Solvation of carboxylate ions and of transition-state anions for the reaction of carboxylate ion with ethyl iodide in acetonitrile–methanol mixtures. Thermodynamic and quantum mechanical approaches

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Rate constants and activation parameters for carboxylate ion plus ethyl iodide reactions and enthalpies of solution for the tetraalkylammonium salts of relevant nucleophiles have both been measured in acetonitrile–methanol mixtures and have been analysed from the viewpoint of molecular thermodynamics of solute–solvent interaction. An empirical correlation incorporating nucleophiles and transition-state anions has been found between the derived quantities, namely the specific interaction enthalpies for anions and the number of methanol molecules participating in hydrogen bonding with the anions. The mechanism of the hydrogen-bonding interaction in the transition state could be visualized through rationalization of the specific interaction enthalpies for the transition-state anions in terms of the concept of the 'effective atomic charge on oxygen'.

Carboxylic acids are among the most important acids in organic chemistry. Fundamental concepts such as structural effects on acid–base properties in solution and nucleophilic reactivity of conjugate-base anions,[1–3] together with such advanced concepts as 'concertedness' and 'non-perfect synchronization' in physical organic chemistry[4,5] have been deduced mainly through empirical analysis of thermodynamic and kinetic measurements performed in aqueous or protic phases. Recent developments in experimental procedures and theory have enabled the revelation of the shortcomings of the traditional concepts derived mainly through measurements in the aqueous phase.[6–8]

The entropy change of reaction and of activation have long been invoked to be the key thermodynamic functions which contain molecular mechanistic information on solute–solvent interactions, albeit often giving only a qualitative interpretation deduced from empirical analysis.[9] Recently concurrent analysis of thermodynamic transfer quantities with values of activation quantities has been developed to elucidate molecular mechanistic ideas on nucleophile and on transition-state anion solvation.[10–12]

In this work activation parameters for the reactions of carboxylate ion with ethyl iodide and the single ion enthalpies of transfer for carboxylate ions have both been measured in acetonitrile–methanol mixtures. The results will be analysed from the viewpoint of molecular thermodynamics of solute–solvent interaction, and the physical significance of the derived quantities will be correlated with the results of quantum mechanical calculations.

Results

Rate constants and activation parameters for the reactions of three carboxylate ions with ethyl iodide are summarized in Table 1. With all of these reactions, the rate constant and activation enthalpy indicate very sharp variations in a narrow range of solvent composition with small content of methanol, followed by rather smaller variations over the other regions of solvent composition. The incomplete compensation between the solvent effects on activation free energy and those on activation enthalpy results in the appearance of a maximum in activation entropy *versus* solvent composition profile, and these are the characteristic features of a reaction in which a nucleophile–protic solvent interaction determines the kinetic behaviour.[10,12,13]

Enthalpies of solution for tetramethylammonium diphenylacetate, and for uncharged reaction products, ethyl diethylacetate, ethyl 4-methoxybenzoate and ethyl diphenylacetate have also been determined in the same solvent mixtures and are summarized in Table 2. Single ion enthalpies of transfer for an anion from acetonitrile to solvent mixtures, $\Delta_t H^{\mathrm{AN}\rightarrow\mathrm{mix}}$ have been calculated on the basis of the tetrabutylammonium/tetrabutylborate assumption[13] and are summarized in Table 3. Transfer enthalpies for transition-state anions have been calculated according to a thermodynamic cycle combining the single ion enthalpies for the anions,[11] the activation enthalpies and transfer enthalpies of ethyl iodide,[13] and are summarized in Table 3. All the single ion enthalpies, although less pronounced for transition-state anions, show a quite sharp decrease over the solvent compositions of low content of methanol, followed by a rather smaller increase over other compositions, in a way analogous to the features observed for rate constants and activation enthalpies. The enthalpies for uncharged reaction products show a rather small and curvi-linear response to changing solvent compositions. The features could quantitatively be reproduced by eqns. (1) and (2).[13,14] In the

