The Geometry of Intramolecular Hydrogen Bonding in 1,2-Dicarboxylic Acids

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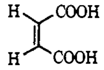
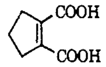
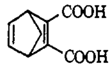
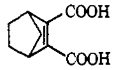
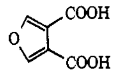
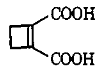
Abstract: The optimum spacing between carboxyl groups to achieve maximum intramolecular hydrogen bonding in 1,2-dicarboxylic acids has been examined. Spacing between the carboxyl groups was controlled by attaching the carboxyl groups to rigid skeletons; distances were determined from the geometry of the rigid skeletons. The following diacids listed in order of increasing space between carboxyl groups were prepared and their dissociation constants (pK_1 and pK_2) and those of the half methyl esters (pK_E) were determined: cyclopentene-1,2-dicarboxylic acid, $pK_1 = 1.64$, $pK_2 = 7.27$, $pK_E = 2.94$; bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylic acid, $pK_1 = 1.32$, $pK_2 = 7.77$, $pK_E = 3.02$; bicyclo[2.2.1]hept-2-ene-2,3-dicarboxylic acid, $pK_1 = 1.32$, $pK_2 = 8.00$, $pK_E = 3.19$; furan-3,4-dicarboxylic acid, $pK_1 = 1.44$, $pK_2 = 7.84$, $pK_E = 3.75$; and cyclobutene-1,2-dicarboxylic acid, $pK_1 = 1.12$, $pK_2 = 7.63$, $pK_E = 3.32$. The degree of hydrogen bonding in the monoanion was determined from pK_1 and pK_E by the method of Westheimer and Benfey. In conjunction with some data in the literature, it is found that the amount of hydrogen bonding increases with increasing distance between the carboxyl groups except for the most widely spaced example, the cyclobutene compound. It is concluded that two requirements must be met for maximum intramolecular hydrogen bonding to occur in the monoanions of dicarboxylic acids in solution: (1) the carboxyl groups should be spaced so that an essentially linear $O \cdots H \cdots O$ bond of length about 2.45 A lying in the intersection of the two planes of the carboxyl groups may be formed; and (2) the carboxyl groups should be attached to a carbon skeleton such that no change in conformation of the carbon skeleton is allowed either before or after requirement 1 is fulfilled.

Intramolecular hydrogen bonding between carboxyl groups has been offered as an explanation of the large K_1/K_2 ratio of acid dissociation constants for a variety of dibasic acids. The hydrogen bond is presumed to stabilize the monoanion, thereby increasing K_1 and decreasing K_2. Effectiveness of such hydrogen bonding is supposed to be related to the distance between the carboxyl groups, and it has been stated or implied that the closer the carboxyl groups approach each other, the stronger will be the bond.[1] However, studies of substituted cyclopropane-*cis*-1,2-dicarboxylic acids[2] and substituted maleic acids[3] lead to the suggestion that carboxyl groups may be forced too close together for effective hydrogen bonding. It is now proposed that maximum intramolecular hydrogen bonding in the monoanions of dicarboxylic acids in solution will occur at some optimum distance between the carboxyl groups, and at greater *or* smaller distances, the bonding will be less. This proposal is examined in the present study.

Experimental Section

Materials. Maleic acid (Matheson Coleman and Bell) was recrystallized from water. All other diacids and half esters examined were prepared by methods reported in the literature or in the case of three of the half methyl esters by a procedure analogous to that for the half methyl ester of 3,4-furandicarboxylic acid. The acids and esters were recrystallized to constant melting point from appropriate solvents, and the half esters were sublimed. In view of the discrepancy in melting point from that reported for bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylic acid, this compound was recrystallized from water, ethyl acetate-*n*-hexane mixture, and finally from ethyl acetate and shown to have the same constant melting point in all three solvent systems. On the same basis and in a similar way, the half methyl ester of bicyclo[2.2.1]hept-2-ene-2,3-dicarboxylic acid had a constant melting point. All of the compounds had infrared spectra consistent with the assigned structures, and except for the half methyl ester of cyclopentene-1,2-dicarboxylic acid, all of the compounds titrated to 100% (±1% or less) of equivalence. Attempted purification of the cyclopentene half ester by vacuum distillation at about 10-mm pressure apparently resulted in appreciable disproportionation to the diacid and diester. Titration of the crude ester indicated the presence of about 5% diacid. This material was used to determine K_E (discussed further in calculation section). Physical constants for the diacids and half esters are reported in Table I.

