

## Studies on Succinic Acids

III. \* Application of the Kirkwood-Westheimer Theory to the Anomalously High  $K_1/K_2$ -Ratios Exhibited by Certain Alkylated Succinic Acids

LENNART EBERSON

*Department of Organic Chemistry, Chemical Institute, University of Lund, Sweden*

The first and second dissociation constants of a number of 1,2-dicarboxylic acids have been measured in 50 % ethanol. It was found that *racem-a,a'*-dialkylsuccinic acids, containing alkyl groups with large steric requirements, and tetraalkylsuccinic acids have  $K_1/K_2$ -ratios of very great magnitudes, the ratio for *racem-a,a'*-di-(*tert.*-butyl)-succinic acid being the highest ever observed. By application of the Kirkwood-Westheimer theory to these molecules it is found that electrostatic effects alone cannot be responsible for this anomaly, but together with the assumption of an intramolecularly hydrogen-bonded monoanion the theory is in satisfactory agreement with experimental data.

The ratio between the first and second dissociation constants of a dibasic acid has been the basis of several attempts to calculate the distance between the dissociating protons<sup>1-6</sup>. This topic has been reviewed by Brown, McDaniel, and Häfliger (up to 1953)<sup>7</sup> and earlier by Adell<sup>8</sup> and Kortüm<sup>9</sup>. The high  $K_1/K_2$ -ratios exhibited by certain highly alkylated short-chain dicarboxylic acids which could not be accounted for by the original simple theory have given rise to a more complicated treatment by Kirkwood and Westheimer<sup>10-12</sup>. This theory treats the molecules as spherical or ellipsoidal cavities of low dielectric constant (assigned a value of 2.0, as for *n*-paraffines), imbedded in a medium of high dielectric constant, *i. e.*, the concept of an "effective" dielectric constant, which is a function of the size and shape of the molecule, was introduced. According to this treatment, the accommodation of alkyl groups in the carbon chain increases the size of the molecule, thereby allowing a greater part of the electrostatic effect to be transmitted through the cavity of low dielectric constant. With this theory reasonable values of the interprotonic

---

\* Part II. *Acta Chem. Scand.* 13 (1959) 203.

distances could be calculated even for acids with high  $K_1/K_2$ -ratios, though it involved a number of important assumptions regarding the size and shape of the molecules. For instance, the calculations were based on molecules with the carboxyl groups in *trans* position, though chemical evidence pointed to other models with the carboxyl groups in *gauche* position. Furthermore, the theory has been criticized for the fact that it does not explain the influence of solvent and temperature on the  $K_1/K_2$ -ratio in a satisfactory manner<sup>13, 14</sup>. Peek and Hill<sup>15</sup> have considered the effect of rotation about the central carbon-carbon bond in succinic acid, and stated that the Kirkwood-Westheimer theory, together with an acceptable value of the energy barrier against internal rotation (about 2 kcal/mole) was in good agreement with experiment.

Davison<sup>16</sup>, Hunter<sup>17</sup>, McDaniel and Brown<sup>18</sup>, and Brown, McDaniel, and Häfliger<sup>7</sup> have discussed hydrogen bonding as a factor in the ionization of dicarboxylic acids and proposed that an anomalously high  $K_1/K_2$ -ratio was best explained by assuming the existence of an intramolecular hydrogen bond in the monoanion. As a summary of the discussions of these authors the formation of such a structure should be favoured by the following factors:

1. The fixation of the carboxyl groups in *cis*-position.
2. The prevention of rotation of the carboxyl groups.
3. The existence of steric strain in the molecule, which should in part be relieved by the formation of a cyclic structure.
4. Lowering of the dielectric constant of the solvent.

The investigations by, among many others, Wotiz and Merrill<sup>19</sup> on highly branched malonic acids, Cookson and Trevett<sup>20</sup> on a dicarboxylic acid derived from a *Delphinium* alkaloid and having the carboxyl groups rigidly held in positions near each other, and Mizutani<sup>21</sup> on the strength of maleic acid in methanol-water mixtures of varying composition, confirm these statements.

However, Westheimer and Benfey<sup>22</sup> recently have shown that the ratio  $K_1/K_E$ , where  $K_E$  is the ionization constant of the monomethyl ester of the acid in question, forces an upper limit upon the effect of hydrogen bonding on the  $K_1/K_2$ -ratio, so that it should contribute only to a fraction of the total observed effect.

These discussions have been based on essentially the same material, published before 1940, and surprisingly few new data have appeared since that time. In paper I of this series<sup>23</sup> the author has described the preparation of a number of  $\alpha, \alpha'$ -dialkyl- and tetraalkyl-substituted succinic acids with structures suitable for obtaining more information regarding the factors which influence the  $K_1/K_2$ -ratio. The thermodynamic dissociation constants of these acids have now been measured in 50 % ethanol by weight by the electrometric titration method in cells with liquid junctions. The experimental conditions were mainly those used by Speakman<sup>24, 25</sup> in the determination of  $K_1$  and  $K_2$  for a few dibasic acids in aqueous ethanol, but a simpler calculation method was used. The use of 50 % ethanol was necessary, as a number of the investigated acids were almost insoluble in water. Succinic, *cis*- and *trans*-carbonic acid, maleic and fumaric acid have been included for comparison. The author has previously reported the preparation of a number of  $\alpha, \alpha'$ -dialkylglutaric acids<sup>26, 27</sup>, from which the two forms of  $\alpha, \alpha'$ -di-(*tert.*-butyl)-glutaric acid were

Table 1. Thermodynamic dissociation constants of diacids in 50 % aqueous ethanol at 20°.

