

## Intramolecular Hydrogen Bonding as a Factor in Determining the $K_1/K_2$ Ratios of Dicarboxylic Acids

LENNART EBERSON and INGEMAR WADSÖ

*Department of Organic Chemistry and Thermochemistry Laboratory,  
University of Lund, Sweden*

The ionization enthalpies of racemic 2,3-di-(tert-butyl)-succinic acid have been determined, being for the first step  $-0.94 \pm 0.10$  kcal/mole in 50 % by weight aqueous ethanol and for the second  $+4.0 \pm 0.2$  kcal/mole in water. From the latter value the enthalpy of formation of the intramolecular hydrogen bond in the acid ion was estimated to be  $-4.8 \pm 0.8$  kcal/mole.

The high ratio between the first and second dissociation constant exhibited by certain types of dibasic acids has been explained mainly on the basis of increased electrostatic interaction between the carboxyl groups and the formation of an intramolecular hydrogen bond in the acid ion<sup>1-13</sup>. In all such acids the geometry of the molecule is such as to allow the carboxyl groups to be oriented in close proximity to each other in order that these effects will operate effectively. The geometrical and steric factors favouring a high  $K_1/K_2$  ratio are well known and the problem is to determine to what extent internal hydrogen bonding contributes to a high ratio between the ionization constants.

Infrared and NMR spectral evidence for the existence of such a hydrogen bond has been presented for the acid ions of some highly alkylated succinic acids<sup>14,15</sup> ( $\Delta pK$  values between 6.6 and 9.5 in 50 % by weight ethanol-water<sup>11</sup>) and for the acid maleate ion<sup>16</sup> ( $\Delta pK$  in water 4.42<sup>17</sup> and in 50 % by weight ethanol-water 6.6<sup>11</sup>). Maleic acid is the most frequently cited example of internal hydrogen bonding as a possible cause of a high  $K_1/K_2$ -ratio, and since the acid maleate ion is often used as a model compound for the investigation and discussion of hydrogen bond properties<sup>17-19</sup>, the arguments for the existence of such bonding in this acid will be discussed in some detail.

Dodd, Miller and Wynne-Jones<sup>20</sup> concluded that electrostatic effects, as calculated by the Kirkwood-Westheimer treatment<sup>2,3</sup>, alone are sufficient to account for the high  $K_1/K_2$  ratio found for maleic acid. Nevertheless, they were able to demonstrate by infrared measurements that the intramolecular

hydrogen bond known to be present in crystalline acid maleate<sup>21</sup> is stable enough to withstand competition with external hydrogen bonding from water, but probably not from dioxane. The hydrogen bond in crystalline maleic acid<sup>22</sup> itself is, however, broken up in these solvents. In deuterium oxide it appears possible that both internally and externally, "deuterium bonded" ions are present in comparable equilibrium concentrations and since the relative abilities of deuterium and hydrogen to form hydrogen bonds do not differ appreciably<sup>18,23a</sup>, the same situation probably applies to water. This conclusion is in agreement with calculations by Westheimer and Benfey<sup>23b</sup>, which suggest that hydrogen bonding contributes maximally by a factor of about 30 in the  $K_1/K_2$  ratio of maleic acid. This corresponds to an equilibrium constant of about 10 for the equilibrium between externally and internally hydrogen bonded ions.

Levy and Maguolas<sup>19</sup> calculated an equilibrium constant of 45 by a slightly modified procedure. This value is probably too high, since the calculations were based on the assumption that electrostatic effects are identical in maleic and fumaric acid, which cannot be the case in view of the above results.

Jaffé has pointed out that there is a fundamental thermodynamic difference between inter- and intramolecular hydrogen bonds,<sup>24</sup> which makes even weak (say with a  $-\Delta H$  of 0.5–1 kcal/mole) intramolecular hydrogen bonds observable in polar solvents, such as water and dioxane. The difference appears in the  $T\Delta S$  term that is estimated to be 4–5 kcal/mole for an intermolecular hydrogen bond and negligible for an intramolecular hydrogen bond. This would be the reason for the difficulty of observing intermolecular hydrogen bonds with  $-\Delta H$  less than 3 kcal/mole, whereas intramolecular ones with considerably smaller enthalpies of formation are observable, as there is no unfavourable  $T\Delta S$  term to overcome.

The results obtained by Dodd, Miller, and Wynne-Jones combined with the above-mentioned theoretical considerations are in good agreement with the assumption of a rather weak internal hydrogen bond in the acid maleate ion in aqueous solution. In the absence of any significant  $T\Delta S$  term, this will correspond to an equilibrium between externally and internally hydrogen bonded ions in comparable concentrations. This weak bond contributes significantly but not dominantly to the  $K_1/K_2$  ratio and the main effect is probably electrostatic in origin.