Table I

Compound	Mp,[a,b] °C	Mp (half ester),[a,b] °C
	132–133 (130–131)[c]	
	176–178 (178)[d]	. . .
	165–166 (170)[e]	104–105
	210–211 (212–213)[e]	123–124 (131)[e]
	212–213 (214)[f]	135–136 (135–137)[f]
	169–170 dec (178–178.5 dec)[g]	62–63

[a] Values in parentheses are literature values. [b] All of the diacids were recrystallized from suitable solvents; the half esters were sublimed in addition to recrystallization. [c] "The Merck Index," 6th, ed, p 596; see footnote *d*, Table II. [d] E. Haworth and W. H. Perkin, *J. Chem. Soc.*, **65**, 978 (1894). [e] O. Diels and K. Alder, *Ann.*, **490**, 236 (1931). [f] S. Oae, M. Hamada, Y. Otsuji, and N. Furukawa, *Ann. Rept. Radiation Center Osaka Prefect.*, **2**, 106 (1961). [g] F. B. Kipping and J. J. Wren, *J. Chem. Soc.*, 1733 (1957).

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(1) This suggestion in various forms has been set forth by numerous authors. For example, see: H. C. Brown, D. H. McDaniel, and O. Hafliger, "Determination of Organic Structures by Physical Methods," Vol. 1, E. A. Braude and F. C. Nachod, Ed., Academic Press Inc., New York, N. Y., 1955, pp 628–634.

(2) L. L. McCoy and G. W. Nachtigall, *J. Am. Chem. Soc.*, **85**, 1321 (1963).

(3) L. Eberson, *Acta Chem. Scand.*, **18**, 1276 (1964).

Titrations. These were carried out in a jacketed essentially sealed cell thermostated at 25.0 ± 0.1° using a Radiometer automatic recording titrator. Each titration was recorded automatically, but data used for calculating p*K*'s were obtained directly from the pH meter scale and the micrometer scale of the syringe buret by interrupting the titration at suitable intervals. Prior to each titration, the pH meter was calibrated against two buffers, 4.01 (phthalate) and 7.41 (phosphate) for pK_E and pK_2 determinations and 4.01 (phthalate) and 1.68 (tetroxalate) for pK_1 determinations; a similar check with phthalate or tetroxalate buffer was made immediately following each titration and in no case was the drift greater than 0.02 pH. The acid solutions were about $5\text{-}9 \times 10^{-3}$ *M* for determination of pK_2 and pK_E, and about ten times as concentrated for pK_1; 0.1 *N* sodium hydroxide was used for the more dilute solutions and 1.0 *N* for the more concentrated ones. The basic solutions were standardized against potassium acid phthalate. Four or five sets of data were obtained from each titration and with only one exception, at least two titrations were run on each compound; the one exception was the determination of pK_1 for cyclobutene-1,2-dicarboxylic acid where only one titration was run at the more concentrated level.

Calculations. A. p*K* Values. Because K_1 and K_2 differed by factors of greater than 10^4, the expressions for K_1 and K_2 given by Eberson[4] were used. For K_1 and K_E, the concentration of hydrogen ion was evaluated by an iterative, sequential method.[5a] For K_1, the Debye–Hückel equation for activity coefficients in the form $-\log f = (0.509Z^2\sqrt{\ })/(1 + 1.5\sqrt{I})$ was used while for K_E and K_2, the denominator was set equal to one. All concentration terms involved in the calculations were corrected for volume of added titrant. Table II shows an example of the data observed and the results obtained for a determination for 1,2-cyclopentenedicarboxylic acid (1.000 *N* sodium hydroxide added from a 1-ml syringe (micrometer reading 25.00 equals 1.00 ml) to a 10-ml aliquot of 0.0925 *M* acid). The scatter in all p*K* values determined in this work is ±0.04 or less, more than half having deviations of only ±0.02 based on the total values of all runs for the acid. The value for the half methyl ester of cyclopentene-1,2-dicarboxylic acid cited in this paper is the value calculated directly from the titration data. Recalculation on the basis of 5% of the corresponding diacid being present and making the assumption that one proton of the diacid was completely dissociated at the concentration used resulted in a change of only 0.07 p*K*. Because the assumption made undoubtedly is stronger than justified, the actual p*K* difference owing to the diacid probably is within the experimental error.

