

## The Basicities of *N*-Trimethylammonioacetamidate and of Substituted *N*-Trimethylammonioacetamidates. The Hammett Correlation and the Thermodynamics of Protonation

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The  $pK_a$  values of *N*-trimethylammonioacetamidate and a number of substituted *N*-trimethylammonioacetamidates have been determined over the temperature range 15–55 °C. The  $pK_a$  values show a correlation with Hammett  $\sigma$  constants with  $\rho$   $1.51 \pm 0.03$  at 25 °C. These facts are consistent with an *N*-protonated cation structure, *i.e.* the cations are *N*-trimethylammonioacetamidates, as deduced earlier from spectroscopic studies. The thermodynamic functions of protonation have been compared with those for tertiary amines and a close similarity of the entropies of protonation has been observed. The variation of the entropies of ionisation of *N*-trimethylammonioacetamidates with change of substituent is analogous to that in the benzoic acid series, except that solvation effects are smaller. The substantial difference in the enthalpies of ionisation and their variation with substitution in the two reaction series is largely attributable to that difference in solvation.

*N*-AMMONIOAMIDATES represent compounds which have structural features akin to carboxylate anions (*i.e.* a negatively charged, resonance stabilized moiety) on the one hand, and to tertiary ammonium ions (*i.e.* a positive trimethylammonio-pole) on the other. Recently, several lines of spectroscopic evidence have been adduced, showing that the site of protonation in these compounds is the amidate nitrogen, *i.e.* that the conjugate acids are *N*-trimethylammonioacetamidates or acylhydrazinium ions.<sup>1</sup> We have been interested in finding supporting evidence for this from a Hammett correlation of the  $pK_a$  values of the *N*-trimethylammonioacetamidate series and also information about solvation effects on acid–base equilibria involving these compounds from the thermodynamic functions of protonation. We report our findings in this paper.

### EXPERIMENTAL

**Materials.**—The *N*-trimethylammonioacetamidates were prepared and characterised by the methods already described.<sup>1–3</sup>

**Measurements.**—pH Measurements were carried out using the EIL model 23A pH meter and an EIL wide range combination micro-glass electrode (type 33 1140 100/B). Measurements were made over the temperature range 15–55 °C (attempts to make measurements at 5 °C were abandoned owing to the slow response of the electrode). The temperature was controlled to  $\pm 0.05$  °C. The pH response of the electrode was checked at 20 °C using two buffers, the phthalate buffer of pH 4.00 and the borate buffer of pH 9.2 (both solutions made up from BDH buffer tablets) and was found to be at least 99% of theoretical. The calibration of the pH meter was subsequently carried out using the phthalate buffer only at each temperature and the automatic temperature compensation. Measure-

ments were made on half-neutralised 0.1M solutions of the base. In each set of measurements on a given solution a check was made for the absence of hysteresis in the response of the glass electrode after temperature variation by repeating the measurement at 25 °C. The agreement with the initial measurement was always within 0.01 pH unit. The pH at half-neutralisation of two identically prepared samples always agreed to 0.02 pH unit or better. The titration volume of most samples showed that there was no more than 3–4% of impurity present, but a few derivatives (*p*-CN, *m*-Cl) showed as much as 15% lower titration results. The variation of pH with titrant volume, however, gave no evidence of the presence of any basic impurity in any of the samples.

The thermodynamic  $pK_a$  values were calculated from the pH values at half-neutralisation by the method described by Albert and Serjeant<sup>4</sup> and using the Debye–Hückel expression  $\log \gamma_{\pm} = -A\sqrt{I}/(1 + B\bar{a}\sqrt{I})$  for the activity coefficient. The value taken for  $\bar{a}$  was 5.28 Å, equal to the sum of the radii of the tetramethylammonium and chloride ions.<sup>5</sup> This choice was based on the argument that the effective radius of the acyltrimethylhydrazinium cations could reasonably be taken to be the same as the radius of the tetramethylammonium cation. The  $pK_a$  values obtained are shown in Table 1 and are believed to be accurate to  $\pm 0.01$  pK units. The relative accuracy of  $pK_a$  values at various temperatures is probably better than  $\pm 0.01$  pK units.

In the calculation of thermodynamic functions, the slopes of the  $pK_a$  versus  $1/T$  plots were obtained by the method of least squares. All correlation coefficients were better than 0.98 (most were better than 0.99). Only one or two plots appeared slightly curved to the eye, but the deviations of

<sup>4</sup> A. Albert and E. P. Serjeant, 'The Determination of Ionization Constants,' Chapman and Hall, London, 2nd edn., 1971.