Evidently, we must turn to acids with extremely high  $K_1/K_2$  ratios in order to find intramolecular hydrogen bonding as an important factor in determining the  $K_1/K_2$  ratio. Racemic 2,3-di-(tert-butyl)-succinic acid (I) has the largest  $\Delta pK$  ever reported (9.5 in 50 % by weight ethanol-water<sup>11</sup> and 8.0 in water<sup>25</sup>) and the existence of intramolecular hydrogen bonding in its acid ion has been demonstrated by infrared<sup>15</sup> and NMR<sup>14</sup> measurements. By calculation of the electrostatic effect according to the Kirkwood-Westheimer treatment and the influence of hydrogen bonding according to the method given by Westheimer and Benfey it could also be shown that hydrogen bonding must be the dominating factor in determining the  $K_1/K_2$  ratio<sup>11</sup>.

However, the results from the NMR measurements on maleic acid and I and their potassium salts are contradictory to those obtained by calculations and ionization constant data. If we accept that a stronger hydrogen bond has

the larger chemical shift,<sup>26</sup> the hydrogen bond in the acid maleate ion must be stronger than that in the acid ion of I since monopotassium maleate in dimethyl sulphoxide has the hydrogen bond signal at lower fields ( $\delta = -15.40$  with external water standard) than the monopotassium salt of I ( $\delta = -14.66$  with external water standard). In order to resolve this apparent contradiction it seemed desirable to determine the thermodynamic functions for the ionization stages of I. In this paper we give the results of a calorimetric determination of these ionization enthalpies, which together with data from the literature make possible an estimation of the influence of internal hydrogen bonding on the  $K_1/K_2$  ratio of dibasic acids.

The measurements were carried out with an isothermal jacket calorimeter described by Sunner and Wadsö<sup>27,28</sup>. The enthalpies of ionization were determined by allowing a solution of the monosodium salt to react with hydrochloric acid ( $\Delta H_1$ ) or with 0.1 M sodium hydroxide solution ( $\Delta H_2$ ). As the free acid is very slightly soluble in water the determination of the enthalpy of the first ionization step had to be performed in 50 % by weight ethanol. Appropriate corrections were made for the heats of dilution accompanying the reactions.

The use of a solution of the monosodium salt in both cases is made possible by the large difference between  $K_1$  and  $K_2$ , which means that the acid ion comprises more than 99.9 % of the total acid concentration in a pH interval around neutrality.

## EXPERIMENTAL

*Materials.* Rac.-2,3-di-(tert-butyl)-succinic acid was prepared and purified as described elsewhere<sup>29</sup>. According to titrations the purity was better than 99.7 %. The distilled water used in the preparation of the calorimetric liquids was deionized and made free from carbon dioxide. Ethanol, sodium hydroxide and sodium chloride were of analytical grades.

*Apparatus.* The measurements were performed with an "isothermal-jacket" glass calorimeter, described in detail elsewhere<sup>27,28</sup>. The heat equivalent of the calorimeter including its content was determined by passing a known current for a given time (360 sec) through the heating element. The calibration experiments were performed after the reaction had taken place.

*Units of measurements.* The results of the calorimetric experiments are expressed in terms of the defined calorie, equal to 4.1840 abs. joules, and refer to the isothermal process at 25°C.

### Calorimetric technique

*Determination of  $\Delta H_1$ .* The calorimeter was charged with 100 ml of aqueous ethanol (50.36 % by weight) solution containing 2 mmoles of the monosodium salt of I. The calorimetric liquid was prepared by adding carbonate-free sodium hydroxide solution to the acid solution until the pH was 7.0 as determined by glass electrode. During the preparation and while handling the solution precautions were taken to avoid carbon dioxide uptake.

In the sealed glass ampoule was contained ca. 0.6 ml 1.7 M aqueous hydrochloric acid, i.e. about 1 mmole of acid. To account for the heat accompanying the dissolution of the hydrochloric acid solution in the calorimetric liquid blank experiments were performed.

*Determination of  $\Delta H_2$ .* In the determination of  $\Delta H_2$  for I a supersaturated aqueous solution of the monosodium salt was contained in the ampoule. The calorimetric liquid

consisted of 0.1 M aqueous sodium hydroxide. Blank experiments with 0.1 M sodium chloride solution as calorimetric liquid were performed.

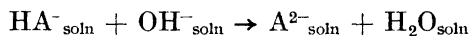
The mono-salt solution was prepared from a weighed amount of the acid by addition of strong carbonate-free sodium hydroxide solution until the pH was 7–7.5. The well-defined neutralization end point was indicated by bromothymol blue and checked in control experiments by using both the indicator and glass electrode. The strong salt solution, containing 0.817 mmole of salt per g of solution, crystallized upon prolonged standing at room temperature. Calorimetric experiments, however, could be performed on the super-saturated liquid, which remained stable in the ampoules for ca. 6 h.