Table II

Micrometer reading	pH	$K_1 \times 10^2$	pK_1
7.240	1.69	2.40	1.620
9.265	1.78	2.29	1.640
11.235	1.86	2.36	1.628
13.215	1.97	2.28	1.642
15.220	2.09	2.25	1.647
		Av 2.32	Av 1.635 ± 0.015

B. The O···H···O Distances. These distances were calculated assuming (1) that the two carboxyl groups are coplanar, and (2) that the C–C (skeleton–carboxyl) bond bisects the external C═C—C angle of the skeleton. The distance between the two carbons to which the carboxyl groups are attached and the internal C═C—C angles, *i.e.*, the skeletal geometry of cyclobutene,[6] cyclopentene,[7] cyclohexene,[8] and furan,[9] are literature values; the same parameters for phthalic acid are based on the assumption of the benzene nucleus as a regular hexagon and using C–C as 1.39 A. For maleic acid, an H–C–H angle (ethylene skeleton) of 117° and a C═C length of 1.34 A were used. The C–C–O (skeleton–carboxyl–hydrogen bond) angle was taken as 120°, the C–C (skeleton–carboxyl) distance as 1.48 A, and the C–O (carboxyl–hydrogen bond) as 1.27 A in all cases. With this information, the statement $d = d_1 + 2.96 \sin (\alpha - 90°) - 2.54 \cos (\alpha + 300°)$ was derived; *d* is the O···H···O distance (assumed to be symmetrical), d_1 is the distance between the carbons to which the carboxyl groups are attached, and α is the C–C–C (skeleton–skeleton–carboxyl) angle. Framework Molecular Orbital (FMO) models were made for each of these skeletons and also for the two bicyclic compounds of this report. Rods representing the two carboxyl groups were attached at the appropriate positions on these models; the rods were of equal length, but only approximated 3 A on the scale used. The distance between the tips of the rods was measured with a millimeter scale. A plot of these measured distances against the calculated O···H···O distances gave a satisfactory linear correlation. From this plot, the O···H···O distances of the bicyclic compounds were evaluated.

C. The Angle of Tilt of the Carboxyl Groups Necessary to Attain an O···H···O Distance of 2.45 A. The carboxyl groups were assumed to rotate about the C–C (carboxyl–ring) bonds and the two carboxyl groups of each diacid were assumed to rotate equally. The same molecular dimensions used to calculate the O···H···O distances were used here. For each diacid, two possible arrangements of the carboxyl groups can provide the required 2.45 A distance, *i.e.*, the carboxyl groups may rotate in the same or in opposite directions. The angles calculated for these two cases are labeled γ_1 and γ_2, and they were determined using the equations

$$\cos \gamma_1 = [d_1 + 4.22 \cos (180 - \alpha) - 2.45]/ 2.20 \cos (\alpha - 90°)$$

and

$$\cos \gamma_2 = [-ab \pm \sqrt{a^2b^2 - (b^2 - c^2)(a^2 + c^2 - 1.500)}]/ (b^2 - c^2)$$

where $a = {}^1\!/_2 d_1 + 2.11 \cos (180 - \alpha)$, $b = -1.10 \cos (\alpha - 90°)$, $c = 1.10$, and d_1 and α have the same meaning as in part B. Smooth plots of the calculated angles *vs.* the FMO model measured distances (see B) were obtained; plots of the cosines of the angles *vs* these measured distances gave nearly linear plots. From either of these plots, values for the angles of tilt of the carboxyl groups attached to the bicyclic systems were obtained.

