Structure-reactivity correlations in the reaction of ethyl bromoacetate with aliphatic carboxylate ions

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Abstract. The second-order rate constants at three different temperatures have been determined for nucleophilic substitution reactions of ethyl bromoacetate with various substituted aliphatic carboxylate ions (XCH_2COO^-) in 90% acetone–10% water (v/v) mixture and the activation parameters have been evaluated. The rate data have been analysed in terms of electronic and steric effects by using various single and multi-parameter equations. Analysis of the results shows that localized and steric effects are more important than the delocalized effect. The regression coefficient of the inductive component is negative indicating that inductively electron-releasing substituents accelerate the reaction and electron-withdrawing substituents retard it. The steric component corresponds to the reaction being subject to steric acceleration by the substituents. The per cent steric effect has been calculated. The Brönsted type correlation is fair, and the β_N value has been determined.

Keywords. Ethyl bromoacetate; substituted aliphatic carboxylate ions; multi-parameter equations; substituent effect; Brönsted relationship.

1. Introduction

Although a number of kinetic studies have been reported on the nucleophilic substitution reactions of α-haloketones, there has been only limited study involving α-haloesters. We have previously reported the kinetics of the reactions of various substituted benzoate (Srinivasan *et al* 1981, 1984) and cinnamate ions (Srinivasan *et al* 1982a), and anilines (Srinivasan *et al* 1982b) with ethyl bromoacetate. As a continuation of our work on the reactivity of ethyl bromoacetate we now report the S_N2 reaction of various aliphatic carboxylate ions with ethyl bromoacetate in 90% acetone–10% water (v/v) mixture. The rate data have been analysed with different single-parameter and multi-parameter extensions of linear free energy relationships in order to investigate the effect of structure on reactivity and to separate the polar and steric effects.

2. Experimental

Ethyl bromoacetate (E Merck) was purified by repeated distillation and the collected middle fraction stored in an amber-coloured bottle in a desiccator over P_2O_5. The

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carboxylic acids were either commercial samples or prepared by literature methods.

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 solutions of sodium salt and ethyl bromoacetate and estimating the bromide ion by the Volhard method. The solutions of ethyl bromoacetate and sodium salt of the carboxylic acids were prepared just prior to use. Solvolysis of ethyl bromoacetate was negligible under the experimental conditions.

Solutions of sodium acetate and ethyl bromoacetate were mixed under experimental conditions and kept overnight. Acetone was then removed under slightly reduced pressure. The residual liquid was extracted with carbon tetrachloride, dried (anhydrous Na_2SO_4), the solvent removed carefully and the residue examined by TLC. TLC showed two spots, one corresponding to the unreacted ethyl bromoacetate and another corresponding to the product. The spot due to the product corresponded to the authentic sample of $CH_3COOCH_2COOC_2H_5$ [^1H NMR ($CDCl_3$): $4.63\,\delta$ (2H, s, CH_2), $4.26\,\delta$ (2H, q, CH_2 adjacent to CH_3), $2.18\,\delta$ (3H, s, CH_3) and $1.30\,\delta$ (3H, t, CH_3 adjacent to CH_2)].

3. Results and discussion

Nucleophilic substitution reactions between ethyl bromoacetate and aliphatic carboxylate ions can be represented by the following general equation,

$$XCOO^- + BrCH_2COOC_2H_5 = XCOOCH_2COOC_2H_5 + Br^-.$$
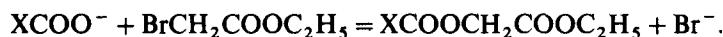
The reaction was studied under second-order conditions at unequal concentrations of the nucleophile and the substrate in 90% acetone–10% water (v/v) mixture. The second-order rate constants measured for the various aliphatic carboxylate ions at 30, 35 and 40°C and the activation parameters are shown in table 1. The rate data have been analysed using various single and multi-parameter extensions of the linear free energy relationships involving inductive, resonance and steric parameters.