## RESULTS

Results from the calorimetric experiments are given in Tables 1 and 2.  $\log R_i/R_f$  is the expression proportional to the temperature change;  $R_i$  and  $R_f$  are the corrected thermistor resistance values at the start and the end, respectively, of the main period.  $\epsilon$  is the heat equivalent of the system. All uncertainties are given as average deviation of the mean.

The dilution of HCl is accompanied by a heat evolution equal to 8.75 kcal/mole. When, following the dilution process, the protons are bound by the acid anions the heat evolution equals 7.77 kcal/mole and thus the enthalpy change accompanying the first ionization step of I ( $\Delta H_1$ ) is derived to be  $-0.94 \pm 0.06$  kcal/mole. When allowances are made for possible systematic errors this value is  $\Delta H_1 = -0.94 \pm 0.10$  kcal/mole.

The heat of dilution of the ampoule contents in 0.1 M aqueous NaCl is accompanied by an enthalpy release equal to 1.48 kcal/mole. When the ampoule contents is diluted to approximately the same concentration and the same ionic strength as in the blank experiments, followed by neutralization of the monosalt solution 10.98 kcal was released per mole of acid anion. Then, for the process



the enthalpy change is calculated to be  $-9.50 \pm 0.06$  kcal/mole. The heat of ionization of water is 13.50 kcal/mole<sup>30</sup> at zero ionic strength and is not expected to deviate significantly from that at an ionic strength of 0.1. (From

Table 1. Determination of  $\Delta H_1$  for I in aqueous ethanol (50 % by weight).  $\epsilon = 7595 \pm 8$  cal/unit of  $\log R_i/R_f$ .

Reaction	mmoles HCl in the ampoule	$10^4 \times \log R_i/R_f$	$-\Delta H$ , kcal/mole
Protonization of $\text{HA}^-$	0.926	9.52	7.81
	1.083	11.15	7.82
	1.104	11.19	7.70
	1.036	10.55	7.73
			Mean $7.77 \pm 0.05$
Blank experiment	1.086	12.46	8.71
	0.895	10.34	8.77
	1.090	12.53	8.73
	1.063	12.27	8.77
			Mean $8.75 \pm 0.02$

Table 2. Determination of the sum of the enthalpy of the second ionization step of I and the heat of neutralization of water in aqueous solution. Ionic strength = 0.1. Ampoule contents: Aqueous solution of the monosodium salt of I.

Reaction, calorimetric liquid, and heat equivalent	mmoles NaHA in the ampoule	$10^4 \times \log R_i/R_f$	$-\Delta H$ , kcal/mole
Neutralization	0.808	9.91	10.07
0.1 M NaOH	0.774	9.47	10.95
$\varepsilon = 8948 \pm 11$	0.792	9.81	11.08
	0.711	8.69	10.93
			Mean $10.98 \pm 0.05$
Blank experiment	0.794	1.32	1.49
0.1 M NaCl	0.709	1.14	1.44
$\varepsilon = 8978 \pm 9$	0.689	1.16	1.51
	0.764	1.27	1.49
			Mean $1.48 \pm 0.02$

recent calorimetric experiments<sup>28,31</sup>, parallel to this investigation, the heat of ionization of water at an ionic strength of 0.2 can be calculated to be 13.54 kcal/mole). The heat of dilution of the sodium hydroxide solution by the water formed at the neutralization is insignificant<sup>32</sup> and thus the enthalpy change for the second ionization step of I is calculated to be  $4.00 \pm 0.15$  kcal/mole. (The assigned uncertainty range includes possible systematic errors.)

#### DISCUSSION

In Table 3 thermodynamic data are compiled for about sixty ionization processes involving many types of carboxylic acids, and in Fig. 1  $-\Delta S$  has been plotted against  $pK$ . From Fig. 1 it is evident that there exists a linear correlation between these quantities, which is to be expected as the ionization enthalpies generally are small as compared with the free energies of ionization. The equation of the straight line was computed by the method of least squares (all points were included except those from the first and second ionization of I) and found to be

$$-\Delta S = 0.3 + 4.94 pK \quad (1)$$

with a probable error of a single value of  $\Delta S$  of  $\pm 2$  e.u. A similar linear relationship was found by Chen and Laidler for a series of substituted phenols<sup>52</sup>. The existence of such linear  $pK$  (or  $\Delta G$ -) $-\Delta S$  relationships is the basis of discussions regarding the influence of inductive and resonance effects on the strength of organic acids. As is seen by inspection of Table 3 and Fig. 1 the inductive effect is largely reflected in the  $T\Delta S$  term, *e.g.* the strength of a given acid is determined to a large extent by the change in orientation and compression of solvent molecules accompanying ionization<sup>56,53</sup>. For a strongly polar acid the  $T\Delta S$  term is small, since orientation and compression of solvent molecules around the solute is appreciable even before ionization<sup>36,54</sup>. There is no indication that the inductive effect should be due to electronic displacements induced by the substituent and propagated through the carbon chain

Table 3. Thermodynamic functions for the ionization of carboxylic acids at 25° in water.

