The Separation of Polar and Steric Effects in the Reaction of *ortho*-Substituted Benzoate Ions with Ethyl Bromoacetate

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The second-order rate coefficients for the reactions of *ortho*-substituted benzoate ions with ethyl bromoacetate have been measured in a 90% acetone–10% water (v/v) mixture at three different temperatures and the results have been compared with those of phenacyl bromide. The order of reactivity of *ortho*-substituted benzoate ions with ethyl bromoacetate is almost the same as that observed for the reaction of *ortho*-substituted benzoate ions with phenacyl bromide. Attempts have been made to analyse the rate data in terms of electronic and steric effects by employing Charton's treatment. Analysis of the results shows that the localized effect is predominant over the delocalized effect in each reaction series and electron-releasing groups favour the reaction and electron-withdrawing groups retard it. The steric term is rate accelerating. The $\Delta S^\ddagger$ values for all the *ortho*-substituted benzoate ions are negative and it appears that the bulk effect of the substituent plays a part in the variation of $\Delta S^\ddagger$.

Analysis of the chemical and physical properties of *ortho*-substituted aromatic compounds is somewhat difficult because of the possible interaction of the substituent with the *ortho*-site through the electrical effect, van der Waals forces, hydrogen bonding, and steric factors. Numerous attempts have been made to analyse and understand the nature and composition of the *ortho*-effect [1-4] quantitatively by separating the component effects from each other. Of the various approaches to the *ortho*-effect, Charton's treatment [3-6] is considered to be a better treatment because of its wider applicability in understanding the nature of the *ortho*-effect.

We have previously reported the kinetics of the reactions of *meta*- and *para*-substituted benzoate and cinnamate ions with ethyl bromoacetate in a 90% acetone–10% water (v/v) mixture.[7,8] As a continuation of our work on the reactivity of ethyl bromoacetate we now report the S_N2 reaction of a few *ortho*-substituted benzoate ions with ethyl bromoacetate in 90% acetone–10% water (v/v) mixture. The rate data have been correlated with various single-parameter equations and extended Hammett equations involving inductive, resonance, and steric parameters. The reaction of ethyl bromoacetate with *ortho*-substituted benzoate ions has been compared with that of phenacyl bromide.

Discussion

The reaction between ethyl bromoacetate and benzoate ions follows second-order kinetics and can be represented by equation (1), where X is the substituent present in the *ortho*-position of the benzene nucleus.

$$XC_6H_4CO_2^- + BrCH_2CO_2Et = XC_6H_4CO_2CH_2CO_2Et + Br^- \quad (1)$$

The procedure employed for the kinetic studies was essentially the same as that employed for the reaction of *meta*- and *para*-substituted benzoate ions with ethyl bromoacetate.[7] The second-order rate constants measured at 30, 35, and 40 °C, activation parameters, and *ortho* to *para* ratio of the rate constants are given in Table 1. For the purpose of comparison, the rate constants for the reaction of *ortho*-substituted benzoate ions with phenacyl bromide [12] at 35 °C are given in Table 2.

The *ortho* to *para* ratio of the rate constants for the reaction of ethyl bromoacetate shows that the *ortho*-methyl-, chloro-, bromo-, and iodo-substituent facilitate the reaction noticeably as compared with the corresponding *para*-substituents whereas the *ortho*-methoxy-, acetamido-, and nitro-substituent retard the reaction. Comparison of the rate data of ethyl bromoacetate with those of phenacyl bromide shows that ethyl bromoacetate is less reactive than phenacyl bromide, as observed in the reactions of *meta*- and *para*-substituted benzoate ions with ethyl bromoacetate and phenacyl bromide.[7]

The rate data were analysed with Taft's linear free energy–polar energy and linear free energy–steric energy relationships.[1] The results may be expressed by equations (2) and (3) for ethyl bromoacetate and by (4) and (5) for phenacyl bromide. The values of σ_o^* and E_s were those given by Taft.[1]

$$\log k = -0.662\sigma_o^* - 2.750 \qquad r = 0.806;\ s = 0.199;\ n = 7 \quad (2)$$

$$\log k = 0.270E_s - 2.994 \qquad r = 0.480;\ s = 0.294;\ n = 7 \quad (3)$$

$$\log k = -0.401\sigma_o^* - 1.726 \qquad r = 0.759;\ s = 0.144;\ n = 7 \quad (4)$$

$$\log k = -0.103E_s - 1.870 \qquad r = 0.279;\ s = 0.212;\ n = 7 \quad (5)$$

The substituents SO_2, SO_2Me, NHCOMe, and OAc were not included since no reliable σ_o^* and E_s values are available. The results of the analyses show that the observed reactivity of *ortho*-substituted benzoate ions with ethyl bromoacetate and phenacyl bromide is not compatible with either the size of the substituents or with their Taft's polar substituent parameter.

