

# Solvation and nucleophilic reactivity of 1,2,4-triazolate ion in acetonitrile–methanol mixtures

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Yasuhiko Kondo,<sup>\*,a</sup> Kouji Yano,<sup>b</sup> Ossun Fang,<sup>a</sup> Hiromi Saito<sup>a</sup> and Tatsuya Takagi<sup>c</sup>

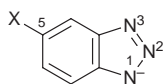
<sup>a</sup> Department of Natural Science, Osaka Women's University, Daisen-cho, Sakai, Osaka 590, Japan

<sup>b</sup> Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan

<sup>c</sup> Genome Information Research Center, Osaka University, Suita, Osaka 565, Japan

The 1,2,4-triazolate ion is a stronger hydrogen-bond accepting base than 5-substituted 1,2,3-benzotriazolate ions. Partly because of this characteristic, the transition-state anion of the 1,2,4-triazolate ion reaction with ethyl iodide indicates the most significant hydrogen-bond accepting basicity of a transition-state anion so far observed. The PM3 atomic charge on the nitrogen atom at the 4-position of the 1,2,4-triazolate ion and the average PM3 atomic charge on the nitrogen atom at the 1- and 3-positions of 5-substituted 1,2,3-benzotriazolate ions make the most significant contribution to the basicity of the relevant anion. The significant basicity for the transition-state anion has been rationalized through an empirical correlation between the specific interaction enthalpy,  $\Delta_t H_{SI}^{AN \rightarrow MeOH}$ , and the PM3 atomic charge.

Triazoles and their benzo derivatives have attracted considerable attention because of their theoretical interest and synthetic value, as well as their numerous applications in industry and agriculture.<sup>1–3</sup> Triazoles are weak bases as well as weak acids ( $pK_a$  values in  $H_2O$  are 10.26 and 8.2 for 1*H*-1,2,4-triazole,<sup>1</sup> and for 1,2,3-benzotriazole,<sup>2</sup> respectively) of comparable strength to succinimide and phthalimide ( $pK_a$  values in  $H_2O$  are 9.66<sup>4</sup> and 8.30<sup>5</sup> for succinimide and phthalimide, respectively) in spite of the different coordination around the reactive nitrogen atom.



X, NO<sub>2</sub>; Cl; H; CH<sub>3</sub>



In previous work, through empirical correlations with the specific interaction enthalpy of the nucleophilic anion,  $\Delta_t H_{SI}^{AN \rightarrow MeOH}$  (single ion enthalpy of transfer due to specific interactions occurring on transfer from acetonitrile to methanol; hydrogen-bond accepting basicity for a nucleophile increases with an increasingly negative value of  $\Delta_t H_{SI}^{AN \rightarrow MeOH}$ ), nucleophilic reactivity has been shown to be controlled mainly through partial desolvation around the nucleophilic anion accompanying activation, while reaction enthalpy is controlled through the atomic propensity of the nucleophilic center but not through partial desolvation.<sup>6,7</sup>

Characterization of solvation and of reactivity patterns for the 1,2,4-triazolate ion (conjugate-base anion of 1,2,4-triazole) is of fundamental importance for planning synthetic routes as well as for critically examining the scope and limitation of empirically established notions for imide ion reactions.

In this work, after the characterization of solvation patterns for triazolate ions (conjugate-base anions of triazoles), the reaction behavior of the 1,2,4-triazolate ion with ethyl iodide will be analyzed in acetonitrile–methanol mixtures. Molecular mechanistic analyses of the derived thermodynamic quantities will be discussed in relation to semi-empirical quantum mechanical properties.

## Results

Enthalpies of solution,  $\Delta_s H$  for the tetramethylammonium salts containing triazolate ion and for 1-ethyl-1,2,4-triazole, a reaction product (as will be described in due course) have been measured in acetonitrile–methanol mixtures and are summarized in Table 1. Single-ion enthalpies of transfer from acetonitrile to mixed solvents,  $\Delta_t H^{AN \rightarrow mix}$  have been calculated on the basis of the TBA/TBB assumption<sup>8,9</sup> and are summarized in Table 2. All these enthalpies pass through a sharp minimum at low methanol content, followed by a steady increase with increasing methanol content, a typically observed pattern for anions which are stabilized through hydrogen-bonding interactions with methanol.<sup>8–10</sup> The results are well simulated by eqns. (1) and (2), where  $x_{AN}$  and  $x_{MeOH}$  are the mole fractions of