Acid	pK	$\Delta H$ kcal/mole	$\Delta S$ e.u./mole	Method <sup>a</sup>	Reference <sup>b</sup>
Formic	3.77	-0.13	-18	C	33
Acetic	4.76	-0.07	-22	C	33
Propionic	4.88	-0.08	-23	C	33
Butyric	4.82	-0.73	-25	C	33
Isobutyric	4.86	-1.01	-26	C	33
Valeric	4.84	-0.72	-25	D	34
Hexoic	4.86	-0.70	-25	D	34
Isovaleric	4.78	-1.22	-26	D	34
Isohexoic	4.85	-0.72	-25	D	34
Trimethylacetic	5.03	-0.72	-25	D	34
Diethylacetic	4.74	-2.03	-28	D	34
Benzoic	4.21	0.09	-19	C	33
Fluoroacetic	2.59	-1.39	-17	D	35
Chloroacetic	2.87	-1.12	-17	D	35
Bromoacetic	2.90	-1.24	-17	D	35
Iodoacetic	3.18	-1.42	-19	D	35
Cyanoacetic	2.47	-0.9	-14	D	36
Glycine	2.35	0.93	- 8	C	37
$\alpha$ -Alanine	2.35	0.62	- 9	C	38
$\beta$ -Alanine	3.55	1.18	-12	D	39
$\gamma$ -Aminobutyric	4.03	0.40	-17	D	40
$\epsilon$ -Aminocaproic	4.37	0.0	-20	D	41
Succinic, 1st	4.21	0.60	-17	C	42
Succinic, 2nd	5.64	0.04	-26	C	42
Oxalic, 2nd	4.27	-1.66	-25	D	43
Malonic, 1st	2.85	0.02	-13	D	44
Malonic, 2nd	5.70	-1.14	-30	D	44
Fumaric, 1st	3.10 <sup>c</sup>	-0.37	-15	C	45
Fumaric, 2nd	4.60 <sup>c</sup>	0.90	-17	C	45
Maleic, 1st	1.91 <sup>c</sup>	-0.26	-10	C	45
Maleic, 2nd	6.33 <sup>c</sup>	-0.21	-29	C	45
<i>cis</i> -Cyclohexane-1,2-dicarboxylic, 1st	4.34 <sup>d</sup>	1.1	-16	C, D	46
<i>cis</i> -Cyclohexane-1,2-dicarboxylic, 2nd	6.76 <sup>d</sup>	-0.30	-31	C, D	46
<i>trans</i> -Cyclohexane-1,2-dicarboxylic, 1st	4.18 <sup>d</sup>	-1.9	-25	C, D	46
<i>trans</i> -Cyclohexane-1,2-dicarboxylic, 2nd	5.93 <sup>d</sup>	-0.24	-27	C, D	46
<i>cis</i> -Caronic, 1st	2.34	-1 <sup>e</sup>	-14	D	47
<i>cis</i> -Caronic, 2nd	8.31	-1 <sup>e</sup>	-41	D	47
<i>trans</i> -Caronic, 1st	3.92	-2 <sup>e</sup>	-21	D	47
<i>trans</i> -Caronic, 2nd	5.32	-2 <sup>e</sup>	-31	D	47
Phthalic, 1st	2.95	-0.64	-16	D	48a
Phthalic, 2nd	5.42	-0.50	-26	D	48b
rac-2,3-Di-tert.-butyl-succinic, 1st	3.58 <sup>f,g</sup>	-0.94 <sup>g</sup>	-19	C	this work
rac-2,3-Di-(tert.-butyl)-succinic, 2nd	10.2 <sup>h</sup>	4.0	-33	C	this work
(+)-Tartaric, 1st	3.04	0.74	-11	D	49
(+)-Tartaric, 2nd	4.31	0.24	-19	D	49
Glutaric, 1st	4.43	0 <sup>e</sup>	-20	D	47
Glutaric, 2nd	5.41	-0.3 <sup>e</sup>	-25	D	47
3-Methylglutaric, 1st	4.25	-0.3 <sup>e</sup>	-20	D	47
3-Methylglutaric, 2nd	5.41	-1 <sup>e</sup>	-28	D	47

Table 3. Cont.