Results. The results are shown in Table III and Figures 1 and 2. In preliminary studies, the strengths of these acids were surveyed by making up six solutions of each acid varying in concentration from about 0.1 to 0.001 *M*. These solutions were titrated automatically and values of pH at half-neutralization for each carboxyl group were obtained from the recordings. It was observed that these pH values for the second dissociation at all concentrations for each acid were essentially constant, the expected behavior for weak acids. On the other hand, the pH values for the first stage (at all concentrations) for each acid were not constant. A plot of these pH values against the negative of the logarithm of the concentrations of the acids (half-neutralized first stage) gave straight lines with slopes of approximately unity; maleic acid, the weakest acid of this study, gave a plot with some curvature at the most concentrated solutions. Titrations using hydrochloric acid (strong acid) gave the same type of plot. These results are what would be expected for relatively strong acids which are very largely dissociated in more dilute solutions. For accurate, reliable results the criteria suggested by Albert and Serjeant[5b] ($pK_a > -\log$ (concentration of acid) was used, *i.e.*, acid solutions of 0.05–0.09 *M* were required. The literature pK_1 values for cyclopentene-1,2-dicarboxylic acid and furan-3,4-dicarboxylic acid shown in Table III are believed to be incorrect. The values reported very likely are representative of the dilute acid concentrations used in the determinations rather than the actual pK_1 values.

The O···H···O values are calculated from the geometry of the molecules except in the cases of the bicyclic compounds. Because the carboxyl group geometry is assumed to be the same for all of the acids, the O···H···O distance is determined largely by the C–C–C (skeleton–skeleton–carboxyl) angle. To the extent that this angle reflects the relative O···H···O spacing, the relative distances in the bicyclic compounds and the cyclopentene compound are consistent with other literature results.[10]

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[4] L. Eberson, *Acta Chem. Scand.*, **13**, 211 (1959).

[5] A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," John Wiley and Sons, Inc., New York, N. Y., 1962: (a) pp 62–63; (b) p 27.

[6] E. Goldish, K. Hedberg, and V. Schomaker, *J. Am. Chem. Soc.*, **78**, 2714 (1956).

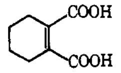
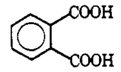
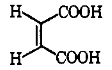
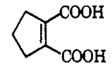
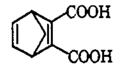
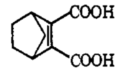
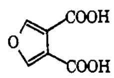
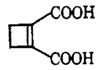
[7] P. Coppens, E. Gil-Av, J. Herling, and J. Shabtai, *ibid.*, **87**, 4111 (1965).

[8] E. J. Corey and R. A. Sneen, *ibid.*, 77, 2505 (1955).

[9] B. Bak, L. Hansen, and J. Rastrup-Anderson, *Discussions Faraday Soc.*, **19**, 30 (1955).

[10] See R. T. LaLonde, S. Emmi, and R. R. Fraser, *J. Am. Chem. Soc.*, **86**, 5548 (1964), and the reference cited in footnote 8 of that article.

Table III. Acid Dissociation Constants at 25° and Calculated O···H···O Distances for Several Dicarboxylic Acids

Acid	pK_1	pK_2	pK_E	$pK_E - pK_1$	O···H···O, A	γ_1°	γ_2°
	(3.3)[a]	(6.2)[a]			1.44	61.5	42.5
	(2.95)[b]	(5.41)[b]		(0.34)[c]	1.60	56.5	40.0
	1.92 (1.91)[d]	6.34 (6.33)[d]	 (3.08)[d]	 (1.17)[d]	1.68	54.0	38.0
	1.64 (3.36)[e]	7.27 (7.18)[e]	2.94	1.30	1.92	45.0	31.0
	1.32	7.77	3.02	1.70	2.07	37.5	26.0
	1.32	8.00	3.19	1.87	2.11	35.5	24.5
	1.44 (2.55)[f] (2.51)[g]	7.84 (7.23)[f] (7.43)[g]	3.75 (4.03)[f] (3.75)[g]	2.31	2.23	29.5	20
	1.12	7.63	3.32	2.20	2.61	...	...