Very often, the ratio of the rate constants for similar *ortho*- and *para*-substituted benzene systems has been taken as a measure of the steric effect of the *ortho*-substituent.[13] A poor correlation is obtained between $\log k_{ortho}/k_{para}$ *versus* E_s, equation (6). These analyses indicate the minor role of the 'primary steric effect.'

$$\log k_{ortho}/k_{para} = 0.196E_s - 0.006 \qquad r = 0.259;\ s = 0.250;\ n = 6 \quad (6)$$

The lack of primary bulk effect can be understood by the fact that the point of attack is the oxygen atom of the carboxylate anion, which is relatively far away from the substituent in the benzene ring.

Since the single-parameter equations did not yield satisfactory correlations, the rate data were analysed using Charton's method.[5] The rate constants were correlated with the following equations (7) and (8). In equations (7) and (8), σ_I, σ_R, and ν are inductive, resonance, and steric substituent

Table 1. Second-order rate constants and activation parameters for the reactions of *ortho*-substituted benzoate ions with ethyl bromoacetate in a 90% acetone–10% water (v/v) mixture $[X\text{-}C_6H_4CO_2^-] = 0.01$ mol dm^{-3}; [ethyl bromoacetate] = 0.0486 mol dm^{-3}. The error quoted in k is the 95% confidence limits of the Student's t.[9,10] The precision of $\Delta H^‡$ and $\Delta S^‡$ values is calculated using the method of Petersen *et al.*[11]

Sample no.	X	10^3k_2/dm^3 mol^{-1} s^{-1} 30 °C	35 °C	40 °C	$\Delta H^‡$/kJ mol^{-1} (at 35 °C)	$-\Delta S^‡$/ J K^{-1} mol^{-1} (at 35 °C)	k_{ortho}/k_{para}
1	Me	1.54 ± 0.04	2.47 ± 0.08	3.62 ± 0.07	65.1 ± 4.1	83.7 ± 13.7	1.68
2	SMe	1.29 ± 0.07	2.03 ± 0.04	2.94 ± 0.06	62.6 ± 5.0	93.7 ± 16.7	
3	I	1.01 ± 0.02	1.58 ± 0.03	2.30 ± 0.05	62.7 ± 3.2	95.2 ± 10.7	1.44
4	H	0.835 ± 0.03	1.35 ± 0.07	2.06 ± 0.07	74.9 ± 6.2	56.9 ± 20.9	1.00
5	OMe	0.801 ± 0.01	1.28 ± 0.03	1.96 ± 0.03	68.2 ± 2.9	79.4 ± 9.7	0.77
6	Br	0.748 ± 0.01	1.24 ± 0.02	1.78 ± 0.05	66.1 ± 3.2	86.3 ± 10.9	1.24
7	Cl	0.744 ± 0.01	1.17 ± 0.04	1.84 ± 0.06	69.0 ± 4.1	77.3 ± 13.6	1.09
8	F	0.565 ± 0.01	0.920 ± 0.01	1.48 ± 0.05	73.7 ± 3.4	64.3 ± 11.4	
9	SO_2Me	0.614 ± 0.01	0.946 ± 0.01	1.38 ± 0.05	61.7 ± 3.4	103.0 ± 11.5	
10	NO_2	0.166 ± 0.01	0.256 ± 0.01	0.385 ± 0.02	64.0 ± 6.6	106.4 ± 22.1	0.39
11	OAc	0.891 ± 0.03	1.30 ± 0.04	1.85 ± 0.10	55.2 ± 6.0	121.3 ± 20.1	
12	NHCOMe	0.473 ± 0.01	0.768 ± 0.03	1.08 ± 0.04	62.8 ± 4.4	101.0 ± 14.8	0.56