3-Isopropylglutaric, 1st	4.30	-1 <sup>e</sup>	-23	D	47
3-Isopropylglutaric, 2nd	5.51	-1.5 <sup>e</sup>	-30	D	47
3,3-Dimethylglutaric, 1st	3.70	-3 <sup>e</sup>	-27	D	47
3,3-Dimethylglutaric, 2nd	6.34	-2.5 <sup>e</sup>	-37	D	47
3,3-Pentamethyleneglutaric, 1st	3.49	-2.5 <sup>e</sup>	-24	D	47
3,3-Pentamethyleneglutaric, 2nd	6.96	-1.5 <sup>e</sup>	-36	D	47
Adipic, 1st	4.43	-1 <sup>e</sup>	-23	D	47
Adipic, 2nd	5.42	-1 <sup>e</sup>	-27	D	47
Citric, 1st	3.13	1.00	-11	D	50
Citric, 2nd	4.76	0.58	-20	D	50
Citric, 3rd	6.40	-0.80	-33	D	50

a. Whenever possible,  $\Delta H$  values have been taken from calorimetric measurements. C = calorimetric, D = dissociation constant data.

b. Source of pK and  $\Delta H$ .

c.  $\Delta pK$  from the work by Dahlgren and Long<sup>19</sup>.

d. Ref.<sup>51</sup>.

e. These values were estimated from the slope of the tangent at  $T = 298^\circ$  to the curve relating  $1/T$  and  $-\log K$ . The uncertainty is estimated at  $\pm 1$  kcal/mole.

f. Ref.<sup>11</sup>

g. In 50 % by weight ethanol-water.

h. Ref.<sup>25</sup>.

to the O—H bond with a resulting strengthening or loosening of this bond. Such an effect would be expected to influence the  $\Delta H$  term but this is, however, not the case. No simple correlation exists between acid strength and heat of ionization. We therefore favor an interpretation of the inductive effect as a field effect operating mainly by changing the solvent structure around the molecule.

The existence of a small and temperature dependent  $\Delta H$  term makes it advisable not to discuss minor pK differences in a series of acids too much in detail, since pK determinations carried out at other temperatures sometimes will reveal a different order of acid strengths<sup>34</sup>.

For the dicarboxylic acids listed in Table 3 the second ionization is accompanied by a larger negative entropy change than the first one. If  $\Delta S_1 - \Delta S_2$  is plotted against  $\Delta pK$  for these acids we obtain a linear correlation, which is shown in Fig. 2 (naturally, this relationship is implied in Fig. 1).  $\Delta H_1$  and  $\Delta S_1$  of I could not be determined in water due to the insolubility of the acid but from eqn. (1) we estimate a  $\Delta S_1$  of  $-11 \pm 2$  e.u. for the pK<sub>1</sub> of I in water (2.18<sup>25</sup>) and consequently  $\Delta H_1$  in water is  $\sim 0$ . Fig. 2 indicates that the change in orientation and compression of solvent molecules accompanying the second ionization is more pronounced when the carboxyl groups are oriented close to each other.

Starting from the principles discussed above it is possible to analyze the extremely large  $\Delta pK$  of I in terms of electrostatic (or inductive) effect and internal hydrogen bonding. Electrostatic interaction between the carboxyl groups should have little effect on  $K_1$  but should decrease  $K_2$ . Intramolecular hydrogen bonding in the acid ion should facilitate the removal of the first proton, since it stabilizes the monoanion but should decrease  $K_2$  for the same reason. The pK<sub>1</sub> value of I in water is 2.18, which is considerably lower than

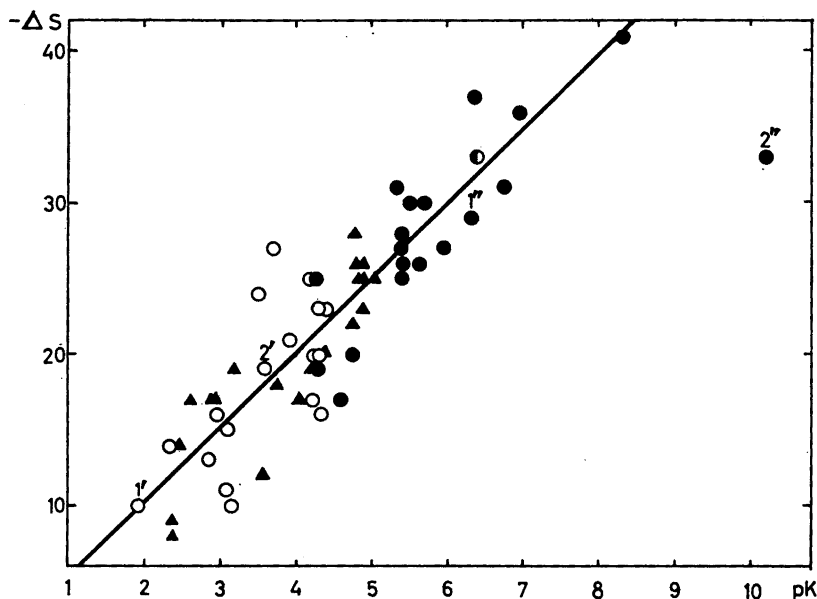


Fig. 1. Plot of  $-\Delta S$  against  $pK$ .  $\blacktriangle$   $pK$  from monocarboxylic acids;  $\circ$   $pK_1$  from dicarboxylic acids;  $\bullet$   $pK_2$  from dicarboxylic acids;  $\odot$   $pK_3$  from a tricarboxylic acid; 1', 1'' are  $pK_1$  and  $pK_2$  of maleic acid; 2', 2'' are  $pK_1$  and  $pK_2$  of I.