[a] Footnote 3. [b] "Dissociation Constants of Organic Acids in Aqueous Solution," G. Kortum, W. Vogel, and K. Andrussow, Ed., Butterworth and Co. Ltd., London, 1961, p 363. [c] Reference 1, p 625. [d] G. Dahlgren and F. A. Long, *J. Am. Chem. Soc.*, **82**, 1303 (1960); the monoethyl ester was used in the determination of K_E. [e] Y. Inoue, K. Kurosawa, K. Nakanishi, and H. Obari, *J. Chem. Soc.*, 3339 (1965). [f] S. Oae, M. Hamada, Y. Otsuji, and N. Furukawa, *Ann. Rept. Radiation Center Osaka Prefect.*, **2**, 106 (1961). [g] S. Oae, N. Furukawa, T. Watanabe, Y. Otsuji, and M. Hamada, *Bull. Chem. Soc. Japan*, **38**, 1247 (1965).

Discussion

To obtain any correlation between hydrogen bonding and the distance between carboxyl groups in a group of dicarboxylic acids it is necessary to measure both factors. In the present work, the degree of hydrogen bonding is measured in terms of the first dissociation constant and the dissociation constant of the corresponding half methyl ester for each dicarboxylic acid, while the spacing between carboxyl groups is determined from the geometry of the rigid carbon skeletons to which the carboxyl groups are attached. The relation between intramolecular hydrogen bonding in the monoanion of a dicarboxylic acid and the dissociation constants mentioned was derived by Westheimer and Benfey[11] and may be expressed in the approximate form (adequate for present purposes): $K_{H'} = K_1/K_E$ or $pK_{H'} = -(pK_E - pK_1)$ where $K_{H'}$ is the equilibrium constant between nonintramolecular hydrogen bonded monoanion and intramolecular hydrogen bonded monoanion. This relation estimates the maximum possible

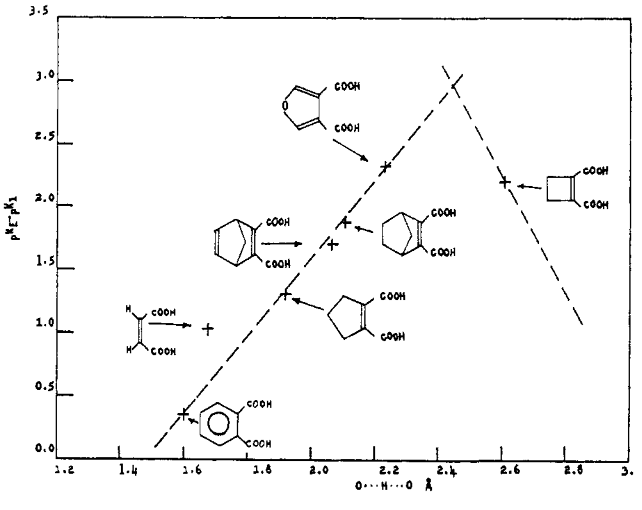


Figure 1. The relation between the degree of intramolecular hydrogen bonding in some 1,2-dicarboxylic acids and the spacing between the carboxyl groups in those acids. The intersection of the two lines is arbitrarily placed at 2.45 A.

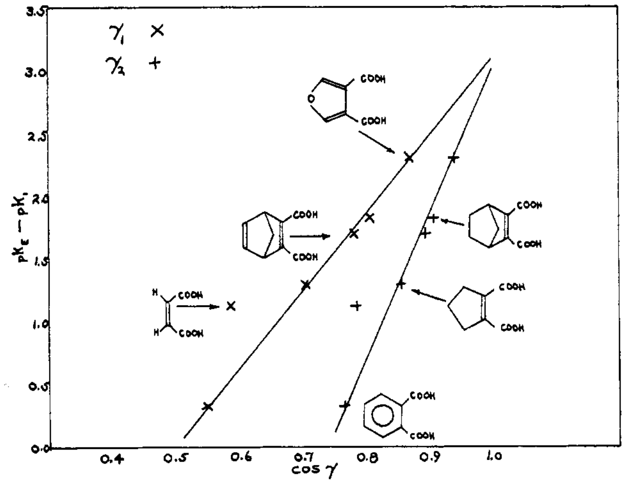


Figure 2. The relation between the degree of intramolecular hydrogen bonding in some 1,2-dicarboxylic acids and the angle of tilt, γ, of the carboxyl groups necessary to attain an O···H···O distance of 2.45 A.

