Kinetics of the Reactions of Phenacyl Bromide and of *para*-Substituted Phenacyl Bromides with Benzoate and Substituted *trans*-Cinnamate Ions

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The second-order rate constants for the reactions of various *para*-substituted phenacyl bromides with benzoate ion and with several substituted *trans*-cinnamate ions have been measured in 90% acetone–10% water (v/v) mixture. Electron-releasing substituents in cinnamate ion and electron-withdrawing substituents in phenacyl bromide increase the rate of substitution reaction. Results of correlation analysis show constant selectivity in the reactions of various phenacyl bromides with a given cinnamate ion (ρ *ca.* 1.05) and also in various cinnamates with a given phenacyl bromide (ρ *ca.* −0.2). In these simple S_N2 reactions, the reactivity–selectivity effects are absent.

Although the remarkable ease with which phenacyl halides undergo nucleophilic substitution reactions has long attracted attention,[1,2] opinions still differ about the precise mechanism.[3-11] This is due to two available reaction centres in phenacyl halides for a nucleophile to attack in the rate-limiting step leading to different types of transition-state structures. The study of substituent effects provides one of the most powerful tools for probing the structure of transition states. The present study was undertaken in order to arrive at the probable transition state in the reactions of *para*-substituted phenacyl bromides with benzoate ion and cinnamate ion. The rate studies have been made by changing the substituent in the nucleophile as well as in the substrate in order to investigate the effect of structure on reactivity in nucleophilic substitution reactions.

Discussion

The reactions of benzoate and *trans*-cinnamate ions with phenacyl bromides proceed according to equation (1).

$$p\text{-}ZC_6H_4COCH_2Br + RCOO^- = p\text{-}ZC_6H_4COCH_2OCOR + Br^-$$
$$R = C_6H_5 \text{ or } m\text{- or } p\text{-}XC_6H_4CH{=}CH\text{-} \qquad (1)$$

The reactions were studied under second-order conditions at equal concentrations of the nucleophile and the substrate in 90% acetone–10% water (v/v) mixture. The rate constants for the reactions of benzoate ion with various *para*-substituted phenacyl bromides at 35 °C and for cinnamate ion with several *para*-substituted phenacyl bromides at 30, 35, and 40 °C are

Table 1. Second-order rate constants and activation parameters for the reactions of sodium cinnamate–benzoate with substituted phenacyl bromides. [Sodium cinnamate/benzoate] 0.01 mol dm^{-3}; [phenacyl bromide] 0.01 mol dm^{-3}; solvent 90% acetone–10% water (v/v)

		Sodium cinnamate $10^3\,k_2$/dm^3 mol^{-1} s^{-1}					Sodium benzoate $10^3\,k_2$/dm^3 mol^{-1} s^{-1}
No.	Z	30 °C	35 °C	40 °C	$\Delta H^‡$/kJ mol^{-1} at 35 °C	$-\Delta S^‡$/J K^{-1} mol^{-1}	35 °C
1	OMe	5.20 ± 0.17	7.78 ± 0.17	12.2 ± 0.4	64.9 ± 4.6	74.9 ± 15.4	8.25 ± 0.22
2	Me	6.90 ± 0.20	9.46 ± 0.21	14.7 ± 0.2	56.9 ± 3.4	99.4 ± 11.4	10.8 ± 0.4
3	H	9.66 ± 0.09	14.9 ± 0.4	21.3 ± 0.8	60.1 ± 4.0	85.1 ± 13.3	14.2 ± 0.4
4	F	15.3 ± 0.5	23.0 ± 0.3	33.1 ± 0.3	58.7 ± 3.1	86.2 ± 10.3	21.5 ± 1.0
5	Cl	20.1 ± 0.5	28.8 ± 0.2	44.7 ± 0.4	60.5 ± 2.1	78.4 ± 6.9	33.1 ± 1.1
6	Br	21.5 ± 0.8	31.9 ± 1.6	48.2 ± 2.0	61.3 ± 6.7	75.1 ± 22.5	34.4 ± 1.1
7	NO_2	59.6 ± 3.3	101 ± 2	127 ± 7	57.7 ± 5.8	77.1 ± 19.4	97.7 ± 3.5

The error quoted in *k* is the 95% confidence limits of the 'Student t' test. The precision of $\Delta H^‡$ and $\Delta S^‡$ values is calculated using the method of Peterson *et al.*[21]