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

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

acetonitrile and of methanol in the solvent mixtures, and  $K_{se}$  is the equilibrium constant for a solvent exchange process on the solvation site around an ion.<sup>8–10</sup> In these equations, the term  $\Delta_t H_{PHYS}^{AN \rightarrow MeOH}$  indicates the enthalpy of transfer from acetonitrile to methanol due to 'more physical' interactions such as electrostatic, protophobic and cavity forming interactions, and the term  $\Delta_t H_{SI}^{AN \rightarrow MeOH}$  indicates more 'specific' or more 'chemical' interactions such as hydrogen-bonding and charge-transfer interactions which are observed for a specific solute and solvent pair.<sup>8–10</sup> Curve fittings were repeated until the optimum fit of the calculated values to the experimental one was attained through systematic variation of  $K_{se}$  and  $\Delta_t H_{SI}^{AN \rightarrow MeOH}$  under the constraints of eqn. (2); one of the most plausible sets of values is given in Table 2. Usually experimental results were simulated with these equations within the maximum deviation of  $\pm 1.6$  kJ mol<sup>-1</sup>. Amongst all the ions studied, the 1,2,4-triazolate ion is the most hydrogen-bond accepting of all.

Rate constants and activation parameters for the reaction of

**Table 1** Enthalpies of solution,  $\Delta_s H$  in acetonitrile–methanol mixtures (25 °C) (in kJ mol<sup>-1</sup>)<sup>a</sup>

$x_{\text{MeOH}}$	TMA 1,2,4-triazolate	1-Ethyl-1,2,4-triazole	TMA 5-Me-BTA	TMA BTA	TMA 5-Cl-BTA	TMA 5-NO <sub>2</sub> -BTA
0.0	13.0	0.79	21.2	19.5	21.2	27.3
0.1	-30.1	-2.01	-10.6	-8.68	-4.20	9.63
0.25	-32.8	-3.78	-14.3	-12.4	-7.73	5.94
0.50	-29.3	-4.25	-12.1	-10.4	-7.12	7.13
0.75	-24.3	-3.50	-9.42	-7.11	-4.46	10.7
1.0	-17.5	-1.70	-3.31	-1.67	-0.13	14.9

<sup>a</sup> TMA, tetramethylammonium; BTA, 1,2,3-benzotriazolate.

**Table 2** Single ion enthalpies of transfer (in kJ mol<sup>-1</sup>) from acetonitrile to acetonitrile–methanol mixtures,  $\Delta_t H^{\text{AN} \rightarrow \text{mix}}$ , interaction parameters and solvation number  $Z$ <sup>a</sup>

$x_{\text{MeOH}}$	1,2,4-Triazolate	TS-anion	1-Et-1,2,4-triazole	5-Me-BTA	BTA	5-Cl-BTA	5-NO <sub>2</sub> -BTA
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.1	-42.2	-25.7	-2.8	-30.9	-27.3	-24.5	-16.8
0.25	-44.5	-24.0	-4.6	-34.2	-30.6	-27.6	-20.1
0.50	-41.95	-23.75	-5.0	-32.95	-29.55	-27.95	-19.85
0.75	-37.6	-19.7	-4.3	-30.9	-26.9	-26.0	-16.9
1.0	-33.2	-10.7	-2.5	-27.2	-23.9	-24.0	-15.1
$\Delta_t H_{\text{PHYS}}^{\text{AN} \rightarrow \text{MeOH}}$	14.8	20.3	5.0	10.3	10.1	7.0	7.9
$\Delta_t H_{\text{SI}}^{\text{AN} \rightarrow \text{MeOH}}$	-48.0	-31.0	-7.5	-37.5	-34.0	-31.0	-23.0
$K_{\text{se}}$	75.0	60.0	8.50	53.0	50.0	40.0	33.0
$Z$	4.3	2.3	—	—	—	—	—

<sup>a</sup>  $T = 25$  °C.

**Table 3** Rate constants and activation parameters for the reaction of 1,2,4-triazolate ion with ethyl iodide in acetonitrile–methanol mixtures<sup>a</sup>

$x_{\text{MeOH}}$	$k/10^{-5} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	$\Delta H^\ddagger/\text{kJ mol}^{-1}$	$\Delta S^\ddagger/\text{J K}^{-1} \text{ mol}^{-1}$
0.0	$2.00 \times 10^4$	63.6	-48.6
0.1	231	80.1	-31.3
0.25	55.0	84.2	-29.7
0.50	20.3	82.2	-44.6
0.75	9.64	82.4	-50.1
1.0	3.80	87.7	-40.4

<sup>a</sup>  $T = 30$  °C.

ethyl iodide with 1,2,4-triazolate ion were determined in acetonitrile–methanol mixtures and are summarized in Table 3. The rate constant shows a very significant decrease, while the activation enthalpy undergoes a sharp increase, at low methanol contents. In contrast to these, the activation entropy goes through a maximum. These are all typically observed trends for the reactions in which the hydrogen-bonding interaction of a nucleophile with methanol plays a significant role.<sup>8,10</sup> On the basis of a thermodynamic cycle, single ion enthalpies of transfer for the transition-state anion were calculated and are summarized in Table 2. Interaction parameters are also calculated as described above and are also given in Table 2. The value of  $-31.0 \text{ kJ mol}^{-1}$  for  $\Delta_t H_{\text{SI}}^{\text{AN} \rightarrow \text{MeOH}}$  for the transition-state anion, which is equal to that for 5-chloro-1,2,3-benzotriazolate ion, is the largest negative value for a transition-state anion so far observed by the authors.