| Acid   | pK <sub>1</sub> | pK <sub>2</sub> | ΔpK  | K <sub>1</sub> /K <sub>2</sub> in<br>50 %<br>aq. ethanol | K <sub>1</sub> /K <sub>2</sub> in<br>water <sup>7</sup> |
|--|-----------------|-----------------|------|--|---|
| Succinic   | 5.44            | 7.35            | 1.91 | 81   | 19.2  |
| Racem- <i>a,a'</i> -dimethylsuccinic                                 | 5.04            | 8.17            | 3.13 | 1 350  | 181   |
| Meso- <i>a,a'</i> -dimethylsuccinic                                  | 4.97            | 7.58            | 2.61 | 410  | 147   |
| Racem- <i>a,a'</i> -diethylsuccinic                                  | 4.76            | 9.22            | 4.46 | 29 000   | 1 220   |
| Meso- <i>a,a'</i> -diethylsuccinic                                   | 5.37            | 7.43            | 2.06 | 115  | 672   |
| Racem- <i>a,a'</i> -diisopropylsuccinic                              | 3.66            | 11.44           | 7.78 | 60 000 000   |   |
| Meso- <i>a,a'</i> -diisopropylsuccinic                               | 5.98            | 8.10            | 2.12 | 130  |   |
| Racem- <i>a,a'</i> -di-( <i>tert.</i> -butyl)-succinic               | 3.58            | 13.12           | 9.54 | 3 500 000 000  |   |
| Meso- <i>a,a'</i> -di-( <i>tert.</i> -butyl)-succinic                | 6.43            | 8.29            | 1.86 | 73   |   |
| Racem- <i>a,a'</i> -dineopentylsuccinic <sup>a</sup>                 | 5.22            | 9.56            | 4.34 | 22 000   |   |
| Racem- <i>a,a'</i> -bis-(trimethylsilylmethyl)-succinic <sup>a</sup> | 4.96            | 9.96            | 5.00 | 100 000  |   |
| Racem- <i>a,a'</i> -dicyclohexylsuccinic                             | 3.83            | 11.59           | 7.76 | 58 000 000   |   |
| Meso- <i>a,a'</i> -dicyclohexylsuccinic                              | 6.06            | 8.35            | 2.29 | 195  |   |
| <i>Cis</i> -caronic  | 3.33            | 10.68           | 7.35 | 22 000 000   | 929 000   |
| <i>Trans</i> -caronic  | 5.45            | 7.24            | 1.79 | 62   | 31.8  |
| Maleic   | 2.22            | 8.82            | 6.60 | 4 000 000  | 20 200  |
| Fumaric  | 4.37            | 6.19            | 1.82 | 66   | 23.2  |
| Tetramethylsuccinic  | 4.84            | 10.13           | 5.29 | 200 000  | 6 130   |
| <i>a,a'</i> -dimethyl- <i>a,a'</i> -diethylsuccinic                  | 4.86            | 10.16           | 5.30 | 200 000  |   |
| Tetraethylsuccinic   | 4.78            | 11.42           | 6.64 | 4 400 000  |   |
| <i>a,a'</i> -diethyl- <i>a,a'</i> -diisopropylsuccinic               | 4.55            | 12.61           | 8.06 | 110 000 000  |   |
| <i>a,a,a'</i> -bis-(ethylene)-succinic                               | 5.80            | 8.78            | 2.98 | 960  |   |
| <i>a,a,a'</i> -bis-(trimethylene)-succinic                           | 5.68            | 9.55            | 3.87 | 7 400  |   |
| <i>a,a,a'</i> -bis-(tetramethylene)-succinic                         | 5.87            | 9.83            | 3.96 | 9 100  |   |
| <i>a,a'</i> -di-( <i>tert.</i> -butyl)-glutaric, high-melting        | 6.64            | 8.34            | 1.70 | 50   |   |
| <i>a,a'</i> -di-( <i>tert.</i> -butyl)-glutaric, low-melting         | 6.68            | 8.35            | 1.67 | 47   |   |

a. The *meso* form of this acid was almost insoluble in 50 % ethanol. The dissociation constants in 75 % ethanol were estimated from the titration curves as the pH-values at 25 and 75 % neutralization. The K<sub>1</sub>/K<sub>2</sub>-ratio was of the order 1 000.

Table 2. Thermodynamic dissociation constants for monomethyl esters in 50 % aqueous ethanol at 20°.

| Monomethyl succinate                           | pK <sub>E</sub> | pK <sub>1</sub> | K <sub>1</sub> /K <sub>E</sub><br>in 50 %<br>aq. ethanol | K <sub>1</sub> /K <sub>E</sub><br>in water <sup>7,28</sup> |
|--|-----------------|-----------------|--|--|
| Racem- <i>a,a'</i> -dimethyl-                  | 5.98            | 5.04            | 8.7  | 2.7  |
| Meso- <i>a,a'</i> -dimethyl-                   | 5.92            | 4.97            | 8.9  | 3.1  |
| Racem- <i>a,a'</i> -diethyl-                   | 6.01            | 4.76            | 17.8   |  |
| Meso- <i>a,a'</i> -diethyl-                    | 6.04            | 5.37            | 4.7  |  |
| Racem- <i>a,a'</i> -diisopropyl-               | 6.63            | 3.66            | 930  | 20   |
| Meso- <i>a,a'</i> -diisopropyl-                | 6.40            | 5.98            | 2.6  | 1.7  |
| Racem- <i>a,a'</i> -di-( <i>tert.</i> -butyl)- | 7.44            | 3.58            | 7 300  |  |
| Meso- <i>a,a'</i> -di-( <i>tert.</i> -butyl)-  | 6.83            | 6.43            | 2.5  |  |
| Tetramethyl-                                   | 6.80            | 4.84            | 91   | 27.0   |
| Tetraethyl-                                    | 7.35            | 4.78            | 370  |  |