<sup>5</sup> R. A. Robinson and R. H. Stokes, 'Electrolyte Solutions,' 2nd revised edn., Butterworths, London, 1965, Table 62, p. 125 and Appendix 31, p. 461.

<sup>1</sup> M. Liler and D. G. Morris, *J.C.S. Perkin II*, 1977, 909.

<sup>2</sup> A. F. Cameron, N. J. Hair, and D. G. Morris, *J.C.S. Perkin II*, 1972, 1071.

<sup>3</sup> A. M. Murray, Thesis, Glasgow, 1975.

the points from a straight line were seldom greater than the experimental accuracy of  $\pm 0.01$ . The uncertainties in the slopes were obtained also by statistical treatment,

TABLE 1

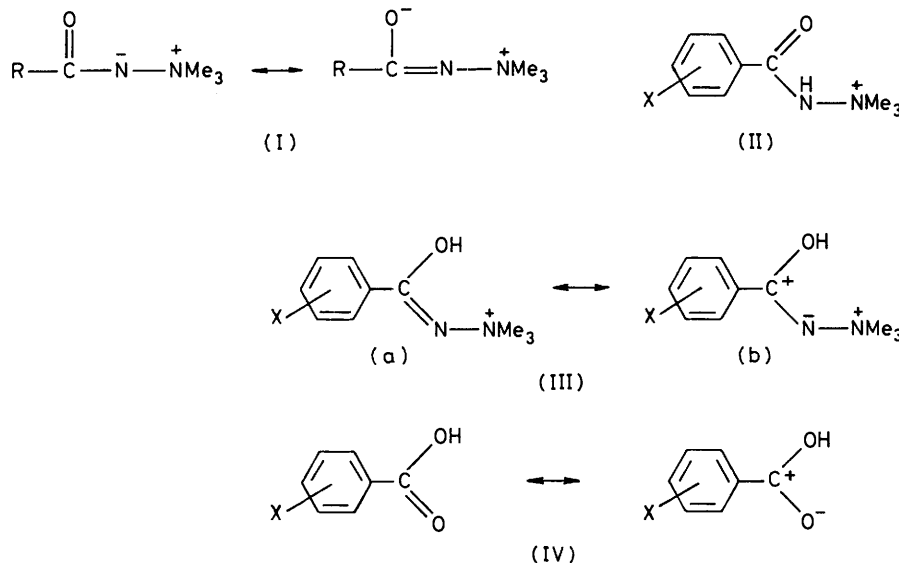
The  $pK_a$  values for *N*-ammonioamidates over the temperature range 15–55 °C

	$\sigma$	15°	25°	35°	45°	55°
Acetamidate		5.45	5.39	5.30	5.26	5.21
Substituted in benzamidate						
H	0	4.32	4.26	4.20	4.17	4.12
<i>p</i> -NO <sub>2</sub>	0.778	3.14	3.09	3.06	3.03	3.00
<i>p</i> -MeO	-0.268	4.68	4.60	4.55	4.52	4.45
<i>p</i> -F	0.062	4.20	4.12	4.08	4.04	3.99
<i>p</i> -Cl	0.227	4.02	3.95	3.92	3.88	3.82
<i>p</i> -CF <sub>3</sub>	0.48	3.64	3.58	3.54	3.49	3.45
<i>p</i> -CN	0.66	3.31	3.25	3.20	3.18	3.16
<i>m</i> -Cl	0.373	3.77	3.71	3.66	3.63	3.60
<i>m</i> -F	0.337	3.81	3.74	3.70	3.67	3.63
<i>m</i> -Br	0.391	3.74	3.70	3.65	3.62	3.60
<i>m</i> -NO <sub>2</sub>	0.710	3.19	3.14	3.11	3.08	3.04
<i>m</i> -CF <sub>3</sub>	0.43	3.60	3.55	3.50	3.46	3.43
<i>m</i> -CN	0.678	3.28	3.24	3.20	3.18	3.16
<i>m</i> -MeO	0.115	4.15	4.09	4.05	4.01	3.98

using a Gauss program on the Hewlett-Packard 2000E computer. The values obtained for  $\Delta H^\circ$  and  $\Delta S^\circ$  are summarized in Table 3.

#### RESULTS AND DISCUSSION

*The Hammett Correlation.*—There are two possible protonation sites in these compounds owing to resonance



(I), analogous to that in carboxylate anions. Although in the second structure the negative charge appears on the more electronegative atom, and this should therefore be favoured, it also involves a large charge separation, which is unfavourable electrostatically (an X-ray structure determination<sup>2</sup> showed that O and N<sup>+</sup>Me<sub>3</sub> are in fact *syn*, presumably on electrostatic grounds). In

<sup>6</sup> R. Stewart and K. Yates, *J. Amer. Chem. Soc.*, 1958, **80**, 6355.