Table 2. Second-order rate constants [a] for the reaction of phenacyl bromide with *ortho*-substituted benzoate ions in a 90% acetone–10% water (v/v) mixture at 35 °C

Sample no.	Substituent	10^3k_2/dm^3 mol^{-1} s^{-1}
1	Me	30.2
2	SMe	22.3
3	I	18.6
4	H	12.6
5	OMe	16.0 [b]
6	Br	12.4
7	Cl	11.5
8	F	10.5 [b]
9	SO_2Me	10.7
10	NO_2	7.1

[a] Data from ref. 12. [b] Data obtained in the present investigation.

constants and the values used were those compiled by Aslam *et al.*[6] The results of the regression equation (7) may be expressed by the correlation given in equation (9) with ethyl bromoacetate.

$$\log k_{ortho} = \alpha\sigma_I + \beta\sigma_R + h \qquad (7)$$

$$\log k_{ortho} = \alpha\sigma_I + \beta\sigma_R + \varphi\upsilon + h \qquad (8)$$

$$\begin{gathered}\log k = -0.762\sigma_I - 0.262\sigma_R - 2.725 \qquad (9)\\ \pm 0.283 \quad \pm 0.294\\ R = 0.695;\ \text{s.e.} = 0.197;\ n = 12;\ \text{c.l.} < 90\%\end{gathered}$$

The correlation is slightly improved by the exclusion of OAc and NHCOMe groups, equation (10) with ethyl bromoacetate, equation (11) with phenacyl bromide. In the multiple regression analysis using the regression equation (7), the correlation coefficients are poor, and the standard errors of estimate and regression coefficients are high. The absence of significant correlation with equation (7) leads to the conclusion that the electrical effects alone are not sufficient to account for the *ortho*-substituent effect in these two series of reactions.

$$\begin{gathered}\log k = -0.810\sigma_2 - 0.307\sigma_R - 2.698 \qquad (10)\\ \pm 0.322 \quad \pm 0.358\\ R = 0.758;\ \text{s.e.} = 0.198;\ n = 10;\ \text{c.l.} < 90\%\end{gathered}$$

$$\begin{gathered}\log k = -0.562\sigma_I - 0.195\sigma_R - 1.686 \qquad (11)\\ \pm 0.195 \quad \pm 0.203\\ R = 0.760;\ \text{s.e.} = 0.135;\ n = 10;\ \text{c.l.} < 90\%\end{gathered}$$

The correlations with equation (8) were performed at temperatures of 30, 35, and 40 °C. The correlation obtained for the *ortho*-substituted benzoate ions with ethyl bromoacetate using the equation (8) is not very successful when all 12 substituents are included. The correlation is very much improved by excluding the *o*-OAc and *o*-NHCOMe groups. This may be due to the uncertainty in the υ value for these two groups. The correlation results for the reaction of ethyl bromoacetate with *ortho*-substituted benzoates are given in equations (12), (13), and (14), at 30, 35, and 40 °C, respectively.

$$\begin{gathered}\log k = -1.099\sigma_I - 0.517\sigma_R + 0.550\upsilon - 3.129 \qquad (12)\\ \pm 0.157 \quad \pm 0.156 \quad \pm 0.117\\ R = 0.952;\ \text{s.e.} = 0.099;\ n = 10;\ \text{c.l.} = 99.5\%\end{gathered}$$

$$\begin{gathered}\log k = -1.111\sigma_I - 0.535\sigma_R + 0.543\upsilon - 2.923 \qquad (13)\\ \pm 0.163 \quad \pm 0.163 \quad \pm 0.122\\ R = 0.950;\ \text{s.e.} = 0.103;\ n = 10;\ \text{c.l.} = 99.5\%\end{gathered}$$

$$\begin{gathered}\log k = -1.081\sigma_I - 0.549\sigma_R + 0.507\upsilon - 2.742 \qquad (14)\\ \pm 0.170 \quad \pm 0.169 \quad \pm 0.126\\ R = 0.943;\ \text{s.e.} = 0.107;\ n = 10;\ \text{c.l.} = 99.5\%\end{gathered}$$