Table 2. Second-order rate constants for the reactions of *para*-substituted phenacyl bromides with substituted sodium cinnamates in 90% acetone–10% water (v/v) at 35 °C. [Sodium cinnamate] 0.01 mol dm^{-3}; [phenacyl bromide] 0.01 mol dm^{-3}

	Phenacyl bromide $10^3\,k_2$/dm^3 mol^{-1} s^{-1}						
X	Z = OMe	Me	H	F	Cl	Br	NO_2
p-Me	8.98 ± 0.17	10.6 ± 0.1	15.6 ± 0.2	24.3 ± 0.7	33.8 ± 0.9	36.3 ± 1.5	114 ± 2
m-Me	8.25 ± 0.07	10.2 ± 0.2	14.9 ± 0.3	23.7 ± 0.9	30.8 ± 0.5	34.9 ± 0.7	102 ± 8
H	7.78 ± 0.17	9.46 ± 0.21	14.9 ± 0.4	23.0 ± 0.3	28.8 ± 0.2	31.9 ± 1.6	101 ± 2
p-Cl	6.69 ± 0.22	8.99 ± 0.42	12.0 ± 0.6	20.5 ± 0.4	24.4 ± 0.5	28.5 ± 0.9	84.9 ± 1.5
p-Br	6.67 ± 0.02	8.62 ± 0.11	12.8 ± 0.3	21.0 ± 0.1	25.9 ± 1.0	28.9 ± 0.2	85.4 ± 1.2
m-Cl	6.51 ± 0.07	8.34 ± 0.13	11.7 ± 0.2	19.3 ± 0.2	22.9 ± 0.4	27.5 ± 1.3	81.2 ± 3.4
m-NO_2	5.74 ± 0.24	6.90 ± 0.09	10.4 ± 0.5	16.7 ± 0.2	20.2 ± 1.0	23.6 ± 0.7	67.4 ± 2.7
p-NO_2	5.31 ± 0.14	6.47 ± 0.19	9.73 ± 0.47	15.8 ± 0.3	19.5 ± 0.1	22.4 ± 0.9	62.0 ± 1.3

The error quoted in *k* is the 95% confidence limit of the 'Student t' test.

given in Table 1. The kinetic data for several substituted *trans*-cinnamate ions with different *para*-substituted phenacyl bromides are presented in Table 2. An examination of the rate data in Table 1 reveals that there is an enhancement in the rate of nucleophilic substitution for a given nucleophile (benzoate or cinnamate) when electron-withdrawing substituents are present in the substrate. The rates of reactions of benzoate and cinnamate ions with all the substrates at 35 °C are comparable implying that the strengths of the two nucleophiles are almost identical. Satisfactory correlations of log k_2 with σ at 35 °C for the two reaction series exist. The ρ values are 1.05 (r 0.988; s 0.020, 95% confidence level on $\rho \pm 0.19$) for the reaction of benzoate ion and 1.08 (r 0.990; s 0.057, 95% confidence level on $\rho \pm 0.17$) for the reaction of cinnamate ion with *para*-substituted phenacyl bromides.

Transition State.—Many mechanisms have been proposed to account for the reactivity of α-halogenoketones. According to Hughes[3] the inductive effect of the carbonyl group enhances the normal polarity of the carbon–halogen bond by increasing electron deficiency at the α-carbon. Consequently a direct displacement of the halogen from the α-carbon atom is envisaged. On the other hand, Baker[4] suggested that the first and rate-determining step is the addition of the nucleophile to the carbonyl carbon from which the addend is transferred to the α-position, with the displacement of halogen. This involves the formation of an intermediate in which the nucleophile is covalently bonded to the carbonyl carbon. Other modes of interaction[6,7] of the nucleophile with the carbonyl group have been proposed. The enhanced reactivity has been attributed to orbital overlap with the nucleophile by the π-molecular orbital of the C–C–O system[6] and to the electrostatic effect exerted by the carbonyl group on the approaching nucleophile.[7] These models involve bridging between the carbonyl carbon and the α-carbon. The orbital overlap mechanism has been shown to be operating in many cases.[8,9] It has also been shown that the enhanced reactivity of phenacyl halides is due to the combination of field and conjugative effects.[11] We felt that a comparison of ρ values for the reactions of various substituted phenacyl bromides with other nucleophiles in related S_N2 type reactions reported in the literature may provide a clue in identifying the nature of the transition state. The ρ value for the nucleophilic substitution of bromide ion in the reactions of phenacyl bromide with pyridine in acetone[12] at 20 °C is 0.558, with pyridine in methanol[11] is 0.257 at 33 °C, and with aniline in methanol[13] at 40 °C is 0.390. For the solvolysis of phenacyl bromide in aqueous ethanol[14] the ρ value is 0.350. The low values of ρ observed in these series have been attributed to the normal direct displacement mechanism which does not involve the carbonyl participation. Baker's mechanism involving carbonyl addition requires a high value of ρ. In the equilibrium addition reactions of the carbonyl group of substituted benzaldehydes[15–19] the ρ value has been found to be *ca.* 2.0. The ρ values of 1.05 and 1.08 observed in the present study for benzoate and cinnamate ions respectively are higher than those involving direct displacement and lower than those observed for carbonyl addition. These intermediate values of ρ may be construed as an indication of carbonyl participation leading to a bridged transition state. The steps leading to the product after the formation of bridged transition state may be fast. More information is needed to arrive at the exact description of the transition state.