<sup>7</sup> R. Stewart and K. Yates, *Canad. J. Chem.*, 1959, **37**, 664.

<sup>8</sup> R. Stewart and K. Yates, *J. Amer. Chem. Soc.*, 1960, **82**, 4059.

the benzoyl series, the two types of cation, the *N*-protonated cations (II) and the *O*-protonated cations (III), both have structural analogies with the molecules of corresponding benzoic acids. There is little reason to suppose that for the acid ionisation of cations (II) a correlation of  $pK_a$  values with  $\sigma$  constants would not be observed, because of the close similarity of charge distributions in substituted derivatives of both the conjugate acid and the base with those of substituted derivatives of benzoic acid and benzoate anion. A correlation with  $\sigma$  constants is indeed found (Figure 1, correlation coefficient  $r$  0.997) and this may be regarded as supporting evidence for cation structure (II). However, cation structure (III) does not rule out the possibility of a correlation with  $\sigma$  constants either. Only to the extent that one might argue that the positive *N*-trimethylammonio-pole would tend to localize the negative charge on the adjacent nitrogen and thereby increase the relative importance of structure (IIIb) in the resonance hybrid (III), might a correlation with  $\sigma^+$  constants be expected, because of the possibility of more extensive delocalisation of the positive charge on the carbonyl carbon by *para*-substituents in that type of cation. Correlations with  $\sigma^+$  constants have been observed for the ionisation of a number of protonated carbonyl compounds (acetophenones,<sup>6</sup> benzaldehydes,<sup>7</sup> benzoic acids,<sup>8</sup> and benzoyl chlorides<sup>9</sup>), but not for that

of protonated benzamides,<sup>10</sup> which are *N*-protonated in <60% sulphuric acid.<sup>11</sup> The above argument, however, is equivalent to the assumption that the electronegativity of the amidate nitrogen is increased by the adjacent positive pole to become greater than that of the carbonyl oxygen in the molecule of benzoic acid (IV). We have no certain way of deciding about this possible difference in electronegativities, but the fact that the  $pK_a$  values

<sup>9</sup> M. Liler, *J. Chem. Soc.*, 1966, 205.

<sup>10</sup> J. T. Edward, H. S. Chang, K. Yates, and R. Stewart, *Canad. J. Chem.*, 1960, **38**, 1518.

<sup>11</sup> M. Liler, *J.C.S. Perkin II*, 1974, 71.

are comparable in the two series suggests that there is little difference. Therefore, cation structure (III) may

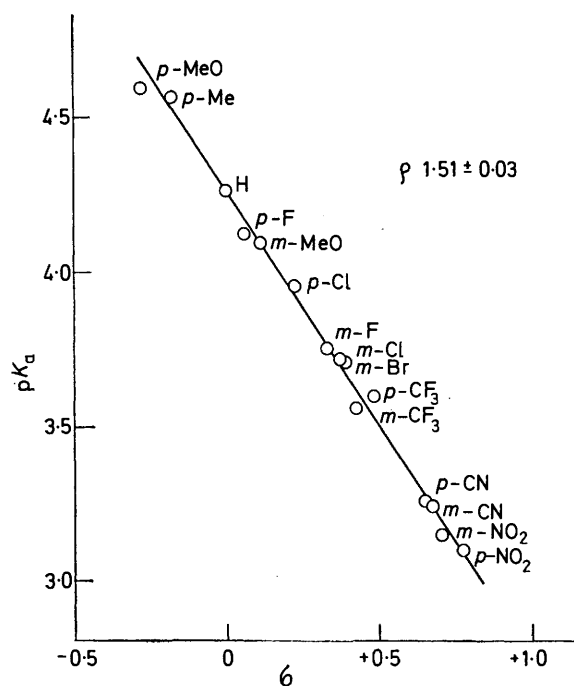


FIGURE 1 The Hammett correlation of the  $pK_a$  values of  $N$ -ammoniobenzamidates

also be consistent with a correlation of  $pK_a$  values with  $\sigma$  constants.