## Discussion

In 5-substituted 1,2,3-benzotriazolate ions, the anion becomes a weaker base with increasing electron withdrawing ability of the substituent as expressed by Hammett  $\sigma$  values and specific interaction enthalpies are correlated with  $\sigma_p$  and the average of  $\sigma_m$  and  $\sigma_p$  values,  $(\sigma_m + \sigma_p)/2$  to a similar extent. The latter correlation is given by eqn. (3). This, although only indicating

$$\Delta_t H_{\text{SI}}^{\text{AN} \rightarrow \text{MeOH}} = -34.1 + 16.0(\sigma_m + \sigma_p)/2 \quad (3)$$

$$n = 4, r = 0.99$$

a trend, suggests hydrogen-bonding interactions take place at

lone-pair electrons of the nitrogen atoms at the 1- and 3-positions (N-1 and N-3), which constitute one of the  $sp^2$  hybrid orbitals and are in the same plane as the aromatic ring. The contribution from resonance interaction *via* the  $\pi$ -electron system between the lone-pair electrons in a p-orbital at a hydrogen-bonding site and the nitro group at the 5-position in the phenyl ring, *para* to N-1, could not be detected through our analysis. This is partly in contrast to the participation of a p-orbital in the nucleophilic substitution of benzyl chloride by the carbazole ion.<sup>11</sup> By dividing the coefficient by the factor  $2.30RT$  ( $=5.71 \text{ kJ mol}^{-1}$ ), the  $\rho$  value amounts to 2.80 which is, although partly fortuitous, close to the  $\rho$  values for the dissociation equilibria of substituted phenols and of substituted anilinium ions in the aqueous phase, 2.1 and 2.8.<sup>12</sup> In comparison to these anions, the 1,2,4-triazolate ion is a much stronger hydrogen-bond accepting base. Specific interaction enthalpies for three triazolate ions for which  $pK_a$  values for the conjugate acid in the aqueous phase are available, 1,2,4-triazolate, 1,2,3-benzotriazolate and 5-chloro-1,2,3-benzotriazolate ions, give a linear trend for the  $pK_a$  values, according to eqn. (4) ( $pK_a$  values in the

$$\Delta_t H_{\text{SI}}^{\text{AN} \rightarrow \text{MeOH}} = 20.6 - 6.68 pK_a \quad (4)$$

$$n = 3, r = 0.99$$

aqueous phase used in the correlation are: 10.26, 8.2 and 7.7 for 1*H*-1,2,4-triazole,<sup>1</sup> 1,2,3-benzotriazole<sup>2</sup> and 5-chloro-1,2,3-benzotriazole,<sup>2</sup> respectively) and the difference in  $\Delta_t H_{\text{SI}}^{\text{AN} \rightarrow \text{MeOH}}$  between 1,2,4-triazolate and 1,2,3-benzotriazolate ions,  $14 \text{ kJ mol}^{-1}$ , is comparable to the difference in the Gibbs energy of ionization for the conjugate acid in DMSO,  $16.3 \text{ kJ mol}^{-1}$  ( $pK_a$  values for the conjugate acids in DMSO are 14.75 and 11.9 for 1*H*-1,2,4-triazole<sup>13</sup> and 1,2,3-benzotriazole<sup>13</sup>). The 'more' physical interaction enthalpy  $\Delta_t H_{\text{PHYS}}^{\text{AN} \rightarrow \text{MeOH}}$ , becomes more endothermic as a nucleophile becomes more basic (see Table 2). This suggests that more localized negative charge at a hydrogen-bond accepting site brings about two counteracting effects in anion solvation in methanol; one is the stabilization due to hydrogen-bonding with methanol, and the other is the less significant stabilization due to decreased charge–solvent dipole interactions in methanol in comparison to that in acetonitrile. The 'more physical' interaction enthalpy for the transition-state anion is much larger, in comparison to the nucleophilic anion as

usually observed in our analysis<sup>10,14,15</sup> and this would be ascribed to the significant charge–solvent dipole interactions around the incipient iodide ion in the transition state. A quantitative assessment of these counteracting effects on anion solvation is only possible through quantitative analysis of single ion enthalpy of transfer in mixed solvents. Through these analyses, the five triazolote ions treated in this work are likely to conform to one series.