$$\Delta_t H^{\mathrm{AN}\rightarrow\mathrm{mix}} = \Delta_t H_{\mathrm{PHYS}}^{\mathrm{AN}\rightarrow\mathrm{MeOH}} x_{\mathrm{MeOH}}[1 - 1.23x_{\mathrm{MeOH}}(1 - x_{\mathrm{MeOH}})] + \Delta_t H_{\mathrm{SI}}^{\mathrm{AN}\rightarrow\mathrm{MeOH}} K_{\mathrm{se}} x_{\mathrm{MeOH}}/(x_{\mathrm{AN}} + K_{\mathrm{se}} x_{\mathrm{MeOH}}) \quad (1)$$

$$\Delta_t H^{\mathrm{AN}\rightarrow\mathrm{MeOH}} = \Delta_t H_{\mathrm{PHYS}}^{\mathrm{AN}\rightarrow\mathrm{MeOH}} + \Delta_t H_{\mathrm{SI}}^{\mathrm{AN}\rightarrow\mathrm{MeOH}} \quad (2)$$

equations, $\Delta_t H_{\mathrm{PHYS}}^{\mathrm{AN}\rightarrow\mathrm{MeOH}}$ and $\Delta_t H_{\mathrm{SI}}^{\mathrm{AN}\rightarrow\mathrm{MeOH}}$ stand for the single ion enthalpy of transfer from acetonitrile to methanol due to a 'general physical' interaction and that due to a specific interaction, respectively. K_{se} stands for the equilibrium constant of the solvent-exchange process at the solvation site around a solute and x_{AN} and x_{MeOH} stand for the mole fraction of acetonitrile and of methanol in the solvent mixture.[13,14]

The first term of the right hand side of eqn. (1), which expresses the response of transfer enthalpy to solvent

Table 1 Rate constants and activation parameters in acetonitrile–methanol mixtures at 30 °C

	Diethylacetate + EtI			4-Methoxybenzoate + EtI			Diphenylacetate + EtI		
x_{MeOH}[a]	k/10^{-5} dm^3 mol^{-1} s^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}	k/10^{-5} dm^3 mol^{-1} s^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}	k/10^{-5} dm^3 mol^{-1} s^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}
0	3.56×10^4	60.8	−53.1	6.76×10^3	66.8	−47.1	6.74×10^3	63.1	−59.3
0.1	6.24×10	92.2	−2.3	3.22×10	90.8	−12.4	4.45×10	90.6	−10.3
0.25	9.82	93.8	−12.3	5.45	93.2	−19.2	7.81	92.7	−17.9
0.50	2.37	95.1	−19.9	1.27	96.2	−21.4	1.93	93.3	−27.5
0.75	0.874	96.7	−22.9	0.588	91.2	−44.3	0.720	94.9	−30.4
1.0	0.280	100.8	−18.8	0.186	100.9	−21.9	0.257	96.5	−33.7

[a] x_{MeOH} is the mole fraction of methanol.

Table 2 Enthalpies of solution (kJ mol^{-1}) in acetonitrile–methanol mixtures at 25.0 °C

x_{MeOH}	Tetramethylammonium diphenylacetate	Ethyl diethylacetate	Ethyl 4-methoxybenzoate	Ethyl diphenylacetate
0	20.5	3.55	3.73	28.9
0.1	−9.76	—	—	—
0.25	−12.8	3.01	3.91	28.6
0.50	−10.7	2.83	4.44	29.45
0.75	−7.64	2.65	5.12	30.1
1.0	−1.23	2.54	6.24	32.2

Table 3 Single ion enthalpies of transfer (kJ mol^{-1}) from acetonitrile to solvent mixtures and interaction parameters (kJ mol^{-1})

x_{MeOH}	Diphenylacetate ion	TS anion (Diethylacetate + EtI)	TS anion (4-Methoxybenzoate + EtI)	TS anion (Diphenylacetate + EtI)
0	0	0	0	0
0.1	−29.4	−10.35	−9.7	−1.9
0.25	−32.0	−12.1	−9.55	−2.5
0.50	−30.85	−10.35	−5.15	−1.05
0.75	−28.4	−7.05	−7.50	2.50
1.0	−24.4	−0.9	5.50	7.40
$\Delta_t H_{PHYS}^{AN \rightarrow MeOH}$	−11.1	15.6	19.0	13.4
$\Delta_t H_{SI}^{AN \rightarrow MeOH}$	−35.5	−16.5	−13.5	−6.0
K_{se}	56.0	26.0	48.0	12.0
Z	2.9	1.4	1.0	0.5