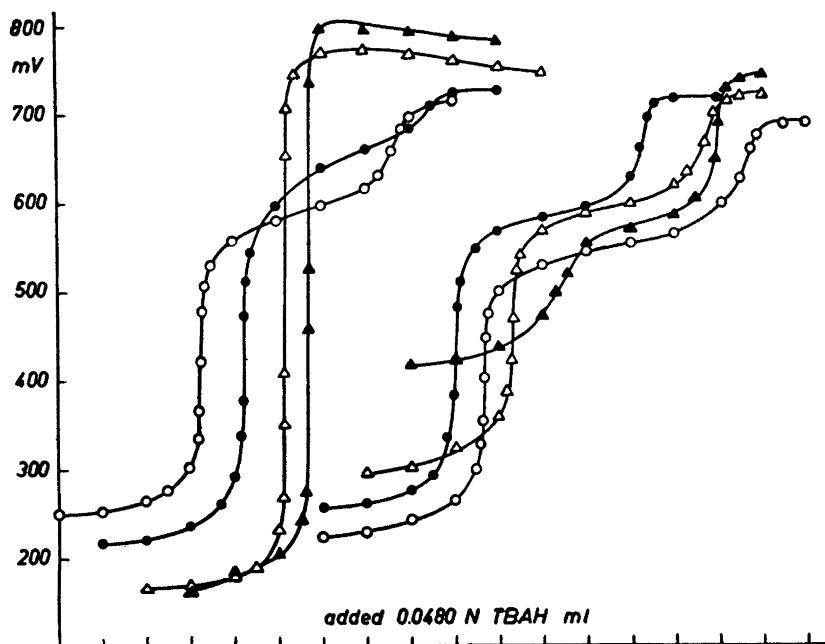


Fig. 1. Titration of  $\alpha, \alpha'$ -dialkylsuccinic acids with TBAH.

- $\alpha, \alpha'$ -dimethylsuccinic acid
- $\alpha, \alpha'$ -diethylsuccinic acid
- △—△—△—△—△  $\alpha, \alpha'$ -diisopropylsuccinic acid
- ▲—▲—▲—▲—▲  $\alpha, \alpha'$ -di(*tert.*-butyl)-succinic acid

The racemic acid titration curves are the left ones.

chosen for  $pK$ -measurement, representing glutaric acids with a large bulk of alkyl substituents. The values of  $pK_1$ ,  $pK_2$ ,  $\Delta pK$  and  $K_1/K_2$  are shown in Table 1 together with the results of earlier determinations in water.

The monomethyl esters of *meso*- and *racem*- $\alpha, \alpha'$ -dimethyl-, *meso*- and *racem*- $\alpha, \alpha'$ -diethyl-, *meso*- and *racem*- $\alpha, \alpha'$ -diisopropyl-, *meso*- and *racem*- $\alpha, \alpha'$ -di(*tert.*-butyl)-, tetramethyl-, and tetraethylsuccinic acid have been prepared and their  $pK_E$ -values determined in 50 % aqueous ethanol, as shown in Table 2. Furthermore, some of the acids listed in Table 1 were titrated electrometrically in pyridine with tetrabutylammonium hydroxide (TBAH)\* in methanol-benzene solution. This titration method has recently been applied to dibasic acids<sup>29-31</sup> and has been found to give two sharp inflection points in the titration curves of a number of acids, namely *m*- and *p*-hydroxybenzoic, malic,

\* These titrations were carried out at the Department of Analytical Chemistry, University of Lund.

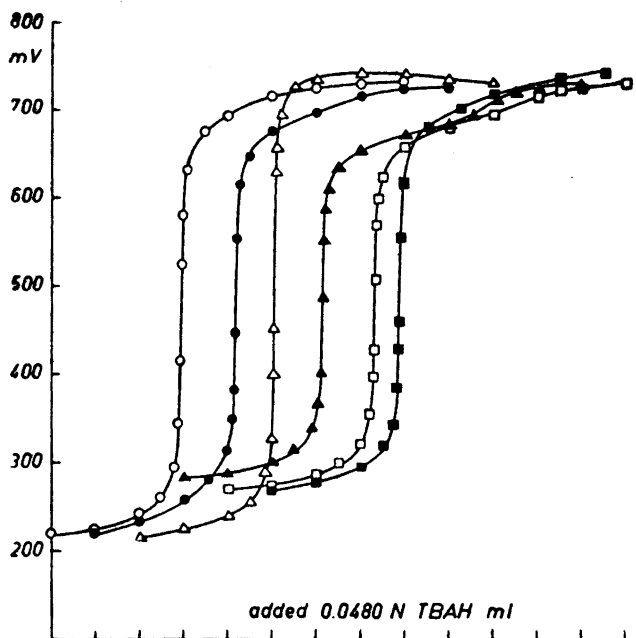


Fig. 2. Titration of tetraalkylsuccinic acids with TBAH.

- tetramethylsuccinic acid
- *a,a'*-dimethyl-*a,a'*-diethylsuccinic acid
- △—△—△—△—△ tetraethylsuccinic acid
- ▲—▲—▲—▲—▲ *a,a,a',a'*-bis-(ethylene)-succinic acid
- *a,a,a',a'*-bis-(trimethylene)-succinic acid,
- *a,a,a',a'*-bis-(tetramethylene)-succinic acid.

oxalic, malonic, maleic, fumaric, succinic, *o*-phthalic, and sulphuric acid. Salicylic acid titrated as a monobasic acid and had a very large break in the titration curve. The results of the TBAH-titrations are given in the form of titration curves in Figs 1 and 2.