Specific interaction enthalpies indicate that as the reaction proceeds from the initial state, through the transition state, to the final state, hydrogen-bonding interactions become weaker, but are still significant in the final state (see Table 2).

Activation parameters in the mixed solvents are composed of ‘more physical’ and of specific interaction quantities and are given by eqn. (5), where  $Y$  represents the relevant thermo-

$$\delta\Delta Y^\ddagger = \delta\Delta Y_{\text{PHYS}}^\ddagger + \delta\Delta Y_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}}(\text{TS}^-) - \delta\Delta Y_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}}(\text{Nu}^-) \quad (5)$$

dynamic quantities. In order for a detailed discussion on the behavior of the reaction to be given in the solvent mixtures, a quantitative analysis through reconstruction of the thermodynamic quantities is indispensable. This can be carried out through the following procedures.<sup>14,15</sup>

1. Activation enthalpies due to ‘more physical’ interactions can be derived through eqn. (6), substituting into the equation

$$\delta\Delta H_{\text{PHYS}}^\ddagger = [\Delta_{\text{t}}H_{\text{PHYS}}^{\text{AN}\rightarrow\text{MeOH}}(\text{TS}^-) - \Delta_{\text{t}}H_{\text{PHYS}}^{\text{AN}\rightarrow\text{MeOH}}(\text{Nu}^-)]x_{\text{MeOH}}[1 - 1.23x_{\text{MeOH}}(1 - x_{\text{MeOH}})] - \Delta_{\text{t}}H^{\text{AN}\rightarrow\text{MeOH}}(\text{EtI}) \quad (6)$$

the relevant values given in Table 2 and enthalpies of transfer for ethyl iodide.<sup>8</sup>

2. Activation entropies due to ‘more physical’ interactions can be derived through the division of the enthalpies calculated above by an assumed value for the isokinetic temperature  $\beta_{\text{PHYS}}$  in the reactions for which an isokinetic relationship holds between activation parameters arising from ‘more physical’ interactions.

$$\delta\Delta S_{\text{PHYS}}^\ddagger = \delta\Delta H_{\text{PHYS}}^\ddagger/\beta_{\text{PHYS}} \quad (7)$$

3. Single ion enthalpies of transfer due to specific interactions can be calculated through the substitution of the relevant quantities given in Table 2 into eqn. (8).

$$\Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}} = \Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}}K_{\text{se}}x_{\text{MeOH}}/(x_{\text{AN}} + K_{\text{se}}x_{\text{MeOH}}) \quad (8)$$

4. The quantity  $\Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}}$  can be separated into several components, the number of methanol molecules participating in specific interactions with the relevant solute,  $Z$ , and the enthalpy of the solvent exchange process on the solvation site around the anion,  $\Delta H_{\text{se}}$  according to eqn. (9). Single ion

$$\Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}} = Z\Delta H_{\text{se}} \quad (9)$$

entropies of transfer due to specific interactions can be derived using eqn. (10) by substituting into the equation the relevant

$$\Delta_{\text{t}}S_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}} = (Z\Delta H_{\text{se}}/T)(K_{\text{se}}x_{\text{MeOH}})/(x_{\text{AN}} + K_{\text{se}}x_{\text{MeOH}}) + ZR\ln(x_{\text{AN}} + K_{\text{se}}x_{\text{MeOH}}) \quad (10)$$

quantities given in Table 2, together with the assumed values of  $Z$  and  $\Delta H_{\text{se}}$ .

5. Substitution of these derived quantities into eqn. (5) gives the desired thermodynamic quantities. The procedures 1–5 were repeated until optimum fits between the calculated and experimental values were attained. One of the most plausible sets of parameters, solvation numbers  $Z$  for the 1,2,4-triazolote ion

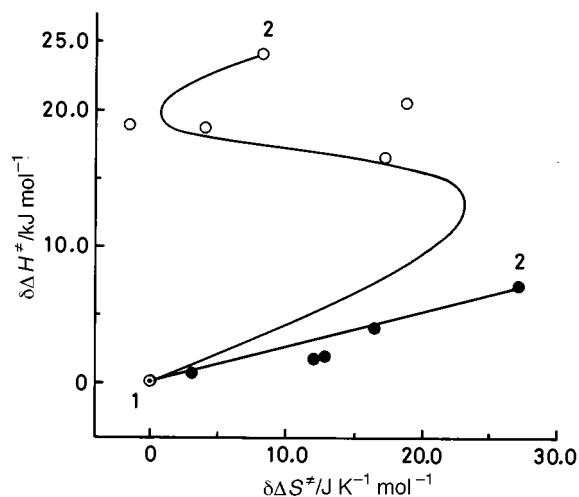


Fig. 1 Activation enthalpy vs. activation entropy correlations for the reaction of the 1,2,4-triazolote ion with ethyl iodide in acetonitrile–methanol. O, Overall quantity; ●, ‘more physical’ interaction quantity; curve, calculated quantity. 1, Acetonitrile; 2, methanol.

and for the transition state anion are also given in Table 2; the final value,  $\beta_{\text{PHYS}}$  is 260 K. General trends observed for the activation parameters ( $S$ -shaped character of the  $\delta\Delta H^\ddagger$  vs.  $\delta\Delta S^\ddagger$  correlation) could be reproduced even for reactions in which very significant hydrogen-bonding interactions are present in the transition state, by the procedures as described above (see Fig. 1). This is another example which indicates that the linear enthalpy vs. entropy correlation does not hold generally, even when it holds between particular constituent quantities.