composition, has been found empirically to simulate the enthalpy of transfer for the perchlorate ion and is likely to contain the contributions from 'general physical' interactions such as cavity term, protophobic interactions, ion–dipole interactions and dipole–dipole interactions.[13,14] The second term which expresses the steep changes of transfer enthalpy over the region of low methanol content, has been derived on the basis of the assumption of solvent-exchange equilibria at the solvation site around a solute and contains contributions from such specific and 'more chemical' interactions as hydrogen-bonding, charge-transfer and dipole–dipole association interactions.[13,14]

The search for the most plausible parameters, K_{se} and $\Delta_t H_{SI}^{AN \rightarrow MeOH}$ which give the optimum fit of the calculated enthalpies, $\Delta_t H^{AN \rightarrow mix}$ to the experimental enthalpies, were repeated step by step, gradually changing these parameters. The enthalpies have been simulated by the equations usually with a maximum deviation of ± 1 kJ mol^{-1} for nucleophiles and ± 2 kJ mol^{-1} for transition-state anions, except for the enthalpy at $x_{MeOH} = 0.75$ for the transition-state anion of the reaction of 4-methoxybenzoate with ethyl iodide. The most plausible sets of parameters obtained are also summarized in Table 3. With uncharged reaction products no definite minimum is observed in the enthalpy profile and this did allow the dissection of transfer enthalpies into their constituent terms. The endothermic change of enthalpy accompanying the transfer from acetonitrile to methanol for ethyl diphenylacetate and for ethyl 4-methoxybenzoate by comparison with the exothermic change of enthalpy for the ethyl diethylacetate (Table 2) have an analogy in the sequence of physical interaction enthalpies for the relevant anions, $\Delta_t H_{PHYS}^{AN \rightarrow MeOH}$ (Table 3 and ref. 11). The significant solvation change around the carboxylate group on going from reactants to uncharged reaction products, could quantitatively be grasped, by comparing the large negative specific interaction enthalpies for nucleophiles, small negative values for transition-state anions and near-zero values for uncharged products. The differential responses of the thermodynamic activation parameters to changing solvent composition lead to non-linear empirical correlations between the activation parameters; one example is shown in Fig. 1.

Discussion

Linear correlations between activation enthalpies and activation entropies, or more recently between activation enthalpies and activation free energies, and the slope values of these correlations have long been invoked as an empirical diagnosis of mechanistic chemistry, while the credibility of the classical form has had to be scrutinized only from a viewpoint of statistics without recourse to any physico-chemical theory of reactions in solution.[1,2,15,16] Recently the molecular thermodynamic approach to such correlations has been developed to

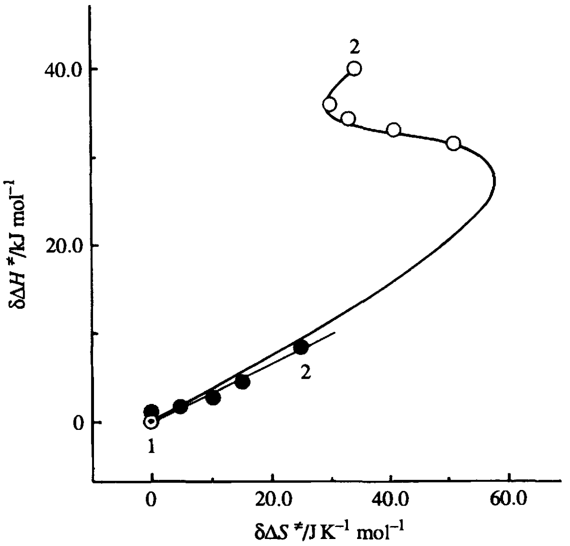


Fig. 1 Activation enthalpy *vs.* activation entropy correlations for the reaction of diethylacetate plus ethyl iodide in acetonitrile–methanol mixtures: ○, overall quantity; ●, 'general physical' interaction quantity; curve, calculated values (see text). 1, Acetonitrile; 2, methanol.

enable the solvation number of the nucleophile and of the transition-state anion to be evaluated.[10–12]