A similar correlation for the reaction of phenacyl bromide with *ortho*-substituted benzoate at 35 °C is given in equation (15). In both reaction series the effect of the *o*-NO_2 group is consistent with the orthogonal conformation.[6]

$$\begin{gathered}\log k = -0.761\sigma_I - 0.346\sigma_R + 0.360\upsilon - 1.835 \qquad (15)\\ \pm 0.120 \quad \pm 0.120 \quad \pm 0.090\\ R = 0.941;\ \text{s.e.} = 0.076;\ n = 10;\ \text{c.l.} = 99.5\%\end{gathered}$$

The significance of the correlation was tested by means of the F-test. The confidence levels of the F-test for both ethyl bromoacetate and phenacyl bromide sets are greater than 95%. The confidence levels for the significance of the φ term were obtained by means of Student's t-test. The confidence levels of the t-test are greater than 95%, indicating the operation of a significant steric effect. These results show that the two sets belong to case 1 of the classification given by Charton.[5]

The regression coefficients of σ_I and σ_R are all negative, which shows that electron-releasing groups accelerate the reaction and electron-withdrawing groups retard it, as found for *meta-* and *para*-substituents. The positive regression coefficient for the steric term corresponds to the reaction being subject to steric acceleration by *ortho*-substituents. The composition of the electrical effect,[5] P_R, was calculated using equation (16).

$$P_R = \beta 100/\alpha + \beta \qquad (16)$$

The values of P_R are estimated to be 32.5 and 31.3 for the reactions of ethyl bromoacetate and phenacyl bromide with *ortho*-substituted benzoate ions, respectively. The values of P_R show that the localized effect is more dominant than the delocalized effect. The low value of P_R in these two reaction series may be due to the twisting of the carboxylate group from the plane of the benzene ring. The magnitude (per cent.) of the steric effect,[5] P_s, was calculated using relationship (17).

$$P_S = \frac{|\varphi|\,100}{|\alpha| + |\beta| + |\varphi|} \qquad (17)$$

The magnitudes (per cent.) of the steric effect are found to be 24.8 and 24.5 for the reactions of ethyl bromoacetate and phenacyl bromide, respectively, which shows that the steric effect is considerable in these two series. The magnitudes of α, β, and φ reveal that the reactions are more susceptible to the inductive effect than the resonance and steric effects.

The behaviour of various *ortho*-substituted benzoate ions may be accounted for by both electronic and steric effects. The steric acceleration may arise due to the fact that the carboxylate group can rotate freely about the $Ph-CO_2^-$ bond since the barrier to rotation is low. An *ortho*-substituent may cause the molecule to be in the orthogonal conformation because of its bulkiness. The attack of the benzoate ions on ethyl bromoacetate with such a conformation will be easier as the substrate will be farthest from the *ortho*-substituents.

The *ortho*-methylthiobenzoate ion reacts faster than the *ortho*-methoxybenzoate ion. The low reactivity of *ortho*-methoxybenzoate ion may be due to the predominance of the electron-withdrawing inductive effect of the oxygen atom over sulphur and also to the small size of the methoxy group. The order of reactivity in the halogen-substituted benzoate ions is I > Br ≈ Cl. If the reactivity is due to the electrical effect alone, then there should be a greater inductive effect in the *ortho*-position and this will cause a decrease in the reactivity compared with the corresponding *meta-* and *para*-halogeno compounds. The observed rate increase may be due to the steric acceleration, which may at least in part be due to solvation around the carbon–halogen dipole. The rates of *ortho*-nitrobenzoate and *ortho*-methylsulphonylbenzoate ions are very much lower than that of the unsubstituted benzoate ion and may be attributed to the dominant electronic effect. The reactivity of *ortho*-acetamidobenzoate ion is less than that of the corresponding *para*-substituted compound. The low nucleophilic activity may be due to the stabilisation of carboxylate ion by internal hydrogen bonding between the NH and a negatively charged oxygen in the carboxylate ion.