Imides and triazoles are usually classified as nitrogen acids, although the central nitrogen atom has different coordination. Characteristics of reactivity for imide ions have been analyzed through empirical correlations with the specific interaction enthalpy for the relevant nucleophile,  $\Delta_{\text{t}}H^{\text{AN}\rightarrow\text{MeOH}}$ . Logarithmic rates,  $\log k$  and enthalpies for the reaction of ethyl iodide and imide ion in acetonitrile,  $\Delta_{\text{R}}H$  have been correlated with the specific interaction enthalpy by eqns. (11)<sup>6</sup> and (12).<sup>7</sup>

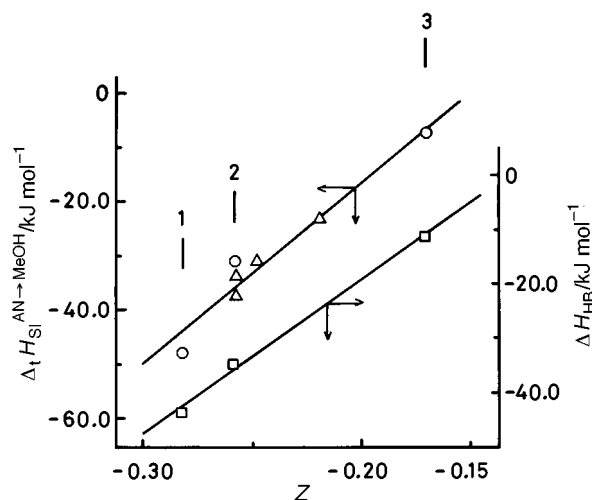
$$3 + \log k = -0.42 - 7.23 \times 10^{-2} \Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}} \quad (11)$$

$$r = 0.97, n = 13$$

$$\Delta_{\text{R}}H = -115.9 + 0.651 \Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}} \quad (12)$$

$$r = 0.91, n = 8$$

Substitution of  $\Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}} = -48.0$  for the 1,2,4-triazolote ion into these equations leads to a larger rate and more exothermic enthalpy in comparison to observed results. The uncharged reaction product of the imide ion reaction,  $N$ -ethylimide, does not show any signs of specific interactions with methanol,<sup>14</sup> that is to say, hydrogen-bond accepting basicity for the nucleophile is lost during the reaction. However, the uncharged reaction product of the triazolote ion reaction, 1-ethyl-1,2,4-triazole retains hydrogen-bond accepting basicity,  $\Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}} = -7.5 \text{ kJ mol}^{-1}$ . The differential value of  $\Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}}$  between the 1,2,4-triazolote ion and 1-ethyl-1,2,4-triazole [ $-40.5 = -48.0 - (-7.5)$ ] would be taken as the variation of specific interactions during the reaction, and equivalent to a genuine  $\Delta_{\text{t}}H_{\text{SI}}^{\text{AN}\rightarrow\text{MeOH}}$  value for the imide ion. When the differential value has been substituted into eqns. (11) and (12), the calculated rate constant,  $0.322 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$  and the calculated reaction enthalpy,  $-142.3 \text{ kJ mol}^{-1}$  are close to the observed value for the 1,2,4-triazolote ion reaction,  $0.200 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$  (see Table 3) and  $-135.8 \pm 2 \text{ kJ mol}^{-1}$  (see Experimental section). For imide ion reactions, a linear correlation has been established between the specific interaction enthalpy and the number of methanol molecules participating in hydrogen-bonding with the imide ion,  $Z$ , eqn. (13).<sup>15</sup>



**Fig. 2** Empirical correlation between specific interaction enthalpy,  $\Delta_t H_{Si}^{AN \rightarrow MeOH}$ , and PM3 atomic charge, *i.e.* PM3 atomic charge on N-4 in nucleophile moiety for the 1,2,4-triazolate ion reaction and PM3 average charge on N-1 and N-3 for 1,2,3-benzotriazolate ions.  $\circ$ , 1,2,4-Triazolate ion reaction;  $\triangle$ , 5-substituted 1,2,3-benzotriazolate ions. Empirical correlations between the enthalpy change of hydrogen-bonding,  $\Delta H_{HB}$  and the atomic charge on N-4,  $\square$ . Both quantities are calculated by PM3 procedures.<sup>16</sup> 1, 1,2,4-Triazolate ion; 2, transition state anion for the 1,2,4-triazolate ion reaction; 3, 1-methyl-1,2,4-triazole, an uncharged reaction product.