The most striking fact in Table 1 is the enormous increase of the  $K_1/K_2$ -ratio of the *racemic* acids when the steric requirements of the alkyl substituents are increased, the value for *racem-a,a'*-di-(*tert.*-butyl)-succinic being the highest ever observed, while on the contrary the corresponding *meso* forms have ratios of about the same relatively small magnitude. The  $K_1/K_2$ -values listed in Table 2 show the same general trend. Among the tetra-alkylated acids the trend is a substantial increase of the  $K_1/K_2$ -ratio with higher "degree of alkylation" and a much greater ratio for the open-chain acids than the cyclic ones. As is seen from Fig. 1, this corresponds to a change in titration curve type for the *racemic* acids from a curve with two inflection points to a curve with one

very strong break (compare salicylic acid). The curves of the *meso* acids all have two inflection points. Fig. 2 shows the titration curves of the tetra-alkylated acids, which all have very strong breaks for the first equivalence point but the second ones either very small or totally absent. Also in 50 % ethanol *racem*- $\alpha,\alpha'$ -di-(*tert.*-butyl)-succinic acid titrates as a monobasic acid, thus resembling the highly branched malonic acids investigated by Wotiz and Merrill<sup>19</sup>.

#### DISCUSSION

Kirkwood and Westheimer based their calculations of interprotonic distances in symmetrical dibasic acids on the formula

$$\log \frac{K_1}{\sigma K_2} = \frac{e^2}{2.303 k T R D_E} \quad (1)$$

where  $K_1$  and  $K_2$  are the first and second dissociation constants,  $e$  the electronic charge,  $k$  the Boltzmann constant,  $R$  the interprotonic distance, and  $\sigma$  a statistical factor, in this instance equal to four.  $D_E$  is the effective dielectric constant and is a function of the shape of the molecule, the positions of the protons within the molecule, the dielectric constant of the solvent, and the dielectric constant of the acid molecule. For the calculations of  $D_E$  it was necessary to assume the shape of the molecule to be either a sphere or a prolate ellipsoid of revolution, owing to the mathematical difficulties associated with other models. In the former case  $D_E$  is calculated as a function of the positions of the protons within the sphere, in the latter as a function of the eccentricity of the ellipsoid. An intersection of the spherical model is shown schematically in Fig. 3.

In this Figure  $b$  is the radius of the sphere (estimated from the partial molar volume obtained according to Traube<sup>32</sup>),  $r$  the distance from the center of the sphere to the ionizable protons,  $\vartheta$  the angle between the distances  $r$ , and  $R$  the interprotonic distance. In the case of the ellipsoidal model the mathematical treatment requires the protons to be placed at the foci of an ellipsoid of revolution with the eccentricity  $\lambda_0$ . The interfocal distance is  $R$ , and  $\lambda_0$  is obtained from the formula

$$\lambda_0^3 - \lambda_0 = \frac{6 V}{\pi R^3} \quad (2)$$

where  $V$  is the partial molar volume.

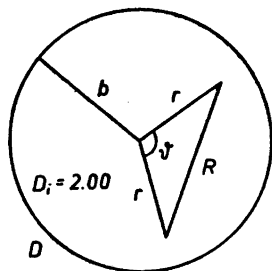


Fig. 3.

For a number of succinic acids (*meso*- and *racem*- $\alpha,\alpha'$ -diethylsuccinic acid, tetramethylsuccinic acid) the spherical model was used and in other cases (*meso*- and *racem*- $\alpha,\alpha'$ -dimethylsuccinic acid, succinic acid) the ellipsoidal one, but in all cases the carboxyl groups were supposed to be *trans* to each other<sup>12</sup>.

Now there is evidence that a number of the acids investigated in this paper and also some of those treated by Kirkwood and Westheimer should have *gauche* carboxyl groups in their most favoured conformations. Thus equilibration of *meso*- and *racem*- $\alpha,\alpha'$ -dialkylsuccinic acids indicates that the *racemic* form is the more stable isomer<sup>33</sup> contrary to the stability order predicted by conformation analytical reasoning<sup>34,35</sup>. The presence of an intramolecular hydrogen bond in the preferred conformation of the *racemic* acid could explain this anomaly. The extreme ease of anhydrization of certain succinic acids<sup>23</sup> also makes it reasonable to assume that the carboxyl groups have been forced into *gauche* position, partly by the possibility of an intramolecularly hydrogen-bonded ring structure being formed, which should relieve part of the steric strain in the open-chain acid, partly by the orienting effects of large alkyl groups. For example in  $\alpha,\alpha'$ -di(*tert.*-butyl)-succinic acid the bulky alkyl groups should entirely determine the conformation of the molecule, and consequently in the *meso* acid the carboxyl groups become orientated *trans* to each other, and in the *racemic* from *gauche* to each other.