The observed effects of solvent composition on activation parameters, $\delta Y^{\ddagger}$, are a combination of 'general physical' and specific interaction quantities and are given by eqn. (3), where Y refers to a relevant thermodynamic quantity.[10,12,13]

$$\delta\Delta Y^{\ddagger} = \delta\Delta Y^{\ddagger}_{\mathrm{PHYS}} + \Delta_t Y^{\mathrm{AN}\to\mathrm{mix}}_{\mathrm{SI}}(\mathrm{TS}^-) - \Delta_t Y^{\mathrm{AN}\to\mathrm{mix}}_{\mathrm{SI}}(\mathrm{Nu}^-) \quad (3)$$

The enthalpy of transfer due to a specific interaction is given by eqn. (4).

$$\Delta_t H^{\mathrm{AN}\to\mathrm{mix}}_{\mathrm{SI}} = \Delta_t H^{\mathrm{AN}\to\mathrm{MeOH}}_{\mathrm{SI}} K_{\mathrm{se}} x_{\mathrm{MeOH}}/(x_{\mathrm{AN}} + K_{\mathrm{se}} x_{\mathrm{MeOH}}) \quad (4)$$

The entropy of transfer due to a specific interaction is given by eqn. (5) and the specific interaction enthalpy, $\Delta_t H^{\mathrm{AN}\to\mathrm{MeOH}}_{\mathrm{SI}}$ is

$$\Delta_t S^{\mathrm{AN}\to\mathrm{mix}}_{\mathrm{SI}} = \left(\frac{Z\Delta H_{\mathrm{se}}}{T}\right)\left(\frac{K_{\mathrm{se}} x_{\mathrm{MeOH}}}{x_{\mathrm{AN}} + K_{\mathrm{se}} x_{\mathrm{MeOH}}}\right) + ZR\ln(x_{\mathrm{AN}} + K_{\mathrm{se}} x_{\mathrm{MeOH}}) \quad (5)$$

the product of a number of methanol molecules participating in the hydrogen-bonding interaction with an anion, Z, and the enthalpy change of the solvent exchange process on the solvation site around an anion, ΔH_{se}, eqn. (6).[10–12] Hence

$$\Delta_t H^{\mathrm{AN}\to\mathrm{MeOH}}_{\mathrm{SI}} = Z\Delta H_{\mathrm{se}} \quad (6)$$

solvent effects on the activation enthalpy due to a 'general physical' interaction can be calculated by the following procedure; first, by substituting relevant parameters given in Table 3 into eqn. (4) and then by substituting the calculated values of $\Delta_t H^{\mathrm{AN}\to\mathrm{mix}}_{\mathrm{SI}}$ into eqn. (3). Solvent effects upon the activation entropy value due to a 'general physical' interaction can also be calculated according to two steps; first by substituting relevant parameters given in Table 3 and an assumed value of the solvation number, Z into eqn. (5) and then by substituting the calculated values of $\Delta_t S^{\mathrm{AN}\to\mathrm{mix}}_{\mathrm{SI}}$ into eqn. (3). The procedures were repeated step-by-step gradually changing the solvation numbers, Z, for nucleophiles and for transition-state anions, until a linear correlation holds between the activation parameters due to a 'general physical' interaction, $\delta\Delta H^{\ddagger}_{\mathrm{PHYS}}$ and $\delta\Delta S^{\ddagger}_{\mathrm{PHYS}}$. The solvation numbers determined by the procedures are summarized in Tables 3 and 4. Isokinetic temperatures due to 'general physical' interactions, β_{PHYS} and some of the characteristics for carboxylate ion reactions are compared in Table 4. One example of the final result is shown in Fig. 1.