Substitution of  $Z$  values for the 1,2,4-triazolate ion and for the transition state anion, 4.3 and 2.3, into eqn. (13) leads to the

$$\Delta_t H_{Si}^{AN \rightarrow MeOH} = -0.80 - 11.6Z \quad (13)$$

$$r = 0.98, n = 13$$

following specific interaction enthalpies,  $-50.7$  and  $-27.5$   $\text{kJ mol}^{-1}$ , which are fairly close to the observed values (see Table 2). As far as the three types of correlations, eqns. (11)–(13) are concerned, the 1,2,4-triazolate ion reaction could be grouped into the imidide ion reaction series, in spite of the structural dissimilarity of the two types of anions.

Empirical correlations between thermodynamic quantities and quantum mechanical properties allow us to understand macroscopic solute–solvent interactions from a molecular mechanistic viewpoint. Quantum mechanical calculations were performed with the PM3 Hamiltonian which has been documented to lead to a more credible enthalpy of formation<sup>16</sup> and has successfully been used in previous work.<sup>6,7</sup> The PM3 atomic charge on the nitrogen atom at the 4-position (N-4) in the 1,2,4-triazolate ion has the largest negative value and this is in a way analogous to the trend observed for substituted 1,2,4-triazoles.<sup>17</sup> The charge shows a gradual increase as the reaction proceeds from the initial, through the transition, to the final state, and an analogous trend is reflected in the variation of the specific enthalpies (see Table 2). This is shown in Fig. 2 in the form of an empirical correlation between specific interaction enthalpies and atomic charge on the nitrogen atom at the 4-position (N-4) (circles in Fig. 2). The specific interaction enthalpies are plotted against the average charge on the nitrogen atoms at the 1- and 3-positions, (atomic charge on N-1 + atomic charge on N-3)/2 for 5-substituted 1,2,3-benzotriazolate ions (triangles in Fig. 2). These data together with the data for the 1,2,4-triazolate ion series result in one correlation, the statistical analysis of which leads to eqn. (14).

$$\Delta_t H_{Si}^{AN \rightarrow MeOH} = 50.5 + 333.7 \times \text{Atomic charge} \quad (14)$$

$$n = 7, r = 0.97$$

It is to be noted that the result for the transition state anion, which is not a thermodynamic quantity but a pseudo-

thermodynamic one having been derived through a thermodynamic cycle from the combination of activation enthalpy with the enthalpies of reactants, falls on the correlation observed for genuine thermodynamic quantities. In addition, calculated enthalpy changes of hydrogen-bond formation at N-4 with a methanol molecule are linearly correlated with the atomic charges on N-4 for the molecular entities at stationary points along the reaction coordinate for the 1,2,4-triazolate ion reaction (squares in Fig. 2, all points are calculated with PM3 procedures<sup>16</sup>). Specific interaction enthalpy,  $\Delta_t H_{Si}^{AN \rightarrow MeOH}$  has been suggested to be related to the enthalpy change of hydrogen-bond formation between the anion and methanol and this supposition is now given theoretical support.

Variation of the specific interaction enthalpy along the reaction coordinate can be taken as the effect of the substituent on the hydrogen-bond accepting basicity for the 1,2,4-triazolate ion moiety, *i.e.* no substituent for the 1,2,4-triazolate ion, substituent is ethyl iodide for the transition state anion, and is the ethyl cation for the uncharged reaction product. An empirical correlation, eqn. (14), indicates that the average charges at N-1 and at N-3 for 5-substituted 1,2,3-benzotriazolate ions, (atomic charge on N-1 + atomic charge on N-3)/2 and the charges at N-4 for the 1,2,4-triazolate ion reaction conform to one series. The successful use of average charge on N-1 and N-3 in the empirical correlation, eqn. (14), is conceptually equivalent to the use of the average  $\sigma$  value,  $(\sigma_m + \sigma_p)/2$  in the empirical correlation, eqn. (3). This is not unreasonable, considering that for a series of 1,2,3-benzotriazolate ions the effects of the substituent are transferred to the nitrogen atom at the 3-position through two bonds in the phenyl ring and one C–N bond in the triazole ring, and to the nitrogen atom at the 1-position through three bonds in the phenyl ring and one C–N bond in the triazole ring, while for the 1,2,4-triazolate ion reaction the effects of the substituent on the nitrogen atom at the 4-position are transferred through two bonds in the ring in one direction and through three bonds in the other direction.