$pK_1$  of succinic acid (4.21). Nevertheless, if we assume that I exists in a conformation with gauche carboxyl groups (COOH-group separation about 4.5 Å), its  $pK$  will lie on the smooth curve relating  $pK$  and calculated maximal interprotonic distance ( $R_{\max}$ ) for acids of the type  $\text{HOCO}(\text{CH}_2)_n\text{COOH}$  (Fig. 1 in Ref.<sup>20</sup>). Thus, we conclude that  $pK_1$  for I is not anomalous but may be accounted for by the electrostatic effect alone. This is also shown by the fact that the thermodynamic functions for the first ionization in 50 % ethanol-water obey the relationship in Fig. 1 in a satisfactory manner.

On the other hand, none of the relationships given in Fig. 1 in Ref.<sup>20</sup> or in Fig. 1 of this paper is satisfied by the  $pK_2$  of I. The deviation from normal behaviour is due to the large positive enthalpy of ionization ( $\Delta H_2 = +4.0$  kcal/mole) and it seems reasonable to assume that this anomalous value is caused by intramolecular hydrogen bonding in the acid ion, which would be expected to influence  $\Delta H_2$  in this direction.

In order to estimate the hydrogen bond strength of the acid ion of I we assume that  $\Delta H_2$  is the sum of (1) the enthalpy of breaking the intramolecular hydrogen bond ( $\Delta H_3$ ) and (2) the heat of ionization of the non-hydrogen bonded acid ion ( $\Delta H_2'$ ), *i.e.*

$$\Delta H_2 = \Delta H_2' + \Delta H_3 \quad (2)$$

$\Delta H_2'$  can be estimated by putting  $\Delta S_2 = -33$  e.u. (Table 3) into eqn. (1), which gives  $pK_2' = 6.6$ . This value may be considered to be the  $pK$  of the



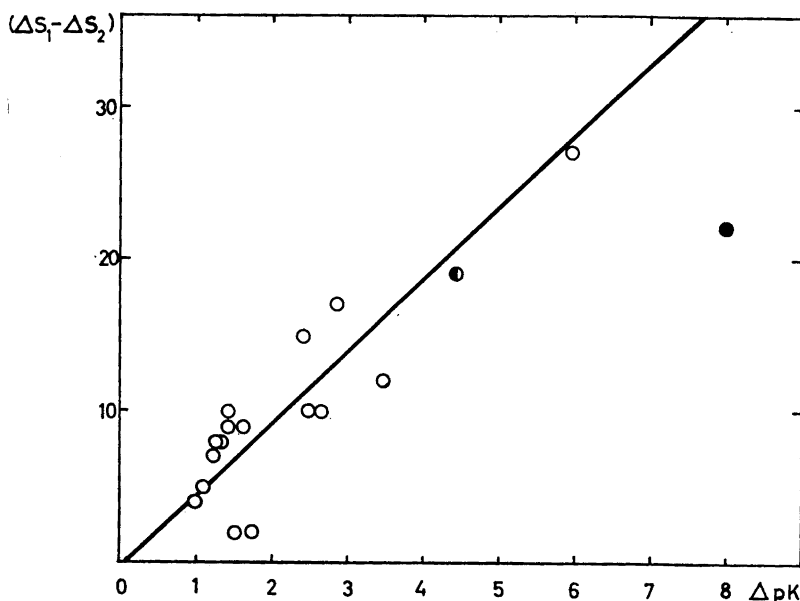


Fig. 2. Plot of  $(\Delta S_1 - \Delta S_2)$  against  $\Delta pK$ . ○ for maleic acid; ● for I.

second ionization of I with only the inductive effect operating. The equation  $\Delta G = \Delta H - T\Delta S$  immediately gives  $\Delta H_2' = -0.8$  kcal/mole and from eqn. (2) we obtain  $\Delta H_3 = 4.8$  kcal/mole. The uncertainty of  $\Delta H_3$  caused by experimental errors is estimated at  $\pm 0.8$  kcal/mole. If we, following the arguments given by Jaffé,<sup>24</sup> neglect the  $T\Delta S$  term for this process we arrive at a free energy of formation of the intramolecular hydrogen bond in the acid ion of  $-4.8 \pm 0.8$  kcal/mole.