The internal consistency of the parameters derived above will be tested by the back calculation of activation enthalpy and of activation entropy, which can be carried out by three procedures; (*i*) values of activation enthalpy due to a 'general physical' interaction can be derived by substituting the relevant parameters summarized in Table 3 and transfer enthalpies for ethyl iodide[13] into eqn. (7), (*ii*) the activation entropy due to

$$\delta\Delta H^{\ddagger}_{\mathrm{PHYS}} = [\Delta_t H^{\mathrm{AN}\to\mathrm{MeOH}}_{\mathrm{PHYS}}(\mathrm{TS}^-) - \Delta_t H^{\mathrm{AN}\to\mathrm{MeOH}}_{\mathrm{PHYS}}(\mathrm{Nu}^-)]x_{\mathrm{MeOH}} \times [1 - 1.23x_{\mathrm{MeOH}}(1 - x_{\mathrm{MeOH}})] - \Delta_t H^{\mathrm{AN}\to\mathrm{mix}}(\mathrm{EtI}) \quad (7)$$

a 'general physical' interaction can be derived by substituting the results calculated above and β_{PHYS} into eqn. (8), (*iii*)

$$\delta\Delta S^{\ddagger}_{\mathrm{PHYS}} = \delta\Delta H^{\ddagger}_{\mathrm{PHYS}}/\beta_{\mathrm{PHYS}} \quad (8)$$

substitution of the above results and of the calculated values of transfer enthalpy and of entropy due to a specific interaction into eqn. (3), which have been derived by substituting the relevant parameters given in Table 3 into eqns. (4) and (5), lead to the desired quantities. Comparison of the back-calculated values with experimental results is shown in Fig. 1. The calculated values simulate well the pattern shown by experimental quantities. In other words, a non-linear or skewed S-shape character of an activation enthalpy *vs.* activation entropy correlation is confirmed through these procedures. The substitution of the calculated values of $\delta\Delta H^{\ddagger}$ and of $\delta\Delta S^{\ddagger}$ into eqn. (9) gives the value, $\delta\Delta G^{\ddagger}$, and this enables the consistency

$$\delta\Delta G^{\ddagger} = \delta\Delta H^{\ddagger} - T\delta\Delta S^{\ddagger} \quad (9)$$

check of the parameters to be carried out in terms of the correlation of $\delta\Delta H^{\ddagger}$ *versus* $\delta\Delta G^{\ddagger}$, which is recommended on the basis of statistics.[16] The set of parameters summarized in Tables 3 and 4 confirmed the non-linear character of the $\delta\Delta H^{\ddagger}$ *versus* $\delta\Delta G^{\ddagger}$ correlation. The characterization of these empirical correlations through molecular thermodynamic calculation is well beyond the scope of statistical analysis on an enthalpy *vs.* entropy and an enthalpy *vs.* free energy correlation,[1,2,15,16] which could indicate the credibility of the linearity in these correlations.

Until now seven substitution reactions of ethyl iodide using carboxylate ion as a nucleophile have been studied in acetonitrile–methanol mixtures and analysed according to the same lines of arguments (present work and ref. 10). Least-squares analysis of the specific interaction enthalpy, $\Delta_t H^{\mathrm{AN}\to\mathrm{MeOH}}_{\mathrm{SI}}$ leads to eqn. (10), encompassing seven nucleophiles and seven

$$\Delta_t H^{\mathrm{AN}\to\mathrm{MeOH}}_{\mathrm{SI}} = 1.9 - 12.9\,Z \quad (10)$$
$$n = 14 \text{ and } r = 0.99$$

transition-state anions. This indicates that the enthalpy change of the solvent exchange process on the solvation site is constant throughout for carboxylate and transition-state anions and that $\Delta H_{\mathrm{sc}} = -12.9$ kJ mol^{-1} [*cf.* eqn. (6)]. The same type of analysis on the substitution reactions using the imidide ion as the nucleophile led to the result, $\Delta H_{\mathrm{se}} = -11.6$ kJ mol^{-1}.[12]

Within the transition state at least three atoms are supposed to act as a hydrogen-bond accepting site; the reacting oxygen

Table 4 Comparison of the characteristics of carboxylate ion reactions

Reaction	$2 + \log k_{AN}$[a]	$\Delta H^{\ddagger}_{AN}$[b]	β_{PHYS}/K	$\Delta_t H_{SI}^{AN\rightarrow MeOH}(Nu^-)$[b]	$\Delta_t H_{SI}^{AN\rightarrow MeOH}(TS^-)$[b]	$Z(Nu^-)$
Diethylacetate + EtI	1.55	60.8	340	−48.0[c]	−16.5	3.8
Pivalate + EtI	1.46[d]	63.2[d]	360[d]	−43.5[e]	−12.0[d]	3.4[d]
4-MeO-benzoate + EtI	0.83	66.8	330	−39.0[c]	−13.5	3.3
Benzoate + EtI	0.68[d]	61.9[d]	340[d]	−36.0[e]	−9.0[d]	3.0[d]
Diphenylacetate + EtI	0.83	63.1	290	−35.5	−6.0	2.9

[a] $2 + \log k_{AN}$ values are at 30.0 °C. [b] Enthalpies are in kJ mol^{-1}. [c] Ref. 11. [d] Ref. 10. [e] Ref. 14.