Table 3 gives the calculated  $\Delta pK$ -values in 50 % ethanol for a number of the acids investigated in this paper.  $D_E$ -functions were worked out for the solvent 50 % ethanol\*. These curves are shown in Figs 4 and 5. The geometrical

Table 3. Comparison between calculated and found  $\Delta pK$ -values in 50 % ethanol.

| Succinic acid  | Calculated $\Delta pK$<br>(spherical model)   |  |  | Calculated $\Delta pK$<br>(ellipsoidal model) | Found<br>$\Delta pK$ |
|--|---|--|--|---|----------------------|
|  | COOH-<br>groups<br>in <i>gauche</i><br>position.<br>$\text{Cos } \vartheta =$<br>$+ 0.07$ | COOH-<br>groups<br>in <i>trans</i><br>position.<br>$\text{Cos } \vartheta =$<br>$- 1.00$ | Corrected<br>for intra-<br>molecular<br>H-bonding.<br>COOH-<br>groups<br><i>gauche</i> | COOH-groups<br>in <i>trans</i><br>position    |                      |
| <i>Racem</i> - $\alpha,\alpha'$ -dimethyl-                 | 1.70  | 1.17   | 2.98   | 1.50  | 3.13                 |
| <i>Meso</i> - $\alpha,\alpha'$ -dimethyl-                  | 1.70  | 1.17   | 3.00   | 1.50  | 2.61                 |
| <i>Racem</i> - $\alpha,\alpha'$ -diethyl-                  | 2.19  | 1.34   | 4.09   | 1.73  | 4.46                 |
| <i>Meso</i> - $\alpha,\alpha'$ -diethyl-                   | 2.19  | 1.34   |  | 1.73  | 2.06                 |
| <i>Racem</i> - $\alpha,\alpha'$ -diisopropyl-              | 2.93  | 1.60   | 8.26   | 1.98  | 7.78                 |
| <i>Meso</i> - $\alpha,\alpha'$ -diisopropyl-               | 2.93  | 1.60   |  | 1.98  | 2.12                 |
| <i>Racem</i> - $\alpha,\alpha'$ -di( <i>tert.</i> -butyl)- | 3.64  | 1.84   | 10.76  | 2.23  | 9.54                 |
| <i>Meso</i> - $\alpha,\alpha'$ -di( <i>tert.</i> -butyl)-  | 3.64  | 1.84   |  | 2.23  | 1.86                 |
| Tetramethyl-   | 2.19  | 1.34   | 5.51   | 1.73  | 5.29                 |
| Tetraethyl-  | 3.64  | 1.84   | 8.17   | 2.23  | 6.64                 |

\* The author wishes to express his thanks to Laborator C.-E. Fröberg and Fil.mag. E. Larsson at the Institute of Numerical Analysis, University of Lund, for their kind help with the calculation of the  $D_E$ -function in the ellipsoidal case.

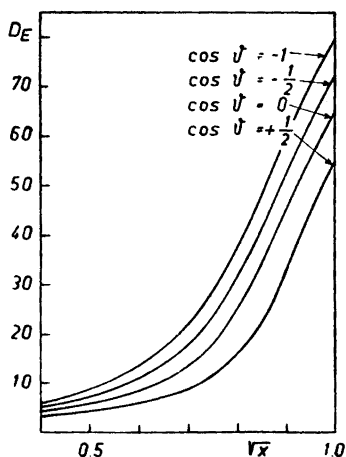


Fig. 4. Plot of  $D_E$  versus  $\sqrt{x} = r/b$  for  $\cos \vartheta = +\frac{1}{2}, 0, -\frac{1}{2}, -1$ .  $D_1 = 2.00$ ;  $D = 50.4$ .

relations between the carboxyl groups were obtained from the bond lengths and angles in succinic acid. The proton was placed on the extension of the bond between the carboxyl carbon atom and its nearest carbon neighbor at a distance of 1.45 Å from the former one. The factors for the correction of the effect of hydrogen bonding in the monoanion were calculated from the  $K_1/K_E$ -values in Table 2 according to Westheimer and Benfey. This correction is calculated for the case that hydrogen bonding exists in the monoanion but not in the free acid and its monomethyl ester. As mentioned above, available data<sup>33, 36</sup> point to the existence of an intramolecular hydrogen bond also in the diacid, which should reduce the magnitude of the correction. However, with regard to the approximate nature of this theory, no attempt was made to estimate this effect. It is also quite obvious that a measured  $\Delta pK$  in reality does not refer to a single conformation but to an equilibrium mixture between several rotation isomers of acids and ions with or without interactions between

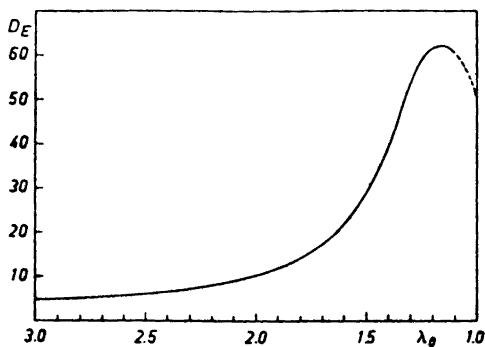


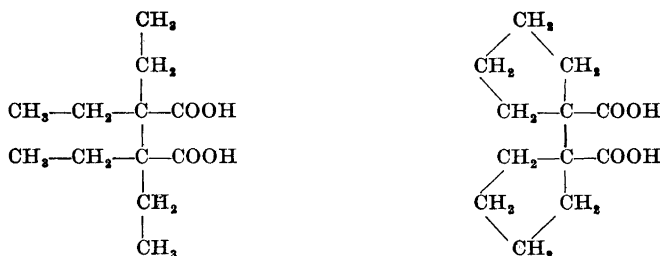
Fig. 5. Plot of  $D_E$  versus  $\lambda_0$ .  $D_1 = 2.00$ ;  $D = 50.4$ .



the carboxyl groups. By comparing calculated and measured  $\Delta pK$ -values it should, however, be possible to get an idea about which conformations are the most preferred ones.

