \ldots (3)$$

The substituent $PhSCH_2$ was not included in the regression analysis (2) as no reliable σ^* constant was available. Similarly, the substituent $PhSO_2CH_2$ was excluded in the correlation (3) since no E_s value was available. The results of the analyses show that the observed reactivity does not depend entirely either on σ^* or E_s. Poor correlation with steric parameter also shows the minor role of the 'primary steric effect' or 'bulk effect' which may be due to the fact that the oxygen of the carboxylate ion is far away from the substituent.

According to Charton[11], ionisation of aliphatic carboxylic acids in water should be the basis of σ_I values for all substituents of aliphatic series and he derived σ_I values for various substituents. Hence, the present rate data were also correlated with Charton's σ_I values. The result of correlation is represented by Eq. (4).

$$\log k_{35°} = -1.413\,\sigma_I - 1.865$$
$$r = 0.619; \ s = 0.447; \ n = 10 \qquad \ldots (4)$$

The correlation is improved (see Eq. 5) by the exclusion of CH_2COOH substituent.

$$\log k_{35°} = -1.057\,\sigma_I - 1.823$$
$$r = 0.941; \ s = 0.100; \ n = 9 \qquad \ldots (5)$$

Since the single-parameter equations did not give satisfactory correlations, the rate data were examined in terms of multi-parameter Eqs (6) and (7)

$$\log k_{35°} = L\sigma_I + D\sigma_R + h \qquad \ldots (6)$$
$$\log k_{35°} = L\,\sigma_I + D\,\sigma_R + SE_s + h \qquad \ldots (7)$$

where σ_I, σ_R and E_s represent localized, delocalized and steric parameters respectively. The values of σ_I and σ_R were those obtained by Charton[12].

The results of the regression Eq. (6) may be expressed by Eq.(8) (the substituents Ph, PhCH=CH, H and CH_2COOH excluded).

Table 1 — Second Order Rate Constants and Activation Parameters for Reactions of Phenacyl Bromide with Carboxylate
Ions (XCOO⁻) in 90% Acetone-10% Water (v/v) Mixture

([XCOO⁻] = [Phenacyl bromide] = 0.01 mol dm⁻³)

Sl No.	X	$10^3 k_2$ (dm³ mol⁻¹ s⁻¹)			$\Delta H^{\neq}$ (kJ mol⁻¹ at 35°)	$-\Delta S^{\neq}$ (JK⁻¹ mol⁻¹ at 35°)
		30°	35°	40°		
1	Pr	12.77 ± 0.47	18.85 ± 0.87	27.94 ± 1.29	70.3 ± 6.8	85.5 ± 22.8
2	Et	10.85 ± 0.39	15.17 ± 0.99	25.55 ± 0.76	65.1 ± 6.9	68.6 ± 23.1
3	PhCH₂	10.52 ± 0.13	15.05 ± 0.62	22.08 ± 0.70	56.1 ± 4.5	98.1 ± 15.0
4	Ph	10.50 ± 0.10	14.16 ± 0.39	22.70 ± 0.62	54.8 ± 3.4	102.0 ± 11.0
5	PhCH=CH	9.66 ± 0.09	14.93 ± 0.41	21.29 ± 0.82	61.6 ± 4.0	80.3 ± 13.3
6	Me	7.95 ± 0.47	11.54 ± 0.58	18.78 ± 0.48	65.4 ± 7.1	70.1 ± 23.8
7	PhSCH₂	6.51 ± 0.16	10.13 ± 0.39	13.15 ± 0.63	53.1 ± 5.8	111.0 ± 21.0
8	H	4.34 ± 0.30	6.66 ± 0.23	10.27 ± 0.37	62.1 ± 6.4	85.4 ± 21.5
9	PhOCH₂	3.39 ± 0.17	5.38 ± 0.13	8.83 ± 0.28	73.1 ± 5.6	51.4 ± 18.8
10	BrCH₂	2.88 ± 0.17	4.63 ± 0.16	6.88 ± 0.20	66.4 ± 6.4	74.4 ± 21.5
11	PhSO₂CH₂	2.76 ± 0.12	4.24 ± 0.13	6.58 ± 0.20	66.3 ± 5.5	75.5 ± 18.4
12	ClCH₂	2.27 ± 0.14	3.64 ± 0.11	5.47 ± 0.11	67.2 ± 5.8	73.8 ± 19.4
13	HOOCCH₂	0.231 ± 0.004	0.274 ± 0.007	0.581 ± 0.006	70.3 ± 2.8	85.4 ± 9.4