It can be seen from Figure 1 that very few points deviate from the straight line by more than  $\pm 0.05$   $pK$  unit. The deviation of the point for the  $p$ - $CF_3$  substituent deserves comment, because it is very likely due to the uncertainty in the  $\sigma$  value itself. This originates from the paper by Roberts *et al.*,<sup>12</sup> who report two divergent values,  $+0.53$  (based on the ionisation of benzoic acids in 50% EtOH) and  $+0.48$  (based on the rate constants for the reaction of benzoic acids with diazodiphenylmethane). The latter was used in the plot in Figure 1, but a still lower value would fit better.

systems, the benzoate anions and some ylides. The figures for comparison are shown in Table 2. Looking at the formally negatively charged protonation centres in the conjugate bases in series (1)–(5), one can see that they are all isoelectronic, involving some delocalisation of the negative charge into the carbonyl group in every case. The differences in the  $\rho$  values in acid–base systems, for a given length of the side-chain, have often been thought of as arising from differences in the polarisability of the side-chain or the basic centre itself,<sup>13,14</sup> but there are very few quantitative correlations demonstrating this.<sup>15</sup> In series (1)–(5), the polarisability of the atom carrying the formal negative charge should decrease as the nuclear charge increases, and  $\rho$  should decrease in the same sequence, if the protonation site is the formally negatively charged atom in every case. It can be seen from Table 2 that there is such a decrease, and Figure 2 shows that there is indeed a good linear

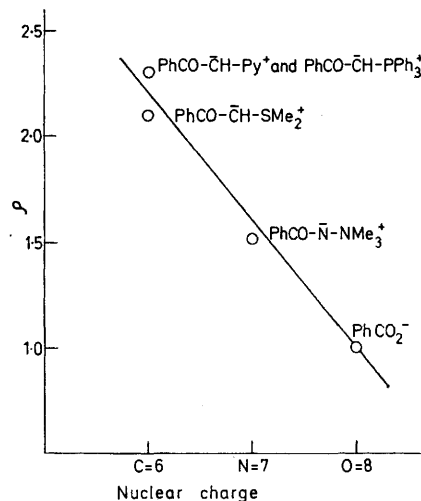


FIGURE 2 The correlation of  $\rho$  constants for the protonation of several structurally similar bases with the nuclear charge of the basic centre

correlation with the nuclear charge ( $r$  0.988). That the positive pole adjacent to the basic centre plays a

TABLE 2

The  $\rho$  constants for proton ionisation in some structurally related series of acids

Parent acid	Conjugate base	Medium	$\rho$	Ref.
(1) Benzoic acid	$PhCO-O^-$	Water	1.00	By definition
(2) $N$ -Ammoniobenzamide ion	$PhCO-\bar{N}-NMe_3^+$	Water	1.51	Present work
(3) $N$ -Phenacylpyridinium ion	$PhCO-\bar{C}H-Py^+$	Water	2.3	<i>a</i>
(4) Phenacylsulphonium ion	$PhCO-\bar{C}H-SMe_2^+$	90% MeOH	2.1	<i>b</i>
(5) Phenacylphosphonium ion	$PhCO-\bar{C}H-PPh_3^+$	80% EtOH	2.3	<i>c</i>

<sup>a</sup> W. G. Phillips and K. W. Ratts, *J. Org. Chem.*, 1970, **35**, 3144. <sup>b</sup> K. W. Ratts and A. N. Yao, *J. Org. Chem.*, 1966, **31**, 1185. <sup>c</sup> S. Fliszar, R. F. Hudson, and G. Salvadori, *Helv. Chim. Acta*, 1963, **46**, 1580.

More positive evidence for nitrogen as the site of protonation in  $N$ -ammonioamidates comes from the comparison of the Hammett reaction constants  $\rho$  for the protonation of these bases with those of the related

<sup>12</sup> J. D. Roberts, R. L. Webb, and E. A. McElhill, *J. Amer. Chem. Soc.*, 1950, **72**, 408.

secondary role in determining  $\rho$  is shown particularly clearly by the series (3)–(5). This is not surprising, since the positive pole is not along the path of trans-

<sup>13</sup> L. P. Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 96.

<sup>14</sup> H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191.

<sup>15</sup> See *e.g.* M. Liler, *Chem. Comm.*, 1965, 244.

mission of substituent effects. The correlation in Figure 2 thus supports the view that the amidate nitrogen is the site of protonation in *N*-ammoniobenzamides and that the cations are *N*-ammoniobenzamides or benzoylhydrazinium ions.