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(11) F. H. Westheimer and O. T. Benfey, *J. Am. Chem. Soc.*, **78**, 5309 (1956).

intramolecular hydrogen bonding and can approach that value closely only if intramolecular hydrogen bonding in the diacid and monoester are essentially the same and negligible. Further, the derivation ignores solvation problems, *e.g.*, steric inhibition of solvation, and a few other probably less important factors. In spite of these difficulties and assumptions, for a set of carboxylic acids rather closely related in structure as the present set is, the Westheimer–Benfey expression should give a valid measure of the *relative* amount of hydrogen bonding for each diacid in the set. To measure the carboxyl group spacing, satisfactory dicarboxylic acids with appropriate rigid carbon skeletons and spacing between carboxyl groups were found in the class of well-known cycloolefinic dicarboxylic acids. With the rigid framework of the carbon skeletons as a base, and assuming the carboxyl groups to be coplanar, O···H···O distances shown in Table III were calculated. A plot of these calculated distances against $-\mathrm{p}K_{\mathrm{H}'}$ is shown in Figure 1. It is clear that for these acids with the exception of the cyclobutene compound, the degree of intramolecular hydrogen bonding increases with increasing separation of the carboxyl groups. For appreciably larger spacings, the intramolecular hydrogen bonding should decrease, *i.e.*, at large enough distances a hydrogen bond could not form at all. Examination of Figure 1 then suggests that a "peak" should occur in the gap between the furan and cyclobutene compounds. An almost symmetrical diagram is produced by locating the "peak" at 2.45 A, the short hydrogen bond distance that is observed in X-ray crystallographic studies of acid salts.[12] The calculated values near the "peak" clearly are comparable to real observed values, while the shorter calculated O···H···O values place the two oxygen atoms much closer than is physically possible. That is, as the calculated O···H···O values show increasing compression and deviation from real O···H···O distances, the amount of hydrogen bonding decreases proportionately as seen in Figure 1. On the basis that the short calculated O···H···O distances might be considered ridiculous, hypothetical, unreal, or otherwise unsatisfactory, one referee has suggested an alternative correlation between $-\mathrm{p}K_{\mathrm{H}'}$ and a real parameter, the angle of tilt of the carboxyl groups, so that an O···H···O distance of 2.45 A is attained. Two possibilities of attaining this distance in each acid exist depending on whether the carboxyl groups rotate in the same or opposite directions (and assuming each carboxyl tilts to the same angle). The two solutions of this problem for each acid were calculated using the same molecular dimensions for the rigid carbon skeletons as were used in calculating the O···H···O distances. Figure 2 shows a plot of $-\mathrm{p}K_{\mathrm{H}'}$ against the cosines of the calculated angles. The cyclobutene compound is missing because the spacing between the carboxyl groups is such that no tilting of the groups is required to attain the optimum distance, only distortion of the carboxyl ring angle is required. These plots clearly show that for a reasonable O···H···O distance of 2.45 A, the greater the deviation of the carboxyl groups from coplanarity, the less effective is the intramolecular hydrogen bonding. Since most diacids with rigid carbon skeletons do not show intramolecular hydrogen bonding of the degree observed in this work even when the optimum O···H···O distance is attainable by suitable conformations of the carboxyl groups, an additional steric condition seems to be required. It is suggested that this requirement is that the hydrogen bond be essentially linear and that it lie in the intersection of the two planes determined by the carboxyl groups. In the systems of the present study, the two planes would coincide, but in some case such as Eberson's racemic disubstituted succinic acids[4] the two planes would intersect at some angle. This requirement follows rather directly from the molecular orbital three-center model[13] of the hydrogen bond if it is assumed that the oxygen atoms of the carboxyl groups are essentially sp^2 hybridized, and the sp^2 hybrid orbitals are the ones taking part in the three-center hydrogen bond. This picture probably is consistent with X-ray crystallographic results.[12,14]