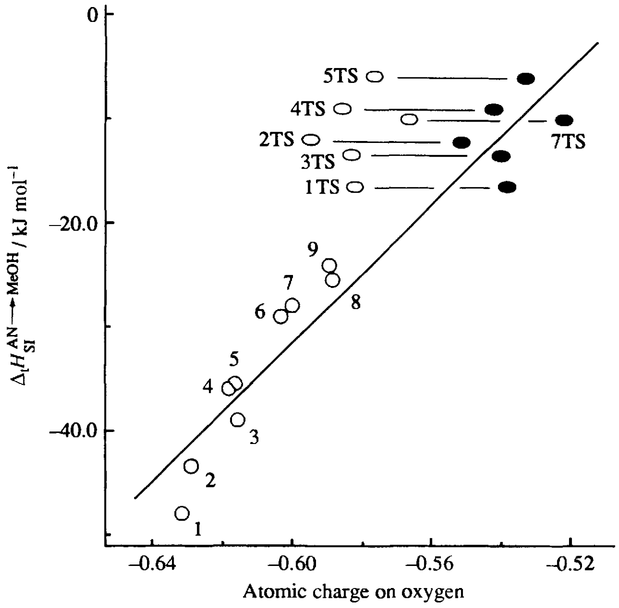
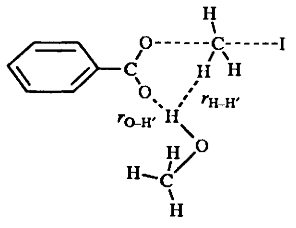


Fig. 2 Empirical correlation between specific interaction enthalpy, $\Delta_t H_{SI}^{AN\rightarrow MeOH}$ and atomic charge on oxygen. ○, carboxylate ions; ⬭, transition-state anions; ⬬, 'effective' atomic charge on oxygen for transition-state anions. 1, Diethylacetate; 2, pivalate; 3, 4-methoxybenzoate; 4, benzoate; 5, diphenylacetate; 6, 3-nitrobenzoate; 7, 4-nitrobenzoate; 8, 3,5-dinitrobenzoate; 9, 3,4-dinitrobenzoate; *i*TS, the transition-state anion of nucleophile *i* from the reaction with ethyl iodide. Experimental results are taken from Table 3 and refs. 10, 11 and 14.

atom and non-reacting oxygen atom in the carboxylate group and the leaving iodine atom. Quantitative molecular mechanistic procedures are required for translating thermodynamic quantities into molecular mechanistic images for nucleophile and transition-state anion solvation. Semi-empirical molecular orbital calculations have been carried out[17] and various empirical correlations were attempted using the calculated results. Specific interaction enthalpies for carboxylate ions show a fair correlation with the calculated partial atomic charge on oxygen, while the enthalpies for transition-state anions seem to systematically deviate upwards; atomic charges on oxygen for 3,4- and 3,5-dinitrobenzoate ions and those on the non-reacting oxygen atom for transition-state anions for diethylacetate, 4-methoxybenzoate, pivalate and benzoate ion reactions are comparable, *ca.* −0.58 to −0.595, while the enthalpies for the transition-state anions exceed those for dinitrobenzoate ions by 8–16 kJ mol^{-1}; this is well beyond the experimental error (Fig. 2). On going from the reactant to the transition state some of the methanol molecules which are hydrogen-bonded to an oxygen atom of the carboxylate ion will have to be removed from the solvation site around the oxygen atom and the extent of the repulsive interaction between the hydrogen atom in the methyl group of an approaching methyl iodide and the hydrogen atom in solvating methanol become more significant. The sum of the coulombic energy acting on the three atom system (the non-reacting oxygen atom, the hydrogen atom in the approaching methyl group and the hydrogen atom in the solvating methanol), *E*, will be given by eqn. (11), where Q_i and r_{i-j} stand for the