In the present reaction series,  $\rho$  depends on temperature in the usual way, decreasing with increasing

TABLE 3

Thermodynamic functions for the protonation of *N*-ammonioamidates

	$pK_a^{25}$	$-\Delta H^\circ/kJ\ mol^{-1}$	$\Delta S^\circ/J\ K^{-1}\ mol^{-1}$
Acetamidate	5.39	$11.25 \pm 0.67$	$65.3 \pm 2.3$
Substituent in benzamidate			
H	4.26	$9.13 \pm 0.34$	$51.0 \pm 1.4$
<i>p</i> -NO <sub>2</sub>	3.09	$6.41 \pm 0.25$	$37.9 \pm 0.8$
<i>p</i> -MeO	4.60	$10.04 \pm 0.77$	$54.4 \pm 2.8$
<i>p</i> -F	4.12	$9.32 \pm 0.60$	$48.0 \pm 2.0$
<i>p</i> -Cl	3.95	$8.75 \pm 0.63$	$46.5 \pm 2.1$
<i>p</i> -CF <sub>3</sub>	3.58	$8.56 \pm 0.26$	$40.0 \pm 0.8$
<i>p</i> -CN	3.25	$6.67 \pm 0.85$	$40.2 \pm 3.0$
<i>m</i> -Cl	3.71	$7.65 \pm 0.55$	$45.6 \pm 1.9$
<i>m</i> -F	3.75	$8.06 \pm 0.58$	$44.9 \pm 1.9$
<i>m</i> -Br	3.70	$6.73 \pm 0.37$	$48.3 \pm 1.4$
<i>m</i> -NO <sub>2</sub>	3.14	$6.50 \pm 0.37$	$38.5 \pm 1.2$
<i>m</i> -CF <sub>3</sub>	3.55	$8.05 \pm 0.21$	$41.0 \pm 0.9$
<i>m</i> -CN	3.24	$5.41 \pm 0.47$	$44.0 \pm 1.5$
<i>m</i> -MeO	4.09	$7.64 \pm 0.34$	$52.9 \pm 0.9$

temperature (from a value of 1.52 at 15 °C to 1.42 at 55 °C), the plot of  $\rho$  against  $1/T$  being linear.

*Thermodynamics of Protonation.*—The thermodynamic functions for the acid–base reaction (1), summarized in

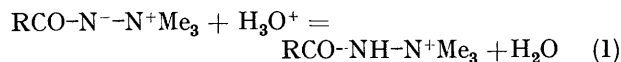
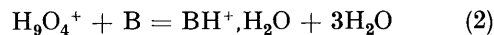


Table 3, show that the protonation of all *N*-ammonioamidates is exothermic and accompanied by an entropy increase. The entropy increase for the protonation of *N*-trimethylammonioacetamidate is closely similar to that found for trimethylamine ( $\Delta S^\circ +63.6\ J\ K^{-1}\ mol^{-1}$ ),<sup>16</sup> while the value for *N*-trimethylammoniobenzamidate is rather smaller, comparable with that reported for triethylamine ( $\Delta S^\circ +56.7\ J\ K^{-1}\ mol^{-1}$ ).<sup>17</sup> These similarities are not unexpected in view of the fact that cations akin to tertiary ammonium ions are formed by protonating *N*-ammonioamidates. The entropy changes in reactions of this type are believed to be largely due to solvation changes. The positive sign of the entropy changes arises from the greater solvation of the proton as compared with a tertiary ammonium ion, so that all these protonation reactions are accompanied by a net release of water molecules of solvation. Solvation by hydrogen bonding 'freezes' water molecules, with a loss of *ca.* 22 J K<sup>-1</sup> mol<sup>-1</sup> in entropy. In the above reactions, which may be represented, including water of hydration, by equation (2), conjugate acids capable



<sup>16</sup> D. H. Everett and W. F. K. Wynne-Jones, *Proc. Roy. Soc.*, 1941, **A177**, 499.

<sup>17</sup> M. C. Cox, D. H. Everett, D. A. Landsman, and R. J. Munn, *J. Chem. Soc. (B)*, 1968, 1373.

of binding only one water molecule by hydrogen bonding are generated, and three water molecules of solvation regain their translational and rotational freedom. This should result in an entropy increase of *ca.* 66 J K<sup>-1</sup> mol<sup>-1</sup>, a figure closely comparable to the experimental entropies of protonation of *N*-trimethylammonioacetamidate and of trimethylamine. The smaller entropy of protonation of triethylamine has been ascribed<sup>18</sup> to restrictions on the freedom of rotation and vibration of ethyl groups in the cation by the hydrogen-bonded water molecule, resulting in a negative contribution to the entropy change. Alternatively, the same effect would arise from the tendency of the ionic change to repel the hydrocarbon chains.<sup>19</sup> Similar interpretations may be given for the less positive entropy of protonation of *N*-trimethylammoniobenzamidate, since a water molecule hydrating the NH group may interfere with the rotational freedom of the bulky benzene ring or the benzoyl group may be stiffened by repulsion. These interpretations ignore the probable presence of hydrogen-bonding hydration of the uncharged bases, but this is justified to the extent that such hydration may be weaker than that of the conjugate acids. In terms of these ideas, the much more positive entropy of protonation of benzoate anions ( $\Delta S^\circ +81.33\ J\ K^{-1}\ mol^{-1}$ )<sup>20</sup> arises from the additional solvation of the anion, coupled with probably weaker hydrogen-bonding solvation of the neutral acid as compared with cation acids.