The hydrogen maleate ion and hydrogen chloromaleate ion apparently are the only intramolecularly hydrogen bonded monoanions of dicarboxylic acids whose molecular dimensions have been determined in detail.[12a,e] The observed "optimum" O···H···O distance and near coplanarity of the carboxyl groups are possible because of rather marked distortions in other bond lengths and angles. It is now suggested that in all of the dicarboxylic acid systems which show strong intramolecular hydrogen bonding, the optimum O···H···O distance, 2.45 A, probably is present or very closely approximated, and the carboxyl groups are conformationally arranged such that the hydrogen bond lies on the intersection of the two planes determined by the two carboxyl groups. The "degree" of intramolecular hydrogen bonding observed then represents a balance in energy between a very strong hydrogen bond (possibly 8–10 kcal) and the amount of "distortion energy" required to produce the necessary configuration for that hydrogen bond.

The present results clearly establish a high degree of intramolecular hydrogen bonding in the monoanions of the acids studied. However, the extent to which this hydrogen bonding actually contributes to the large K_1/K_2 ratio is not shown directly. Although the

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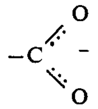
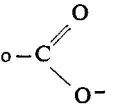
[12] Some examples are: (a) hydrogen maleate ion, 2.437 ± 0.004 A, S. F. Darlow and W. Cochran, *Acta Cryst.*, **14**, 1250 (1961); S. F. Darlow, *ibid.*, **14**, 1257 (1961); (b) ammonium hydrogen cinnamate, 2.51 ± 0.03 A, R. F. Bryan, H. H. Mills, and J. C. Speakman, *J. Chem. Soc.*, 4350 (1963); (c) potassium hydrogen di-*p*-chlorobenzoate, 2.457 A, H. H. Mills and J. C. Speakman, *ibid.*, 4355 (1963); (d) sodium hydrogen diacetate, 2.444 ± 0.010 A, J. C. Speakman and H. H. Mills, *ibid.*, 1164 (1961); (e) neutron diffraction studies of potassium hydrogen chloromaleate [R. D. Ellison and H. A. Levy, *Acta Cryst.*, **19**, 260 (1965)] gave an O···H···O distance of 2.403 A.

[13] G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman and Co., San Francisco, Calif., 1960, pp 236–238.

[14] A somewhat different grouping can be imagined if the oxygens of the O···H···O bond are sp^3 hybridized. Recent work by E. Spinner [*J. Chem. Soc.*, 4217 (1964)] on the vibration spectra of some substituted acetate ions suggests two extremes and implies a range of carboxylate ion structures from  (symmetrical) to  (unsymmetrical). In the latter structure, the O^- quite likely could be sp^3 hybridized and, consequently, the C–O–H angle would be tetrahedral. This would alter, but not eliminate, the requirement that the O···H···O bond lie in some specific orientation with respect to the planes of the two carboxyl groups, but the other general conclusions concerning linearity and length would remain unchanged. Because of the possible variation in carboxylate ion structure, a similar variation in the total grouping of a carboxylate ion and a carboxyl group hydrogen bonded together might be expected.

K_1/K_2 ratios for the acids of this study are very large, unlike the measure of hydrogen bonding, $K_{H'}$, they do not increase as uniformly with increasing spacing between the carboxyl groups. These results could arise from appreciable intramolecular hydrogen bonding within the undissociated diacid and/or the monoester[11] and also by the influence of several factors which have been suggested to explain large K_1/K_2 ratios. Certainly some of these factors make some contribution in the present examples, but because of the structures chosen, the contributions probably are minimal and possibly negligible in most cases. That is, the structures of the carbon skeletons are such that no hindrance to solvation of the acid or anions should be anticipated,[15] and no restriction of rotation of the carboxyl groups should be observed except as one carboxyl group may effect the other.[16]