$$E = (1/4\pi\varepsilon_0)[Q_O Q_{H'}/r_{O-H'} + Q_H Q_{H'}/r_{H-H'}] = (1/4\pi\varepsilon_0)(Q_{H'}/r_{O-H'})[Q_O + Q_H/(r_{H-H'}/r_{O-H'})] \quad (11)$$

atomic charge on atom, *i*, and the distance between atoms, *i* and *j*, respectively, and suffix H′ stands for the hydrogen atom in solvating methanol. The value in square brackets, $Q_O + Q_H/(r_{H-H'}/r_{O-H'})$, reduces to the atomic charge on oxygen, Q_O as $r_{H-H'}$ goes to infinity and which can then be taken as the way in which the effective atomic charge on oxygen acts on the hydrogen atom in methanol, Q_{effect}. The distances, $r_{O-H'}$ and $r_{H-H'}$ have been determined through optimizing the geometry shown in Scheme 1 by the MNDO/PM3 method.[17] The least squares analysis leads to the eqn. (12) which predicts that the specific



Scheme 1

$$\Delta_t H_{SI}^{AN\rightarrow MeOH} = 169.0 + 333.8[Q_O + Q_H/(r_{H-H'}/r_{O-H'})] \quad (12)$$
$$n = 15, r = 0.96$$

interaction enthalpy, $\Delta_t H_{SI}^{AN\rightarrow MeOH}$ goes to zero at $Q_{effect} \cong -0.51$. MNDO/PM3 charges on the carbonyl oxygen for the reaction products have a range *ca.* −0.37 to −0.38, and this indicates that the atomic charge on oxygen is insufficiently negative for a specific interaction enthalpy to be detected by our procedures. Thus, an insignificant specific interaction enthalpy for uncharged reaction products (Table 2 and *loc. cit.*) and the prediction by the empirical correlation, eqn. (12), are consistent. The same line of analysis which has been carried out for the reaction of imidide ion with ethyl iodide led to the analogous correlation to eqn. (12) with a similar slope value, 369.2.[12]

Average values of the specific interaction enthalpies for nucleophiles and for transition-state anions amount to −34.2 and to −11.2 kJ mol^{-1}, respectively (Fig. 2), and this corresponds to *ca.* 67% of solvent reorganization being finished at the transition state stage. For proton transfer reactions the extent of solvent reorganization around methoxide ion in methanol has been estimated to be *ca.* 75–90% at the transition state.[18] Theoretical studies on microsolvent kinetic isotope effects on S_N2 reactions in the gas phase quantitatively rationalized the observed inverse effects in terms of varying the extent of hydrogen-bonding solvation of a nucleophile on going from the reactant to the transition state.[19,20] Thus the extent and the mechanistic significance of the hydrogen-bonding interaction on the reaction behaviour at the transition-state has been substantiated by these procedures.

In imidide ions the negative charge is mainly distributed over three atoms, the two carbonyl oxygens and the imidide nitrogen, while in carboxylate ions the charge is mainly over two oxygen atoms. Correspondingly MNDO/PM3 charges on the oxygen atom of carboxylate ions are *ca.* 3/2 more negative than those on imidide ions (Fig. 2 and Fig. 2 in ref. 12). In spite of the difference in the atomic charge, the values of the slopes of the linear empirical correlation between specific interaction enthalpy, $\Delta_t H_{SI}^{AN \rightarrow MeOH}$ and solvation number, Z, eqn. (10) and those of the empirical correlation between specific interaction enthalpy, $\Delta_t H_{SI}^{AN \rightarrow MeOH}$ and atomic charge on oxygen, eqn. (12), lead to nearly convergent values (*loc. cit.*). One significant difference in the behaviour between the carboxylate ion and imidide ion reactions lies in the observation that the isokinetic temperature due to a 'general physical' interaction, β_{PHYS}, varies according to the nature of the nucleophiles for imidide ion reactions, *i.e.* it becomes higher for more electron delocalized aromatic imidides, while it stays nearly constant for carboxylate ion reactions (Table 4 and Table 3 in ref. 10) in spite of the varied reactivities and the varied solvation patterns of nucleophiles. This might partly be ascribed to the wider molecular cross-section open for solvation and more dispersed anionic charge in imidide ions, which are likely to make interactions in the solvation spheres more sensitive to structural variation.