Turning to Table 3, it must first be established by examination of molecular models whether the various conformations approximate the shapes of spherical or ellipsoidal molecules. It is found that the spherical model is best suited for conformations with *gauche* carboxyl groups and that the ellipsoidal model with the protons at the foci is difficult to associate with the shape of these molecules. For the conformations with *trans* carboxyl groups it was similarly found that both models could be used. By inspection of Table 3 it is obvious that a preferred conformation with *gauche* carboxyl groups together with the assumption of an intramolecular hydrogen bond in the monoanion is in satisfactory agreement with the observed  $\Delta pK$ -values for the *racem*- $\alpha,\alpha'$ -dialkyl- and tetraalkylsuccinic acids. Electrostatic effects alone cannot account for the large  $K_1/K_2$ -ratios in these cases. Likewise, it is probable that the *meso* acids have *trans* carboxyl groups in their most favoured conformations, though *meso*- $\alpha,\alpha'$ -dimethylsuccinic acid appears to be capable of existing also in a conformation with *gauche* carboxyl groups.

Thus, the main cause of an anomalously high  $K_1/K_2$ -ratio appears to be steric in origin. If the steric properties of a dibasic acid are such as to permit a close approach of the carboxyl groups, the pure electrostatic effect transmitted through the solvent and the molecule itself will increase. Besides, formation of an intramolecular hydrogen bond will be possible, which further magnifies the  $K_1/K_2$ -ratio. In the case of highly alkylated dibasic acids it is tempting to compare this effect with the empirically found rule that accommodation of alkyl substituents in a carbon chain capable of ring closure facilitates ring formation<sup>37</sup>. The theoretical background of this rule is not entirely understood, but probably steric strain in the open-chain compound, which is relieved in part in the cyclic structure, together with the existence of preferred conformations with the reacting groups in *gauche* position, is responsible for this effect. The behaviour of the tetraalkylated succinic acids investigated in this paper is consistent with this hypothesis. For example, if in tetraethylsuccinic acid the ethyl groups on each carbon atom are bent back and united with a C—C bond we obtain the structure of  $\alpha,\alpha,\alpha',\alpha'$ -bis-(tetramethylene)succinic acid



By analogy with the investigations on the base strengths of triethylamine and quinuclidine carried out by Brown and Sujishi<sup>38</sup> it may be concluded that the

steric strain should be diminished by this structural change. Actually a much smaller  $K_1/K_2$ -ratio is found for  $\alpha,\alpha,\alpha',\alpha'$ -bis-(tetramethylene)-succinic acid\*.

Lastly, it must be pointed out that the above discussion has neglected the effect of interactions between solvent and solute and of medium changes in the vicinity of the carboxyl groups. As very little is known about the conditions at the boundary surfaces it is, however, difficult to include such a discussion. At present the Kirkwood-Westheimer theory, together with the assumption of an intramolecularly hydrogen-bonded monoanion for molecules with carboxyl groups near each other, accounts for the observed effects, though in a crude manner. Specifically, the theory constitutes a valuable tool for the assignment of conformations in dibasic acids.

### EXPERIMENTAL

**Materials.** Commercial absolute ethanol was freed from water by the magnesium ethylate method and distilled. Equal weights of the ethanol and carbon dioxide-free water were mixed and stored in a container protected from the carbon dioxide of the air. To prepare the standard sodium hydroxide solution the calculated volume of 50 % aqueous carbonate free sodium hydroxide for obtaining a 0.05 N solution was added, followed by the amount of absolute ethanol needed for restoring the original solvent composition.

The preparation and purification of the acids have been described (except those mentioned below) by the author in earlier papers. Before pK-measurement they were recrystallized once more from the appropriate solvents and dried *in vacuo* over concentrated sulphuric acid. Succinic acid was analytical grade reagent, *cis*- and *trans*-caronic acid were prepared and purified according to Fredga and Sikström<sup>38</sup> and commercial samples of maleic and fumaric acid were recrystallized twice from benzene and water, respectively.

The monomethyl esters listed in Table 3 were prepared according to either of the following methods. *Meso*- $\alpha,\alpha'$ -di-(*tert.*-butyl)-succinic acid which does not form an anhydride, was converted into the monosilver salt (contaminated by the disilver salt) and

Table 4. Melting points and analyses of substituted monomethyl succinates.

| Monomethyl succinate  | M.p.<br>°C          | M. p.<br>lit.<br>°C | Analysis |      |                  |       |     |                  |
|---|---------------------|---------------------|----------|------|------------------|-------|-----|------------------|
|   |                     |                     | Found    |      |                  | Calc. |     |                  |
|   |                     |                     | C        | H    | neutr.<br>equiv. | C     | H   | neutr.<br>equiv. |
| <i>Racem</i> - $\alpha,\alpha'$ -dimethyl-                  | 35—37               | 38 <sup>40</sup>    |          |      |                  |       |     |                  |
| <i>Meso</i> - $\alpha,\alpha'$ -dimethyl-                   | 45—47               | 49 <sup>40</sup>    |          |      |                  |       |     |                  |
| <i>Racem</i> - $\alpha,\alpha'$ -diethyl-                   | liquid <sup>a</sup> |                     | 56.9     | 8.7  | 188              | 57.4  | 8.6 | 188              |
| <i>Meso</i> - $\alpha,\alpha'$ -diethyl-                    | 60—63               |                     | 57.3     | 8.8  | 189              | 57.4  | 8.6 | 188              |
| <i>Racem</i> - $\alpha,\alpha'$ -diisopropyl-               | 63—66               |                     | 61.0     | 9.5  | 217              | 61.1  | 9.3 | 216              |
| <i>Meso</i> - $\alpha,\alpha'$ -diisopropyl-                | 120—121             |                     | 60.8     | 9.4  | 217              | 61.1  | 9.3 | 216              |
| <i>Racem</i> - $\alpha,\alpha'$ -di-( <i>tert.</i> -butyl)- | 106—108             |                     | 63.9     | 10.0 | 246              | 63.9  | 9.9 | 244              |
| <i>Meso</i> - $\alpha,\alpha'$ -di-( <i>tert.</i> -butyl)-  | 135—137             |                     | 63.3     | 10.1 | 243              | 63.9  | 9.9 | 244              |
| Tetramethyl-  | 66—67               | 63 <sup>40</sup>    |          |      |                  |       |     |                  |
| Tetraethyl-   | 52—55               | 46—48 <sup>41</sup> |          |      |                  |       |     |                  |