The effect of substituents upon the thermodynamics of ionisation of *N*-ammoniobenzamides will now be considered. The  $\Delta H^\circ$  and  $-T\Delta S^\circ$  values (at 298.2 K), derived from data given in Table 3 for variously substituted derivatives, have been plotted against the  $pK_a$  values in Figure 3 (lines A), together with the most recent corresponding data<sup>20</sup> for variously substituted benzoic acids (lines B) for comparison. It is clear that there is a linear correlation between  $\Delta H^\circ$  and  $pK_a$  ( $r\ 0.895$ ) and likewise between  $\Delta S^\circ$  and  $pK_a$  ( $r\ 0.956$ ) in this series, as in the benzoic acid series. Hence a plot of  $\Delta H^\circ$  against  $\Delta S^\circ$  is also linear ( $r\ 0.724$ ). Thus the ionisation of *N*-ammoniobenzamides falls into the same category of reactions as the ionisation of benzoic acids themselves, obeying the Hammett equation because of a linear relationship between  $\Delta H^\circ$  and  $\Delta S^\circ$  [category (c) according to Bolton *et al.*<sup>20</sup>].

There is a further similarity between the two reaction series in that the  $-T\Delta S^\circ$  terms are considerably larger than the  $\Delta H^\circ$  terms in both series and the entropy of ionisation becomes progressively more negative as the strength of the acids decreases. The variation in the benzoic acid series of the  $-T\Delta S^\circ$  term with acid strength is, however, more than twice as large as that in the *N*-ammoniobenzamide series [the slopes  $-\delta(T\Delta S^\circ)/\delta\ pK_a$  are 7.1 and 3.5 kJ mol<sup>-1</sup> (at 298.2 K), respectively].

<sup>18</sup> A. G. Evans and S. D. Hamann, *Trans. Faraday Soc.*, 1951, **47**, 34.

<sup>19</sup> D. H. Everett, D. A. Landsman, and B. R. W. Pinsent, *Proc. Roy. Soc.*, 1952, **A215**, 403.

<sup>20</sup> P. D. Bolton, K. A. Fleming, and F. M. Hall, *J. Amer. Chem. Soc.*, 1972, **94**, 1033.

According to Hepler's analysis of thermodynamic functions of proton ionisation in series obeying the Hammett equation,<sup>21,22</sup> the entropy variation is almost entirely due to the variation in the entropy of solvation, *i.e.*  $\delta\Delta S^\circ \approx \delta\Delta S_{\text{env}}$ , and the variation in the enthalpy of solvation may be taken proportional to the variation in