Activation Parameters.—The $\Delta S^‡$ values are all negative, as expected for S_N2 reactions. It is found that the enthalpies of activation are slightly lower than those reported for the reaction of corresponding *para*-substituted benzoates with ethyl bromoacetate and entropies of activation are slightly more negative. It is found that the $\Delta S^‡$ values for all the *ortho*-substituted compounds are more negative than those of the unsubstituted compounds. It appears that the bulk effect of the substituents plays a role in the variation of $\Delta S^‡$. The methyl- and bromo-substituents have approximately the same size. However, the $\Delta S^‡$ value for the *ortho*-bromo-compound is found to be slightly more negative, which may be due to the increase in effective radius of the reaction site as a result of increased solvation caused by the negative end of the carbon–bromine dipole. The plot of $\Delta H^‡$ against $\Delta S^‡$ is linear. An Exner plot of log*k* at 40 *versus* log*k* at 30 °C is also linear. The existence of good correlations in both the plots shows that in this reaction series all the *ortho*-substituted benzoate ions follow the same mechanism.[14]

Experimental

Materials.—Ethyl bromoacetate (E. Merck) was purified by repeated distillation and the collected middle fraction stored in an amber-coloured vessel in a P_2O_5 desiccator. Acetone was purified by the method of Sachs.[15] *ortho*-Substituted benzoic acids were either commercial samples or prepared by literature methods. *s*-Methylthiosalicylic acid and *ortho*-methylsulphonylbenzoic acid were prepared from thiosalicylic acid.[6]

Rate Measurements.—The solvent employed in all the kinetic measurements was a 90% acetone–10% water (v/v) mixture. The kinetics were followed by mixing equal volumes of equimolar solutions of sodium benzoate and ethyl bromoacetate and estimating the bromide ion by the Volhard method as reported previously.[7] The solutions of ethyl bromoacetate and sodium benzoate were prepared just prior to use. The second-order rate constants were calculated by the method of least-squares using a Micro 2200 Diskette recorder (Hindustan Computers). The precision of the k_2 values is given in terms of 95% confidence limits,[9,10] calculated with Student's *t*. The activation parameters were evaluated from the Arrhenius plots. The precision of $\Delta H^‡$ and $\Delta S^‡$ values was calculated using the method of Petersen *et al.*[11] Solvolysis of ethyl bromoacetate was negligible under the experimental conditions.

Acknowledgements

The authors thank the University Services and Instrumentation Centre for providing facilities to perform calculations on a Micro 2200 Diskette recorder (Hindustan Computers). One of the authors (A. S.) expresses his thanks to the Madurai Kamaraj University and the U.G.C., New Delhi, for the award of a Teacher Fellowship under FIP and to the VHNSN college for permitting acceptance of the fellowship.

References

1 R. W. Taft, 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, John Wiley, New York, 1956, ch. 13.
2 W. A. Pavelich and R. W. Taft, Jr., *J. Am. Chem. Soc.*, 1957, **79**, 4935.
3 M. Charton, *Prog. Phys. Org. Chem.*, 1971, **8**, 235.
4 T. Fujita and T. Nishioka, *Prog. Phys. Org. Chem.*, 1976, **12**, 49.
5 M. Charton, *J. Org. Chem.*, 1975, **40**, 407.
6 M. H. Aslam, A. G. Burden, N. B. Chapman, J. Shorter, and M. Charton, *J. Chem. Soc., Perkin Trans. 2*, 1981, 500.
7 C. Srinivasan, A. Shunmugasundaram, and N. Arumugam, *Indian J. Chem., Sect. B*, 1981, **20**, 1057.
8 C. Srinivasan, A. Shunmugasundaram, and N. Arumugam, *Indian J. Chem., Sect. B*, 1982, **21**, 355.
9 R. J. Cvetanovic, D. L. Singleton, and G. Paraskevopoulos, *J. Phys. Chem.*, 1979, **83**, 50.

10 C. Srinivasan, P. Kuthalingam, and N. Arumugam, *J. Chem. Soc., Perkin Trans. 2*, 1980, 170.

11 R. C. Petersen, J. H. Markgraf, and S. D. Ross, *J. Am. Chem. Soc.*, 1961, **83**, 3819.

12 P. Ananthakrishna Nadar and A. Shunmugasundaram, *Indian J. Chem., Sect. A*, 1976, **14**, 805.

13 R. W. Taft, M. S. Newman, and F. H. Verhoek, *J. Am. Chem. Soc.*, 1950, **72**, 4511.

14 J. E. Leffler, *J. Org. Chem.*, 1955, **20**, 1205.

15 F. Sachs, *Ber. Dtsch. Chem. Ges.*, 1901, **34**, 494.

Received 6th April 1983; *Paper* 3/540