For imidide ion reactions the reaction takes place at the nitrogen atom, while the specific interaction enthalpies are linearly correlated with the atomic charge on the carbonyl oxygen.<sup>15</sup> Similarly for carboxylate ion reactions specific interaction enthalpies are linearly correlated with the atomic charge on the non-reacting oxygen atom.<sup>18</sup> These are all analogous to the observation indicated in Fig. 2, in the sense that the reaction center, N-1, is separated from the hydrogen-bond accepting site, N-4, by two bonds.

## Conclusions

The reaction behaviour of the 1,2,4-triazolate ion conforms to that of the imidide ion reactions according to three empirical correlations which have been established for imidide ion reactions, albeit with minor corrections.

In the carboxylate ion and the imidide ion reaction series, aliphatic nucleophiles have more hydrogen-bond accepting basicity and higher nucleophilic reactivity in comparison to aromatic nucleophiles. Correspondingly, in the triazolate ion series, 1,2,4-triazolate ion is a more hydrogen-bond accepting base by comparison to 5-substituted 1,2,3-benzotriazolate ions.

Atomic charges on the nitrogen atom at the 4-position for the molecular entities at stationary points along the reaction coordinate for the 1,2,4-triazolate ion reaction and the average atomic charges on N-1 and N-3 for 1,2,3-benzotriazolate ions serve as relevant index series for hydrogen-bond accepting basicity. From this study the specific interaction enthalpy and the atomic charge on N-4 serve as a transition state index to locate the relative position of the transition state along the reaction coordinate, in a way analogous to the observation made for imidide ion and carboxylate ion reactions.

**Table 4** Solvents for recrystallization and elementary analysis

	Solvents	Obs. (%)			Formula	Calc. (%)		
		C	H	N		C	H	N
Tetramethylammonium 1,2,4-triazolate	Acetonitrile	50.55	10.07	39.57	C <sub>6</sub> H <sub>14</sub> N <sub>4</sub>	50.68	9.92	39.40
Tetramethylammonium 5-methyl-1,2,3-benzotriazolate	Acetonitrile	64.14	8.65	27.23	C <sub>11</sub> H <sub>18</sub> N <sub>4</sub>	64.05	8.80	27.16
Tetramethylammonium 1,2,3-benzotriazolate	Acetonitrile	62.20	8.27	29.02	C <sub>10</sub> H <sub>16</sub> N <sub>4</sub>	62.47	8.39	29.14
Tetramethylammonium 5-chloro-1,2,3-benzotriazolate	Acetonitrile	53.09	6.68	24.71	C <sub>10</sub> H <sub>15</sub> N <sub>4</sub> Cl	52.98	6.67	24.71
Tetramethylammonium 5-nitro-1,2,3-benzotriazolate	Acetonitrile	50.83	6.42	29.47	C <sub>10</sub> H <sub>15</sub> N <sub>5</sub> O <sub>2</sub>	50.62	6.37	29.52

## Experimental

### Materials

Tetramethylammonium salts containing the conjugate-base anion of triazole have been prepared from tetramethylammonium hydroxide and a relevant triazole in methanol<sup>19</sup> and purified by recrystallization usually three times from the solvents summarized in Table 4. 1-Ethyl-1,2,4-triazole was prepared from tetramethylammonium 1,2,4-triazolate and ethyl iodide in acetonitrile and purified by distillation under reduced pressure (Found: C, 49.22; H, 7.28; N, 43.53. Calc. for C<sub>4</sub>H<sub>7</sub>N<sub>3</sub>: C, 49.47; H, 7.26; N, 43.27%).

### Product analysis and kinetic measurements

Stock solutions of ethyl iodide and of tetramethylammonium 1,2,4-triazolate were mixed in tightly stoppered flasks. After *ca.* ten half lives, the solvents and the unreacted ethyl iodide were removed carefully at reduced pressure. The solid precipitate which formed was washed with several portions of diethyl ether and the purity of the extracted compound was examined by thin layer chromatography and NMR spectroscopy. The result was consistent with predominant alkylation occurring on the nitrogen atom at the 1-position.

Kinetic measurements were carried out as described elsewhere.<sup>8,10,14,15</sup>

### Enthalpy of solution measurements

Enthalpies of solution,  $\Delta_s H$  were measured at  $25.0 \pm 0.1$  °C with a Tokyo Riko Twin Isoperibol calorimeter.<sup>8-10,14</sup> Final concentration ranges of solutes were  $0.4-1.5 \times 10^{-2}$  mol dm<sup>-3</sup> for the salt and  $2.2-2.8 \times 10^{-2}$  for 1-ethyl-1,2,4-triazole. Experimental errors were usually *ca.* 0.7 kJ mol<sup>-1</sup>.