Error quoted in k_2 is the 95% confidence limits of the student-t.

$$\log k_{35°} = -1.099\,\sigma_I - 0.031\,\sigma_R - 1.792$$
$$\quad\quad\quad (\pm 0.173) \quad (\pm 0.236)$$
$$n = 9;\ SE = 0.112;\ R = 0.936;\ CL = 97.5\% \quad\quad (8)$$

The F-test significance of the correlation is 97.5%, indicating meaningful correlation. The confidence levels by student t-test for the significance of localized and delocalized terms are $>95\%$ and $<90\%$, respectively showing that the resonance effect is insignificant. The above result is also confirmed by the fair correlation with σ_I.

Equation (7) involving the localized, delocalized and steric terms gives the following result on regression analysis (see Eq. 9)

$$\log k_{35°} = -1.326\,\sigma_I - 0.054\sigma_R - 0.410 E_s - 1.889$$
$$\quad\quad (\pm 0.0142) \quad (\pm 0.220) \quad (\pm 0.095)$$
$$n = 8;\ SE = 0.056;\ R = 0.988;\ CL = 99.9\% \quad\quad \cdots (9)$$

(X = Me, Et, Pr, CH₂Cl, CH₂Br, CH₂Ph, CH₂SPh and CH₂OPh)

The confidence levels of the t-test for localized and steric terms are $>95\%$ and for delocalized term it is $<90\%$. The dependence of localized and steric effects is also shown by the good correlation of the rate data with σ_I and E_s parameters (see Eq. 10).

$$\log k_{35°} = -1.302\sigma_I - 0.414 E_s - 1.884$$
$$\quad\quad (\pm 0.093) \quad (\pm 0.084)$$
$$n = 8;\ SE = 0.050;\ R = 0.988;\ CL = 99.9\% \quad\quad \cdots (10)$$

The magnitude of the intercept is closer to that of the parent compound. The foregoing analysis leads to the conclusion that the localized and steric effects are important in this reaction.

The regression coefficient of σ_I is negative indicating that inductively electron-releasing groups accelerate

the reaction and electron-withdrawing groups retard it. The magnitude of the steric effect, (P_s) is 30.2%, which shows that the steric effect is important. The steric acceleration of rate by bulky substituent may be due to the fact that a bulky substituent makes the carboxylate group to orient farthest away from the substituent and also reduces the extent of solvation of the carboxylate ion so that the approach of the two molecules is facilitated.

The inductive effect of Me, Et and Pr substituents is almost the same. The observed rate increase with the increase in the number of carbon atoms of the substituents may be due to steric effect. The difference in the reactivity of chloro and bromo compounds may also be due to the bulk effect. The rate of phenylsulphonylacetate ion is lower than that of the phenylthioacetate ion which may be attributed to predominant field effect. Phenoxyacetate ion reacts slower than phenylthioacetate ion. The low reactivity of phenoxyacetate ion may be due to the electron-withdrawing inductive effect of oxygen over sulphur and also the smaller size of the oxygen atom. The low reactivity and deviation from the regression equations of CH₂COOH group may be due to the stabilisation of carboxylate ion by intramolecular hydrogen bonding between the carboxylic acid and negatively charged oxygen of the carboxylate ion.

A useful comparison of the reaction may be made by the correlation of the rate constants with the pK_a values of the corresponding conjugate acid of the nucleophile (CH₂COOH is excluded). A fair correlation ($r = 0.933$) with pK_a values and a positive value of the Brönsted coefficient show that the rate of the reaction increases with increasing basicity of the nucleophile. However, a

lower value of Brönsted coefficient observed here indicates that there is less bond making in the transition state.

The $\Delta S^{\neq}$ values are all negative as expected for S_{N2} reactions. The enthalpies of activation are comparable to those observed for the reactions of phenacyl bromide with benzoate[1] and cinnamate ions[3]. In this reaction series the isokinetic temperature has been calculated ($\beta = 363K$) by the method proposed by Exner[13]. The existence of good correlation in the Exner plot ($r = 0.998$) shows that all the aliphatic carboxylate ions follow the same mechanism in this reaction series.

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