The results of Taft's linear free energy–polar energy relationship and linear free energy–steric energy relationship (Taft 1956) are expressed by (1) and (2) respectively.

$$\log k_{35°} = -0.528\sigma^* - 2.796, \tag{1}$$
$$(\pm 0.416)$$

$$n = 15; r = 0.619; s = 0.344.$$

(the substituent CH_2CH_2COOH is not included in the correlation as there is no reliable σ^* constant),

$$\log k_{35°} = 0.012E_s - 3.054, \tag{2}$$
$$(\pm 0.333)$$

$$n = 15; r = 0.023; s = 0.474.$$

(the E_s value of the substituent, $PhSO_2CH_2$, is not available), where σ^* is the polar substituent constant and E_s is the steric substituent constant. The values of σ^* and E_s were essentially those given by Taft (1956). A poor correlation with σ^* and E_s values

Table 1. Second-order rate constants and activation parameters for the reaction of ethyl bromoacetate with various carboxylate ions in 90% acetone–10% water (v/v) mixture. [XCOO$^-$] = 0·01 mol dm^{-3}; [ethyl bromoacetate] = 0·06 mol dm^{-3}

	$k_2 (10^4 dm^3 mol^{-1} s^{-1})$ at temperatures			$\Delta H^{\neq}$ kJ mol^{-1} (at 35°C)	$-\Delta S^{\neq}$ JK^{-1} mol^{-1} (at 35°C)
X	30°C	35°C	40°C		
CH$_3$CH$_2$CH$_2$	15·72	25·53	40·60	70·2	67·2
(CH$_3$)$_2$CHCH$_2$	14·80	23·67	38·30	68·3	73·8
(CH$_3$)$_2$CH	13·62	20·67	34·31	65·6	83·9
CH$_3$CH$_2$	11·50	17·70	28·43	70·1	70·3
PhCH$_2$	10·93	15·70	26·66	66·9	81·5
Ph	8·35	13·50	20·60	71·7	67·4
CH$_3$	8·34	13·08	19·80	64·8	90·5
PhCH=CH	8·08	12·50	19·70	64·8	90·5
PhSCH$_2$	7·23	11·90	17·63	72·7	65·4
H	5·32	8·99	12·40	78·9	47·1
BrCH$_2$	4·26	6·43	11·01	71·5	74·3
PhSO$_2$CH$_2$	3·77	5·66	8·84	63·3	102
PhOCH$_2$	3·74	5·31	8·63	63·3	102
ClCH$_2$	3·32	5·07	7·90	65·2	96·7
HOOCCH$_2$CH$_2$	1·74	2·27	3·07	42·6	177
HOOCCH$_2$	0·426	0·553	0·776	38·2	209

shows that the reactivity of ethyl bromoacetate with aliphatic carboxylate ions does not solely depend upon either Taft's polar effects of the substituents or the size of the substituents. The lack of correlation with the E_s parameter also shows that there is no primary steric effect. This may be due to the fact that the oxygen atom of the carboxylate anion is far away from the substituent.

In the aliphatic reactions of the compounds, XCH$_2$Y, the substituent X is insulated from resonance by a methylene group and hence the effect of X must be inductive in nature. The rate data for the reaction of ethyl bromoacetate with various substituted aliphatic carboxylate ions were correlated with Charton's σ_I values (Charton 1964), derived on the basis of ionisation of aliphatic carboxylic acids. The result of the correlation is represented by the following expression,

$$\log k_{35°} = -1·278\sigma_I - 2·764,$$
$$(\pm 1·159)$$

$$n = 12; r = 0·614; s = 0·382.$$

(3)

The substituent CH$_2$CH$_2$COOH is not included because of the nonavailability of the σ_I constant. The correlation is found to be improved considerably by the exclusion of the substituent, CH$_2$COOH. The improved correlation is given by the following equation:

$$\log k_{35°} = -1·094\sigma_I - 2·702,$$
$$(\pm 0·219)$$

$$n = 11; r = 0·931; s = 0·105.$$

(4)

The rate data were examined with the following multi-parameter extensions of the Hammett relationship in order to determine the composition of the various effects.

$$\log k_{35°} = \rho^* \sigma^* + SE_s + h,\qquad(5)$$

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

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

where σ_I and σ_R are the inductive and resonance substituent constants, L, D and S are the regression coefficients of localized, delocalized and steric components. The values of σ_I and σ_R are those obtained by Charton (1981). The significance of the correlation with the above equations was tested by means of the F-test. The significance of the regression coefficients was tested by means of the 'student t' test.

The result of the regression equation (5) is given by (8) and (9),

$$\log k_{35°} = -0.645\sigma^* - 0.058E_s - 2.808,\qquad(8)$$
$$(\pm 0.232)\ (\pm 0.117)$$

$$n = 13; R = 0.664; SE = 0.360; CL < 90\%.$$

(The substituents $PhSCH_2$, $PhSO_2CH_2$ and CH_2CH_2COOH are not included in the above correlation.)