### Enthalpy of reaction measurements

A known amount of tetramethylammonium 1,2,4-triazolate (usually  $3.8-6.6 \times 10^{-4}$  mol) was sealed in an ampoule. A large excess of ethyl iodide over the salt (usually  $1.3 \times 10^{-2}$  mol) was dissolved in acetonitrile (100 cm<sup>3</sup>). The solution and the salt sealed in an ampoule were kept in the calorimeter cell. After thermal equilibration the ampoule was broken and the heat evolved was measured. In the calculation of the enthalpy of reaction, enthalpy of solution for the salt was corrected. The enthalpy of reaction,  $\Delta_r H$  was  $-135.8 \pm 2$  kJ mol<sup>-1</sup>.

### Calculations

Semi-empirical molecular orbital calculations were carried out using the PM3 Hamiltonian.<sup>16</sup> In order to save computation time methyl iodide was used as the electrophile instead of ethyl iodide which was used in experiments, and C<sub>3v</sub> symmetry was assumed for the methyl group in methyl iodide and in methanol. Optimization around a saddle point has been carried out step-by-step for a set of 80-100 fixed N-C and C-I distances with restrictions being imposed. Contour diagrams were drawn with the use of the enthalpies calculated above, saddle points were determined by visual inspection, and N-C and C-I distances for the transition-state anion are 2.228 and 2.296 Å. Optimization with the constraints described above were carried

out for hydrogen-bonded complexes with methanol at the nitrogen atom at the 4-position for 1,2,4-triazolate ion and for 1-methyl-1,2,4-triazole. With respect to the hydrogen-bonded complex of the transition-state anion with methanol at the nitrogen atom at the 4-position, optimizations were carried out with N-C and C-I bonds being fixed at the value determined above and other geometries being varied with the C<sub>3v</sub> symmetry of methyl group being retained. The differential enthalpy of formation between the hydrogen-bonded complex and sum of the enthalpies of methanol with that of uncomplexed 1,2,4-triazolate ion was taken as the enthalpy change of complex formation.

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## References

- H. Wamhoff, in *Comprehensive Heterocyclic Chemistry*, eds. A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford, 1984, vol. 5, p. 669.
- J. P. Poyla, in *Comprehensive Heterocyclic Chemistry*, eds. A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford, 1984, vol. 5, p. 733.
- A. R. Katritzky, H.-X. Chang and B. Yang, *Synthesis*, 1995, 503.
- G. Schwarzenbach and K. Lutz, *Helv. Chim. Acta*, 1940, **28**, 1162.
- Landolt Bornstein Tabellen*, Springer-Verlag, Berlin, 1960, vol. 2, ch. 7.
- Y. Kondo, T. Tsukamoto and C. Moriguchi, *J. Chem. Soc., Perkin Trans. 2*, 1996, 1699.
- Y. Kondo, T. Tsukamoto and N. Kimura, *J. Chem. Soc., Perkin Trans. 2*, 1997, 1765.
- Y. Kondo, M. Itto and S. Kusabayashi, *J. Chem. Soc., Faraday Trans.*, 1982, **78**, 2793.
- Y. Kondo, T. Fujiwara, A. Hayashi and S. Kusabayashi, *J. Chem. Soc., Faraday Trans.*, 1989, **85**, 2931.
- Y. Kondo, T. Fujiwara, A. Hayashi, S. Kusabayashi and T. Takagi, *J. Chem. Soc., Perkin Trans. 2*, 1990, 741.
- F. G. Bordwell and D. L. Hughes, *J. Am. Chem. Soc.*, 1984, **106**, 3234.
- C. D. Ritchie, *Physical Organic Chemistry. The Fundamental Concepts*, Marcell Dekker, New York, 2nd edn., 1990.
- F. G. Bordwell, *Acc. Chem. Res.*, 1988, **21**, 456.
- Y. Kondo, K. Kondo and S. Kusabayashi, *J. Chem. Soc., Perkin Trans. 2*, 1993, 1141.
- Y. Kondo, O. Nonaka, K. Iwasaki, T. Kuwamoto and T. Takagi, *J. Chem. Soc., Perkin Trans. 2*, 1994, 473.
- J. J. P. Stewart, *J. Comput. Chem.*, 1989, **10**, 209. MOPAC93 program package, Dr J. J. P. Stewart and Fujitsu Ltd., Tokyo, Japan.
- A. E. Tipping, P. Jimenez, E. Ballesteros, J.-L. M. Abboud, M. Yanez, M. Esseffar and J. Elguero, *J. Org. Chem.*, 1994, **59**, 1039.
- Y. Kondo, W. Sugitani, M. Tokui and T. Takagi, *J. Chem. Soc., Perkin Trans. 2*, 1995, 1049.
- Y. Kondo, S. Kusabayashi and T. Mitsuhashi, *J. Chem. Soc., Perkin Trans. 2*, 1988, 1799.

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