Substituent Effects.—The rate data in Table 2 are as expected for S_N2 reactions. Electron-releasing substituents in the nucleophile as well as electron-withdrawing substituents in the substrate enhance the rate of substitution. The kinetic data for the reactions of various phenacyl bromides with a given cinnamate ion and various cinnamate ions with a given substrate have been correlated with Hammett σ constants. Table 3 gives ρ values at 35 °C for substituent variation in phenacyl bromide for each cinnamate ion while Table 4 contains reaction constants for substituent variation in cinnamate ion for each phenacyl bromide. Results of correlation analysis show only a minor variation of Hammett slopes when we consider substituent variation either in the nucleophile or in the substrate.

Table 3. Results of correlation analysis for the reaction of various phenacyl bromides with a given substituted cinnamate ion

X	ρ	r	s
p-Me	1.09 ± 0.17	0.991	0.055
m-Me	1.07 ± 0.19	0.988	0.062
H	1.08 ± 0.17	0.990	0.057
p-Cl	1.06 ± 0.20	0.986	0.067
p-Br	1.07 ± 0.21	0.986	0.068
m-Cl	1.06 ± 0.20	0.987	0.064
m-NO_2	1.04 ± 0.20	0.987	0.065
p-NO_2	1.04 ± 0.21	0.985	0.069

The number of points is 7 throughout.

Table 4. Results of correlation analysis for the reaction of various cinnamates with a given substituted phenacyl bromide

Z	ρ	r	s
OMe	−0.219 ± 0.044	0.980	0.017
Me	−0.218 ± 0.028	0.992	0.011
H	−0.216 ± 0.041	0.982	0.015
F	−0.199 ± 0.016	0.997	0.006
Cl	−0.241 ± 0.045	0.983	0.017
Br	−0.212 ± 0.028	0.992	0.010
NO_2	−0.260 ± 0.029	0.994	0.011

The number of points is 8 throughout.

Table 5. Correlations by equation (2)

X	a	b	r	s	$\rho_X/\rho_{X=H}$
p-Me	1.00 ± 0.06	0.027	0.999	0.021	1.01
m-Me	0.989 ± 0.045	0.023	0.999	0.016	0.987
H	1.00	0.0	1.00		1.00
p-Cl	0.982 ± 0.070	0.038	0.998	0.025	0.980
p-Br	0.992 ± 0.044	0.014	0.999	0.016	0.988
m-Cl	0.982 ± 0.056	0.028	0.999	0.020	0.980
m-NO_2	0.969 ± 0.037	0.016	0.999	0.013	0.966
p-NO_2	0.969 ± 0.049	0.018	0.999	0.018	0.964

The number of points is 7.

log k_Z/k_H for a given cinnamate has been correlated with the same ratio of another cinnamate by employing equation (2)

$$\log (k_Z/k_H)_X = a \log (k_Z/k_H)_{X=H} + b \qquad (2)$$

and the results are presented in Table 5. In each case it is observed that the intercept b is nearly zero. The values of a are practically coincident with the corresponding ratios of $(\rho_X/\rho_{X=H})$. This provides a significant test of the correlation in these reaction series.[20]