a. B.p. 115—119°/1 mm.

\* Cf. Kuhn's<sup>43</sup> results in his study on intramolecular hydrogen bonding in alkylsubstituted ethanediols, which are quite analogous to those presented here.

treated with methyl iodide. A fair yield of the monomethyl ester was obtained, which was recrystallized twice from methanol.

The other acids were converted into anhydrides by boiling with acetyl chloride, the excess of acetyl chloride was removed *in vacuo*, and the crude anhydride allowed to react with the calculated amount of sodium methylate in absolute methanol. The solution was evaporated to dryness in a vacuum desiccator at room temperature and the residue acidified with dilute hydrochloric acid. The monomethyl ester was then isolated and purified by distillation or recrystallization from aqueous methanol. Melting points and analyses are shown in Table 4.

*Method.* Speakman<sup>24</sup> has developed a graphical method for the evaluation of the dissociation constants of dibasic acids from pH-measurements which is especially well adapted for acids with small  $K_1/K_2$ -ratios, say  $< 50$ . As the purpose of the present investigation was more to get an idea of the relative magnitudes of  $K_1$  and  $K_2$  for a series of dibasic acids rather than to make very precise measurements, and as the  $K_1/K_2$ -ratios in question are generally  $\gg 50$ , the author has used the simple formulae (3) and (4) for the calculations of  $K_1$  and  $K_2$ ,

$$K_1 = \frac{a_{\text{H}^+} (b + [\text{H}^+]) f_1}{(a - b - [\text{H}^+]) f_0} \quad (3)$$

$$K_2 = \frac{a_{\text{H}^+} (b - a - [\text{OH}^-]) f_2}{(2a - b + [\text{OH}^-]) f_1} \quad (4)$$

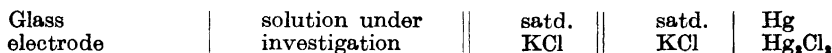
where  $a_{\text{H}^+}$  is the hydrogen ion activity, as measured by the glass electrode,  $a$  the total molar concentration of acid,  $b$  the molar concentration of added base, and  $f_0$ ,  $f_1$ , and  $f_2$  the activity coefficients of diacid, monoanion, and dianion, respectively.

For acids with  $K_1/K_2 > 10^3$  the calculations of  $K_1$  and  $K_2$  are totally independent of each other, and they were based on 5–6 pH-measurements in each of the ranges of 15–35 and 65–85 % neutralization. For acids where  $50 < K_1/K_2 < 10^3$  it can be shown that the influence of the separate dissociation stages on each other is negligible in this connection if  $K_1$  and  $K_2$  were computed from pH-measurements in the ranges of 10–20 and 80–90 % neutralization. As has been shown by Bacarella *et al.*<sup>25</sup> the glass electrode correctly measures  $a_{\text{H}^+}$  in aqueous organic solvents, provided that certain conditions for the handling of the glass electrode are fulfilled. Thus, in this work the glass electrode was standardized before use with an acetate buffer of pH 4.11 and a borate buffer of pH 9.08. It was then equilibrated with 50 % ethanol for several hours before the beginning of the electrometric titrations. It was stored in 50 % ethanol when not in use. No correction was made for the liquid junction potentials. As  $[\text{H}^+]$  normally makes only a small contribution to the expressions  $(b + [\text{H}^+])$  and  $(a - b - [\text{H}^+])$   $a_{\text{H}^+}$  was used in its place.  $[\text{OH}^-]$  could not be neglected in a few cases where  $K_2$  was very small, and it was calculated from the expression  $[\text{OH}^-] = K_w / [\text{H}^+]$ . A rough estimate of  $K_w$  ( $7.2 \times 10^{-16}$ ) was obtained from titration of the pure solvent with standard sodium hydroxide. No correction was made for the presence of ethoxide ions,  $a$  and  $b$  were corrected for dilution during the titration,  $f_0$  was assumed to be unity, and  $f_1$  and  $f_2$  were computed by the Debye-Hückel limiting law,  $\log f_i = -A z_i^2 \sqrt{I}$ , where  $A = 1.01$  in 50 % ethanol at 20°, and  $I$  was approximated as  $(b + [\text{H}^+])$  when  $a < b$  and as  $(2b - a)$  when  $b > a$ <sup>24, 25</sup>.

The dissociation constants of the monomethyl esters were calculated as for monobasic acids.