The correlation is improved with the exclusion of CH_2COOH.

$$\log k_{35°} = -0.496\sigma^* - 0.065E_s - 2.774,\qquad(9)$$
$$(\pm 0.048)\ (\pm 0.024)$$

$$n = 12; R = 0.962; SE = 0.073; CL = 99.9\%.$$

Equations (10) and (11) give results of the correlation with (6) and (7). In both these correlations, CH_2COOH is not included.

$$\log k_{35°} = -1.604\sigma_I + 0.146\sigma_R - 2.688,\qquad(10)$$
$$(\pm 0.167)\ (\pm 0.243)$$

$$n = 10; R = 0.928; SE = 0.115; CL = 99.5\%.$$

$$\log k_{35°} = -2.244\sigma_I - 0.215\sigma_R - 0.265E_s - 2.778,\qquad(11)$$
$$(\pm 0.590)\ (\pm 0.381)\ (\pm 0.134)$$

$$n = 9; R = 0.969; SE = 0.094; CL = 99.5\%.$$

In the above equations, the F-test significance is above 99.5% which shows that the correlations are meaningful. The confidence level for the significance of the localized term tested by the student t-test is above 95% and that of the delocalized term is below 90%. These observations show that the inductive effect is more important than the resonance effect. The confidence level of the t-test significance of the steric term in (11) is above 95% which shows that the steric effect is also important in this reaction series. The negative sign of the σ_I term indicates that the inductively electron-releasing substituents accelerate the reaction while electron-withdrawing groups retard it. The negative sign of the steric term corresponds to steric acceleration by the substituents. The magnitude of the per cent steric effect, P_S, is 17.2%, which shows that the steric

effect also operates in this reaction. The steric acceleration in this reaction may be due to the fact that a bulky substituent makes the carboxylate group orient it self furthest away from the substituent and also due to the reduction of extent of solvation of the carboxylate ion so that the approach of the two molecules is facilitated.

The Brönsted-type relationship between $\log k_{35°}$ and pK_a values of the corresponding conjugate acid of the nucleophile in the reaction of aliphatic carboxylate ions with ethyl bromoacetate may be represented by

$$\log k_{35°} = 0.258 \, pK_a - 3.953, \qquad (12)$$
$$(\pm 0.046)$$

$$n = 14; r = 0.925; s = 0.095,$$

(CH_2COOH and CH_2CH_2COOH substituents are omitted).

A fair correlation 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. The low value of the Brönsted coefficient indicates that there is relatively little bond-making in the transition state.

The enthalpies and entropies of activation are presented in table 1. The entropies of activation are all negative as expected for bimolecular nucleophilic substitution reactions. The entropies of activation of the carboxylate ions, except those of malonate and succinate ions, are comparable to those of benzoate and cinnamate ions (Srinivasan *et al* 1981, 1982a, 1984). The average value $\Delta S^{\neq}$ is very much less than that observed for anilines (Srinivasan *et al* 1982b). These exists a linear relationship between $\Delta H^{\neq}$ and $\Delta S^{\neq}$ ($r = 0.991$). The plot of $\log k_2$ at 313 K versus $\log k_2$ at 303 K is also linear ($r = 0.999$). The existence of a good correlation in the Exner plot shows that all the carboxylate ions in this reaction series have the same mechanism (Leffler 1955).

Acknowledgements

References

Charton M 1964 *J. Org. Chem.* **29** 1222
Charton M 1981 *Prog. Phys. Org. Chem.* **13** 119
Leffler J R 1955 *J. Org. Chem.* **20** 1205
Srinivasan C, Shunmugasundaram A and Arumugam N 1981 *Indian J. Chem.* **B20** 1057
Srinivasan C, Shunmugasundaram A and Arumugam N 1984 *J. Chem. Soc. Perkin 2* 213
Srinivasan C, Shunmugasundaram A and Arumugam N 1982a *Indian J. Chem.* **B21** 355
Srinivasan C, Shunmugasundaram A and Arumugam N 1982b *Indian J. Chem.* **B21** 662
Taft R W 1956 *Steric effects in organic chemistry* (ed.) M S Newman (New York: John Wiley) chap. 13