Activation Parameters.—The enthalpies and entropies of activation for the reactions of cinnamate ion with *para*-substituted phenacyl bromides have been evaluated from the Arrhenius plots and are presented in Table 1. The entropies of activation are negative in all cases as expected for bimolecular nucleophilic substitution reactions. Since $\Delta\Delta H^{\ddagger}$ is 5 kJ mol^{-1} in the reaction series and δ, the calculated maximum probable error in $\Delta H^{\ddagger}$, is 6.7 kJ mol^{-1}, the reaction does not satisfy the error criterion proposed by Petersen *et al.*[21] for the validity of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ correlation to be significant. The small values of $\Delta \log k$ and $\Delta\Delta H^{\ddagger}$ show that all the substrates behave similarly. However, the plot of $\log k_{40^\circ}$ *versus* $\log k_{30^\circ}$ is linear (r 0.999; s 0.015) indicating the operation of one and the same mechanism in all reactions.[22]

Reactivity–Selectivity Principle (*RSP*).—According to the RSP, selectivity as measured by ρ and β parameters in a series of related processes on varying the reagent or substrate bears an inverse relationship to reactivity.[23–25] It has been suggested that the factors [26,27] which contribute to the apparent failure of the RSP are (i) solvent effects, (ii) appreciable structural changes along a reaction series, in either the substrate or the reagent, at or near the reaction site, and (iii) change in mechanism. The present reaction series seem to be suitable for the unambiguous demonstration of RSP since a constant mechanism is assured. But the results of correlation analyses demonstrate constant selectivity either in the reactions of various phenacyl bromides with a given cinnamate ion (ρ *ca.* 1.05) or in the reactions of various cinnamate ions with a given phenacyl bromide (ρ *ca.* -0.20) even though the reactivity range is *ca.* 20 (Table 2). These facts show that in these simple reactions reactivity–selectivity effects are absent. We have reported many simple S_N2 reactions [28–30] where the reactivity–selectivity effects are absent and the present study is yet another example of simple reaction series where RSP fails.

Experimental

Materials.—Substituted *trans*-cinnamic acids used were prepared by the condensation of malonic acid with appropriate benzaldehydes. These acids were crystallised from suitable solvents and their purities were checked by m.p. and ^{1}H n.m.r. Phenacyl bromide and substituted phenacyl bromides were prepared by literature methods.[31,32]

Rate Measurements.—The kinetic procedure was similar to that used by Mishra and his co-workers.[33] The solvent used in all the kinetic measurements was 90% acetone–10% water (v/v). The solutions of the sodium salt of the acids and phenacyl bromides were prepared just before use. The second-order rate constants were calculated by the method of least squares. The precision of k_2 values is given in terms of 95% confidence limit, calculated with the 'Student t' test.

Product Analysis.—Equal volumes of equimolar solutions of sodium salt of the acid and phenacyl bromide in 90% acetone–10% water (v/v) were mixed and kept overnight. The acetone was removed under slightly reduced pressure. The residual liquid was extracted with carbon tetrachloride, dried (anhydrous Na_2SO_4), solvent removed carefully, and the residue (yield 95%) examined by t.l.c. whereupon only one spot was obtained in each reaction. The i.r. and n.m.r. spectral data show that the product in the reaction of sodium benzoate, m.p. 116—117 °C (lit.,[34] 118.5 °C), is $C_6H_5COOCH_2COC_6H_5$, δ ($CDCl_3$) 7.45—8.40 (10 H, m, aromatic) and 5.71 (2 H, s, CH_2) and in the reaction of sodium cinnamate, m.p. 138—139 °C (lit.,[34] 140.5 °C), is $C_6H_5CH{=}CHCOOCH_2COC_6H_5$, δ ($CDCl_3$) 6.5—8.2 (12 H, m, aromatic and 2 H olefinic) and 5.45 (2 H, s, CH_2). The formation of a single product shows that these reactions are purely simple nucleophilic substitution reactions.

Acknowledgements

We thank the University Services and Instrumentation Centre for providing instrument facilities. One of us (A. S.) thanks the Madurai Kamaraj University and the U.G.C., New Delhi, for the award of a Teacher Fellowship under F.I.P and the V.H.N.S.N. College, Virudhunager, for permission to accept the fellowship. We are indebted to Dr. C. D. Johnson, University of East Anglia, for helpful suggestions.

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Received 13*th September* 1983; *Paper* 3/1613