The accuracy of the pK-values of Tables 1 and 2 is estimated at  $\pm 0.15$  unit in pK except for those pK<sub>2</sub>-values which have been corrected for  $[\text{OH}^-]$ , where the error may be as high as  $\pm 0.30$  unit. For comparison within the material of this paper the accuracy is probably rather better. Speakman<sup>25</sup> has determined the pK-values of succinic acid in 50 % ethanol by weight at 20° and found  $\text{p}K_1 = 5.48 \pm 0.05$  and  $\text{p}K_2 = 7.24 \pm 0.05$  (calculated on the basis of molalities). For comparison, the pH-data for succinic acid were also put into the equations given by Speakman and then the pK-values graphically determined. This method gave  $\text{p}K_1 = 5.43$  and  $\text{p}K_2 = 7.36$ , which is in satisfactory agreement with those calculated according to formulae (3) and (4).

*pH-Measurements.* Solutions of the acids in 50 % ethanol (0.004–0.005 M), were electrometrically titrated with standard sodium hydroxide in the same solvent (about 0.05 N), and pH-readings were made for various volumes of added base in the ranges mentioned above. The following cell was used



The glass electrode was Radiometer Type G 202 B. The titrations were run in a carbon dioxide-free atmosphere and the temperature was  $20 \pm 0.5^\circ$ . The titrations were run up to the equivalence points to check the purity of the acids; neutralization equivalents always agreed with the calculated ones within  $\pm 1\%$ .

The author wishes to express his sincere gratitude to Professor Erik Larsson for his kind interest in this work.

#### REFERENCES

1. Bjerrum, N. *Z. physik. Chem.* **106** (1923) 219.
2. Gane, R. and Ingold, C. K. *J. Chem. Soc.* **1931** 2153.
3. Jones, I. and Soper, F. G. *J. Chem. Soc.* **1936** 133.
4. Adell, B. *Über die elektrolytische Dissoziation von Dicarbonensäuren in Alkalichlorid-lösungen* (Diss.) Lund 1938.
5. Adell, B. *Z. physik. Chem. (A)* **185** (1939) 161.
6. Adell, B. *Svensk Kem. Tidskr.* **53** (1941) 89.
7. 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 Inc. New York 1955, p. 622.
8. Adell, B. *Elementa* **26** (1943) 20.
9. Kortüm, G. *Elektrolytlösungen*, Akademische Verlagsgesellschaft, Leipzig **1941**, p. 377.
10. Kirkwood, J. G. and Westheimer, F. H. *J. Chem. Phys.* **6** (1938) 506.
11. Kirkwood, J. G. and Westheimer, F. H. *J. Chem. Phys.* **6** (1938) 513.
12. Westheimer, F. H. and Shookhoff, M. W. *J. Am. Chem. Soc.* **61** (1939) 555.
13. Wynne-Jones, W. F. K. and Rushbrooke, G. S. *Trans. Faraday Soc.* **40** (1944) 99.
14. Westheimer, F. C. and Kirkwood, J. G. *Trans. Faraday Soc.* **43** (1947) 77.
15. Peek, H. M. and Hill, T. L. *J. Am. Chem. Soc.* **73** (1951) 5304.
16. Hunter, L. *Chem. & Ind. London* **1953** 155.
17. Davison, W. H. T. *Chem. & Ind. London* **1953** 408.
18. McDaniel, D. H. and Brown, H. C. *Science* **118** (1953) 370.
19. Wotiz, J. H. and Merrill, H. E. *J. Am. Chem. Soc.* **80** (1958) 866.
20. Cookson, R. C. and Trevett, M. E. *J. Chem. Soc.* **1956** 3864.
21. Mizutani, M. *Z. physik. Chem.* **118** (1925) 318.
22. Westheimer, F. H. and Benfey, O. T. *J. Am. Chem. Soc.* **78** (1956) 5309.
23. Ebersson, L. *Acta Chem. Scand.* **13** (1959) 40.
24. Speakman, J. C. *J. Chem. Soc.* **1940** 855.
25. Speakman, J. C. *J. Chem. Soc.* **1943** 270.
26. Ebersson, L. *Acta Chem. Scand.* **12** (1958) 314.
27. Ebersson, L. *Acta Chem. Scand.* **12** (1958) 1906.
28. Bone, W. A. and Sprankling, C. H. G. *J. Chem. Soc.* **77** (1900) 1299.
29. Harlow, G. A., Noble, C. M. and Wyld, G. E. A. *Anal. Chem.* **28** (1956) 787.
30. Cundiff, R. H. and Markunas, P. C. *Anal. Chem.* **28** (1956) 792.
31. Harlow, G. A. and Wyld, G. E. A. *Anal. Chem.* **30** (1958) 69.
32. Traube, J. *Samml. chem. u. chem.-tech. Vorträge* **4** (1899) 255.
33. Ebersson, L. *Acta Chem. Scand.* **13** (1959) 203.
34. Linstead, R. P. and Whalley, M. *J. Chem. Soc.* **1954** 3722.
35. Barton, D. H. R. and Cookson, R. C. *Quart. Revs. (London)* **10** (1956) 44.
36. Ebersson, L. *Acta Chem. Scand.* **13** (1959) 224.

37. Newman, M. S. *Steric Effects in Organic Chemistry*, J. Wiley & Sons, New York 1956, p. 460.
38. Brown, H. C. and Sujishi, S. *J. Am. Chem. Soc.* **70** (1948) 2878.
39. Fredga, A. and Sikström, Å. *Arkiv Kemi* **8** (1956) 433.
40. Walker, J. *J. Chem. Soc.* **61** (1892) 696.
41. Walker, J. and Walker, A. P. *J. Chem. Soc.* **87** (1905) 961.
42. Bacarella, A. L., Grunwald, E., Marshall, H. P. and Purlee, E. L. *J. Phys. Chem.* **69** (1958) 856.
43. Kuhn, L. P. *J. Am. Chem. Soc.* **80** (1958) 5950.

Received December 24, 1958.