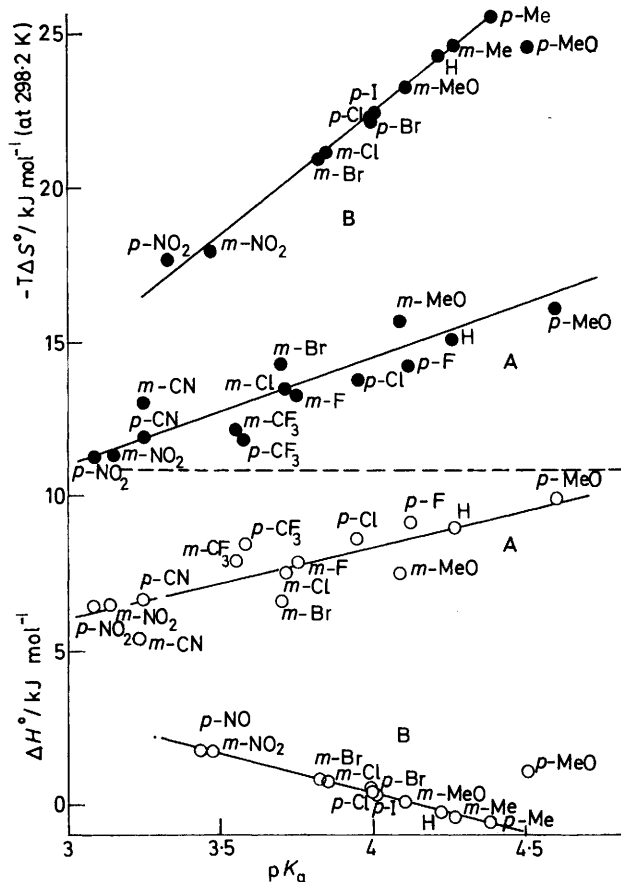


FIGURE 3 Plots of thermodynamic functions ( $-T\Delta S^\circ$  full circles,  $\Delta H^\circ$  open circles) for the proton ionisation of substituted *N*-trimethylammonioacetamidate cations (lines A) and of substituted benzoic acids (lines B) against their respective  $pK_a$  values

the entropy of solvation, *i.e.*  $\delta\Delta H_{\text{env}} \approx \beta\delta\Delta S^\circ$  (with  $\beta$  not very different from  $T$ ). The above slopes (with a minus sign) would thus represent approximately the variations of the solvation enthalpy with acid strength in the two series. The greater variation for the benzoic acids is primarily a consequence of the strong solvation of the benzoate ions, which gets progressively stronger as the anions become more basic, although the simultaneous progressively weaker solvation of the acids probably also makes a contribution. The corresponding effects in the ionisation of *N*-ammonioacetamidates are clearly smaller: there is presumably little variation in the solvation of the

neutral (zwitterionic) bases and the observed variation is due to progressively smaller positive contributions to the enthalpies of solvation as the conjugate acids become weaker and therefore less strongly solvated.

The much greater solvation effects in the ionisation of benzoic acids result (*a*) in close to zero enthalpies of ionisation and (*b*) in decreasing enthalpy values with decreasing acid strength. Since both reaction series have comparable  $\delta\Delta G^\circ$  values, which in terms of Hepler's ideas<sup>21,22</sup> are approximately equal to  $\delta\Delta H_{\text{int}}$ , it is clear that owing to smaller solvation effects in the *N*-ammonioacetamidate series  $\delta\Delta H^\circ$  values parallel  $\delta\Delta H_{\text{int}}$  values, whereas strong solvation effects in the benzoic acid series cause  $\Delta H^\circ$  and  $\Delta H_{\text{int}}$  to vary in opposite directions with variation in acid strength. The fact that  $\delta\Delta H_{\text{int}}$  ( $\approx \delta\Delta G^\circ$ ) values are comparable in both series is consistent with the view expressed in the preceding section that charge distributions are comparable in the benzoate anions and the anionic moiety of acetamidates. The greater 'spread' of  $\Delta G^\circ$  values in the ionisation of *N*-ammonioacetamidate cations, which is reflected in the  $\rho$  value  $>1$ , is associated with the greater 'displaceability' of the negative charge in the anionic moiety of the conjugate bases, as already discussed in the preceding section.

*Some Comparisons of  $pK_a$  Values.*—The basicity of *N*-ammonioacetamidate, with a  $pK_a$  value of 5.39, is closely similar to that reported by Berry and Brocklehurst<sup>23</sup> for *N*-ammoniododecylamidate ( $pK_a$  5.3). A comparison of the  $pK_a$  difference between the conjugate acids of *N*-ammonioacetamidate and *N*-ammonioacetamidate with that between acetic acid and benzoic acid is of interest in connection with the question of mesomerism in the aromatic compounds. It is well known<sup>24</sup> that in benzoic acid an inductive withdrawal of electrons from the carboxy-group by the benzene ring is largely cancelled by the mesomeric electron release (V), so that the  $pK_a$  difference between acetic acid ( $pK_a$  4.74) and benzoic acid ( $pK_a$  4.20) is only 0.54 units. In the amidates studied here, the  $pK_a$  difference between the *N*-ammonioacetamidate cation and the *N*-ammonioacetamidate cation is more than twice as large ( $\Delta pK_a$  1.13). This could be ascribed either (*a*) to a larger inductive electron withdrawal by the ring or (*b*) to a smaller mesomeric electron release, or to both. A larger inductive electron withdrawal is expected if the polarisability of the basic centre is greater in the amidates than in the carboxylates. The above discussion of the  $\rho$  values certainly shows that there is such a difference in polarisability and therefore (*a*) makes a contribution. The mesomeric electron release (VI) is analogous to (V), and only quantum mechanical calculations could give us an idea whether this mesomeric effect is more or less effective in increasing the basicity of the compound than

<sup>23</sup> R. W. H. Berry and P. Brocklehurst, *J. Chem. Soc.*, 1964, 2264.