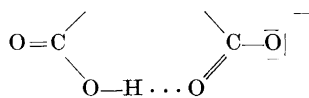
It is possible to estimate the free energy of internal hydrogen bond formation independently from the formula given by Westheimer and Benfey<sup>23</sup>. Using  $pK_1 = 2.18$  and  $pK_E = 5.5$ <sup>25</sup> ( $K_E$  = the ionization constant of the monomethyl ester of I) the equilibrium constant between non-bonded and bonded acid ion species is restricted to values between  $10^3$  and  $2 \times 10^3$ , dependent on the (unknown) degree of internal hydrogen bonding in the monoester. Thus  $\Delta G$  has a value between  $-4.1$  and  $-4.5$  kcal/mole. With regard to the approximate nature of this calculation and the many uncertain factors involved in the interpretation of the calorimetric results the agreement is very satisfactory.

Returning to maleic acid we find that the thermodynamic functions for the first and second ionization do not deviate significantly from the relationships in Figs. 1 and 2. According to the discussion above this will indicate that internal hydrogen bonding in the monoanion is weak and that electrostatic effects make the greatest contribution to the  $K_1/K_2$  ratio. This is essentially the same conclusion as that reached by Dodd, Miller, and Wynne-Jones<sup>20</sup> on the basis of calculations and infra-red measurements.

It was recently suggested on the basis of thermodynamic data that the acid malonate ion should be stabilized by a symmetrical intramolecular hydrogen bond<sup>44</sup>. This could not be confirmed by infrared measurements<sup>55</sup> and the results obtained in this investigation also indicate that such hydrogen bonding must be very weak. Unfortunately the enthalpy data for the remaining high-ratio acids listed in Table 3 (*cis*-caronic acid, 3,3-pentamethyleneglutaric acid) are too uncertain to allow an estimation of the importance of hydrogen bonding in determining their  $K_1/K_2$  ratios.

We conclude that intramolecular hydrogen bonding as a factor in determining  $\Delta pK$  is almost negligible for dicarboxylic acids with  $\Delta pK \leq 4$ . Above this value hydrogen bonding will be increasingly important as  $\Delta pK$  increases. Accordingly the acid maleate ion may be used as a model for the study of hydrogen bond properties<sup>17,19</sup> and also the dialkylmalonic acids used by Levy and Maguolas,<sup>19</sup> although dissociation constant measurements probably are not very well suited for the study of the hydrogen bonds in these acids.

Evidently, the results from the NMR measurements on the acid ions of maleic acid<sup>16</sup> and I<sup>14</sup> in dimethyl sulphoxide are not appropriate for the estimation of the absolute and relative hydrogen bond strengths. It may be assumed that the large chemical shifts observed in the NMR spectra of these compounds are characteristic for the hydrogen bond system II,



II

which differs from other hydrogen bonds by the presence of a negative charge very close to the hydrogen bonded proton. The effect of an electric field on the proton would be a reduction in diamagnetic screening and consequently a shift towards low fields. It has been calculated that a single electronic charge situated at a distance of about 1.4 Å from a free hydrogen atom would produce a shift of 4 ppm towards low fields<sup>56</sup>. It appears probable that this effect operates strongly in II, especially as the charge may be distributed over the whole system. Thus, the electric charge exerts some kind of a levelling effect and shifts due to differences in hydrogen bond energy cannot be estimated.

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## REFERENCES

1. Bjerrum, N. *Z. physik. Chem.* **106** (1923) 219.
2. Kirkwood, J. G. and Westheimer, F. H. *J. Chem. Phys.* **6** (1938) 506, 513.
3. Westheimer, F. H. and Shookhoff, M. W. *J. Am. Chem. Soc.* **61** (1939) 555.
4. Wynne-Jones, W. F. K. and Rushbrooke, G. S. *Trans. Faraday Soc.* **40** (1944) 99.
5. Westheimer, F. H. and Kirkwood, J. G. *Trans. Faraday Soc.* **43** (1947) 77.
6. Peek, H. M. and Hill, T. L. *J. Am. Chem. Soc.* **73** (1951) 5304.
7. Hunter, L. *Chem. Ind. (London)* **1953** 408.
8. McDaniel, D. H. and Brown, H. C. *Science* **118** (1953) 370.