Conclusions

A non-linear correlation between the activation parameters for the reaction of the carboxylate ion with ethyl iodide in acetonitrile–methanol mixtures could successfully be accommodated through our approaches. A linear correlation, for carboxylate ions and transition-state anions, between specific interaction enthalpies and the number of methanol molecules participating in specific interaction is one of the foundations of these approaches. Molecular mechanistic simulations of transition-state solvation could be deduced through the empirical correlation between specific interaction enthalpies and the results of semi-empirical molecular orbital calculations to give partial atomic charges.

Experimental

Materials

Tetramethylammonium diphenylacetate was prepared from tetramethylammonium hydroxide and diphenylacetic acid in methanol according to essentially the same procedures as described elsewhere,[21] recrystallized three times from acetonitrile and dried (phosphorus pentaoxide) (Found: C, 75.5; H, 8.1; N, 4.95. Calc. for $C_{18}H_{23}NO_2$: C, 75.8; H, 8.12; N, 4.91%). Ethyl diethylacetate and ethyl 4-methoxybenzoate were prepared from ethyl iodide and tetramethylammonium salts of the relevant carboxylate ion[11] in acetonitrile and purified by fractional distillation under reduced pressure (for ethyl diethylacetate, Found: C, 66.5; H, 11.0. Calc. for $C_8H_{16}O_2$: C, 66.6; H, 11.2%; for ethyl 4-methoxybenzoate, Found: C, 66.6; H, 6.5. Calc. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71%). Ethyl diphenylacetate was prepared from tetramethylammonium diphenylacetate and ethyl iodide in acetonitrile and recrystallized three times from hexane (Found: C, 79.85; H, 6.6. Calc. for $C_{16}H_{16}O_2$: C, 80.0; H, 6.71%). Other materials were treated as described elsewhere.[10,12,13]

Product analysis and kinetics measurements

Product analyses have been carried out according to the same procedures as described elsewhere[12] and ^1H NMR spectra of both crude and purified products agreed with those of an authentic sample.

Aliquots (5 cm^3) from stock solutions of ethyl iodide and of relevant tetramethylammonium carboxylates were mixed in tightly stoppered glass test-tubes and the mixtures were kept in a thermostatted bath. After a given period, the reaction mixture was poured into a hexane–water mixture. The amount of iodide ion formed was determined by potentiometric titration using silver nitrate solution.

The rate measurements were carried out at four of the following temperatures, 0.0, 10.0, 20.0, 30.0, 40.0, 50.0 and 60.0 °C. The experimental errors were estimated to be *ca.* 2% for rate constants, 1 kJ mol^{-1} for activation enthalpies and 3 J K^{-1} mol^{-1} for activation entropies.

Heats of solution measurements

Heats of solution were measured at 25.0 ± 0.1 °C with a Tokyo Riko twin isoperibol calorimeter.[11,13,14] Final concentration ranges of solutes were $(0.4 - 2.6) \times 10^{-2}$ mol dm^{-3} for salt and $(0.6 - 2.3) \times 10^{-2}$ mol dm^{-3} for uncharged reaction products and experimental errors were *ca.* 0.7 kJ mol^{-1}.

Calculations

Semi-empirical molecular orbital calculations were carried out using the MNDO/PM3 methods.[17] In order to save on computation time, the following restrictions were imposed; the framework of substituted benzoate ions and phenyl groups in diphenylacetate and the transition-state anion have C_{2v} symmetry, methyl groups in carboxylate ions and transition-state anions have C_{3v} symmetry, one of the C–H bonds in the approaching methyl iodide lies in a plane with the O–C–O group of the carboxylate ion and in *syn*-configuration to the non-reacting oxygen atom. Optimization around a saddle point has been carried out step-by-step with the restrictions being imposed for sets of 80–100 fixed O–C and C–I distances. Contour diagrams were drawn with use of the enthalpies calculated above and saddle points were determined by visual inspection.

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