<sup>21</sup> J. W. Larson and L. G. Hepler, in 'Solute-Solvent Interactions,' eds. J. F. Coetzee and C. D. Ritchie, Marcel Dekker, New York, 1969, pp. 1-44.

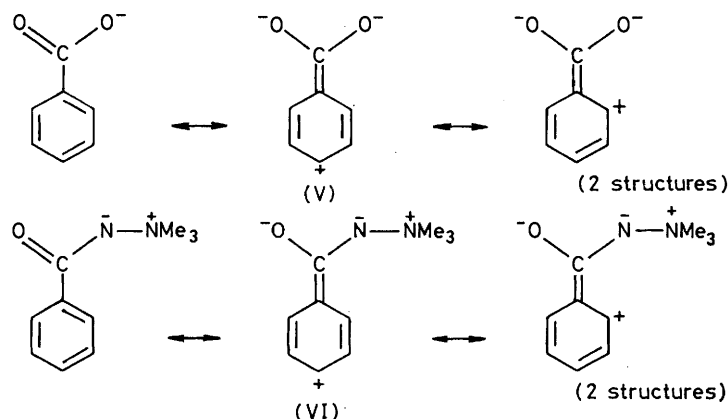
<sup>22</sup> P. D. Bolton and L. G. Hepler, *Quart. Rev.*, 1971, 25, 521.

<sup>24</sup> H. C. Brown, D. H. McDaniel, and O. Häfner, 'Determination of Organic Structures by Physical Methods,' eds. E. A. Braude and F. C. Nachod, Academic Press, New York, 1955, p. 584.

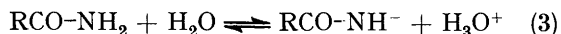
in benzoate anions. Thus the relative importance of effects (a) and (b) remains unknown at present.

Finally, these  $pK_a$  values enable an estimate to be made of the acidifying effect of the positive *N*-trimethylammonio-pole on the acidity of amides. Amides are known to have very weakly acidic properties (*e.g.* from the fact that NH protons show exchange with the solvent protons in weakly alkaline solutions),<sup>25,26</sup> but

It may be mentioned also that the acidifying effect of the *N*-trimethylammonio-pole upon the acidity of cyclopentadiene is only *ca.* 5  $pK$  units, which is less than expected from an estimate of the extra stabilization due to the interaction of opposite charges.<sup>29</sup> This has been ascribed to the electrostatic inhibition of delocalization of charge in the cyclopentadienide ring, since the negative charge becomes partially localized next to the



quantitative measurements on the acid-base equilibrium (3) are made difficult by the onset of base hydrolysis.



Nevertheless, Branch and Clayton<sup>27</sup> have used a conductometric method on mixtures with relatively high concentrations of acetamide and low concentrations of barium hydroxide to estimate the degrees of ionisation of acetamide in alkaline solution and have hence obtained a  $pK_a$  value of 15.1. This taken in conjunction with the present results means that the substitution of a positive pole on the amide nitrogen raises the acidity of the NH proton by some 10 powers of ten. This is comparable in magnitude with the factor of some 9 powers of ten between the first and the second ionisation constants of the doubly protonated hydrazinium ion.<sup>28</sup>

<sup>25</sup> A. Berger, A. Loewenstein, and S. Meiboom, *J. Amer. Chem. Soc.*, 1959, **81**, 62.

<sup>26</sup> M. Liler, *Spectrochim. Acta*, 1972, **28A**, 186.

positive pole (the loss of delocalization energy offsetting to some extent the acid strengthening effect of the pole). Since the enhancement of acidity of the amide by the positive pole is much greater, indeed comparable to that in a system not involving charge delocalization (*i.e.* the hydrazinium cation), this presumably means that the negative charge delocalization in the amidate anionic moiety is not much greater than the delocalization of the nitrogen lone pair electrons in the amide. The reason for this may be the considerable polarity of the CO bond in the amide, *i.e.* the partial negative charge already present on the oxygen, prior to the loss of a proton from the amide nitrogen.

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<sup>27</sup> G. E. K. Branch and J. O. Clayton, *J. Amer. Chem. Soc.*, 1928, **50**, 1680.

<sup>28</sup> G. Schwarzenbach, *Helv. Chim. Acta*, 1936, **19**, 178.

<sup>29</sup> E. M. Kosower, 'An Introduction to Physical Organic Chemistry,' Wiley, New York, 1968, p. 38.