9. Brown, H. C., McDaniel, D. H. and Häfliger, O. in Braude, E. A. and Nachod, F. C. *Determination of Organic Structures by Physical Methods*, Academic Press, New York 1955, p. 622.
10. Wotiz, J. H. and Merrill, H. E. *J. Am. Chem. Soc.* **80** (1958) 866.
11. Ebersson, L. *Acta Chem. Scand.* **13** (1959) 211.
12. Ebersson, L. *Svensk Kem. Tidskr.* **71** (1959) 153.
13. Ebersson, L. *Acta Chem. Scand.* **14** (1960) 614.
14. Ebersson, L. and Forsén, S. *J. Phys. Chem.* **64** (1960) 767.
15. Ebersson, L. *Acta Chem. Scand.* **13** (1959) 224.
16. Forsén, S. *J. Chem. Phys.* **31** (1959) 852.
17. Dahlgren, G., Jr. and Long, F. A. *J. Am. Chem. Soc.* **82** (1960) 1303.
18. McDougall, A. O. and Long, F. A. *J. Phys. Chem.* **66** (1962) 429.
19. Levy, M. and Maguolas, J. P. *J. Am. Chem. Soc.* **84** (1962) 1345.
20. Dodd, R. E., Miller, R. E. and Wynne-Jones, W. F. K. *J. Chem. Soc.* **1961** 2790.
21. Peterson, S. W. and Levy, H. A. *J. Chem. Phys.* **29** (1958) 948.
22. Shahat, M. *Acta Cryst.* **5** (1952) 763.
- 23a. Pimentel, G. C. and McClellan, A. L. *The Hydrogen Bond*, W. H. Freeman and Co., San Francisco and London 1960, p. 210.
- 23b. Westheimer, F. H. and Benfey, O. T. *J. Am. Chem. Soc.* **78** (1956) 5309.
24. Jaffé, H. H. *J. Am. Chem. Soc.* **79** (1957) 2373.
25. Ebersson, L. and Glasoe, P. *To be published.*
26. Pople, J. A., Schneider, W. G. and Bernstein, H. J. *High-resolution Nuclear Magnetic Resonance*, McGraw-Hill Book Company, New York 1959, p. 406.
27. Sunner, S. and Wadsö, I. *Acta Chem. Scand.* **13** (1959) 97.
28. Wadsö, I. *Acta Chem. Scand.* **16** (1962) 479.
29. Ebersson, L. *Acta Chem. Scand.* **13** (1959) 40.
30. Canady, W. J., Papée, H. M. and Laidler, K. J. *Can. J. Chem.* **34** (1956) 1677.
31. Wadsö, I. *Acta Chem. Scand.* **16** (1962) 487.
32. Rossini, F. D., Wagman, D. D., Evans, W. H., Levine, S. and Jaffé, J. *Selected Values of Chemical Thermodynamic Properties*, Circ. of NBS 500, US Government Printing Office, Washington 1952.
33. Ganady, W. J., Papée, H. M. and Laidler, K. J. *Trans. Faraday Soc.* **54** (1958) 502.
34. Everett, D. H., Landsman, D. A. and Pinsent, B. R. W. *Proc. Roy. Soc. A* **215** (1952) 403.
35. Ives, D. J. G. and Pryor, J. H. *J. Chem. Soc.* **1955** 2104.
36. Feates, F. S. and Ives, D. J. G. *J. Chem. Soc.* **1956** 2802.
37. Sturtevant, J. M. *J. Am. Chem. Soc.* **63** (1941) 88.
38. Sturtevant, J. M. *J. Am. Chem. Soc.* **64** (1942) 762.
39. May, M. and Felsing, W. A. *J. Am. Chem. Soc.* **73** (1951) 406.
40. King, E. J. *J. Am. Chem. Soc.* **73** (1951) 155.
41. Smith, P. K. and Smith, E. R. B. *J. Biol. Chem.* **146** (1942) 187.
42. Cottrell, T. L. and Wolfenden, J. H. *J. Chem. Soc.* **1948** 1019.
43. Pinching, G. D. and Bates, R. G. *J. Res. Natl. Bur. Std.* **40** (1948) 405.
44. Das, S. N. and Ives, D. J. G. *Proc. Chem. Soc.* **1961** 373.
45. Wassermann, A. *Z. physik. Chem. A* **146** (1930) 418.
46. Wassermann, A. *Z. physik. Chem. A* **151** (1930) 110.
47. Jones, I. and Soper, F. G. *J. Chem. Soc.* **1936** 133.
- 48a. Hamer, W. J., Pinching, G. D. and Acree, S. F. *J. Res. Natl. Bur. Std.* **35** (1945) 539.
- 48b. Hamer, W. J. and Acree, S. F. *J. Res. Natl. Bur. Std.* **35** (1945) 381.
49. Bates, R. G. and Canham, R. G. *J. Res. Natl. Bur. Std.* **47** (1951) 343.
50. Bates, R. G. and Pinching, G. D. *J. Am. Chem. Soc.* **71** (1949) 1274.
51. Kuhn, R. and Wassermann, A. *Helv. Chim. Acta* **11** (1928) 50.
52. Chen, D. T. Y. and Laidler, K. J. *Trans. Faraday Soc.* **58** (1962) 480.
53. Pitzer, K. S. *J. Am. Chem. Soc.* **59** (1937) 2365. Cf. also the discussion by Laidler, K. J. *Trans. Faraday Soc.* **55** (1959) 1725.
54. Magee, J. L., Ri, T. and Eyring, H. *J. Chem. Phys.* **9** (1941) 419.
55. Lloyd, D. R. and Prince, R. H. *Proc. Chem. Soc.* **1962** 464.
56. Ref.<sup>26</sup>, p. 408.

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