Any discussion of ionization constants of dicarboxylic acids should consider the electrostatic effect of one carboxyl group or carboxylate ion on the second carboxyl group. The theory of Kirkwood and Westheimer[17] is often the starting point of such a discussion. Their theory, in order to be applied in a quantitative sense, requires that the diacid approximate one of two models, either ellipsoidal in shape with the carboxyl groups located at the foci, or a spherical shape. The compounds in the present study cannot fit the ellipsoidal model, and appear to be very poor approximations to spherical (their general shapes seem to be more "pear shaped"). Because of the rigid nature of these molecules, their shape, and the orientation of the carboxyl groups, it is somewhat difficult to apply even the qualitative aspects of the theory. Certainly the observation that the K_1/K_2 ratio increases greatly as the distance between the carboxyl groups increases slighty (implied in Table II) is contrary to the normal expectations of any theory relating K_1/K_2 ratios to electrostatic interactions only. The results of Eberson for the dialkyl-substituted maleic acids which must have their carboxyl groups very close together would seem to put an upper limit on the K_1/K_2 ratio due to electrostatic effects at about 10^3 when the carboxyl groups are oriented as in these compounds.[3,18] The orientation is such as to place the carboxyl groups on the surface of a hydrocarbon cavity, but projecting close to each other into the aqueous medium.

Consequently, a major portion of the K_1/K_2 ratio should be attributed to effects other than electrostatic. Since, with the exception of maleic acid, the compounds can be considered as dialkyl-substituted maleic acids, and the "substituents" are either not bulky or are located at an appreciable distance from the carboxyl groups, the major factor contributing to the large K_1/K_2 (or ΔpK) values would appear to be intramolecular hydrogen bonding.

The present work indicates strongly that intramolecular hydrogen bonding can be the major contributing factor to large K_1/K_2 values in dibasic acids. The present work shows clearly that such intramolecular hydrogen bonding in one series of 1,2-diacids *increases* with *increasing distance* between the carboxyl groups, and suggests that the interaction of the carboxyl groups passes through a maximum at some optimum O···H···O distance, probably about 2.45 A. It is clear that hydrogen bonding does not increase as the carboxyl group spacing is compressed below the optimum distance. It is also clear that possible attainment of the optimum spacing of the carboxyl groups is in itself insufficient to produce a strong hydrogen bond. Thus, numerous flexible compounds, and even moderately restricted molecules such as *cis*-cyclopentane-1,3-dicarboxylic acid, show no large K_1/K_2 values that reflect strong hydrogen bonding. Consequently, two requirements for maximum intramolecular hydrogen bonding in dicarboxylic acids appear to be: (1) the carboxyl groups should be spaced so that an essentially linear O···H···O bond of length about 2.45 A lying in the intersection of the two planes of the carboxyl groups may be formed; and (2) the carboxyl groups should be attached to a carbon skeleton such that no change in conformation of the carbon skeleton is allowed (but the carboxyl groups themselves may rotate) either before or after requirement 1 is fulfilled.

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(15) This acid-weakening effect in aliphatic monoacids was discussed by G. S. Hammond and D. H. Hogle [*J. Am. Chem. Soc.*, 77, 338 (1955)] and elaborated by several other groups: M. S. Newman and H. Boden, *ibid.*, **83**, 115 (1961); H. L. Goering, T. Rubin, and M. S. Newman, *ibid.*, **76**, 787 (1954); M. S. Newman and T. Fukunaga, *ibid.*, **85**, 1176 (1963); L. Eberson, *J. Org. Chem.*, **27**, 3706 (1962). For dibasic acids with closely spaced carboxyl groups, such hindrance to solvation might be expected to be more critical for the dianion than for the monoanion, thereby resulting in a relatively larger decrease of K_2 than K_1 and thus a larger ΔpK value. This might account for part of the very large ΔpK values for racemic di-*t*-butylsuccinic acid observed by Eberson,[4] for *t*-butylmalonic acid observed by van Woerden [*Rec. Trav. Chim.*, **83**, 920 (1963)], and for several disubstituted malonic acids observed by J. H. Wotiz and H. E. Merrill [*J. Am. Chem. Soc.*, 80, 866 (1958)].

(16) Restricted rotation of carboxyl groups in a dibasic acid may have some effect on ΔpK values as suggested by van Woerden[15] and McCoy and Nachtigall.[2] This factor might also contribute to the ΔpK values for the cases mentioned in footnote 15, *i.e.*, racemic di-*t*-butylsuccinic acid, *t*-butylmalonic acid, and several disubstituted malonic acids. Restricted rotation and hindrance to solvation almost certainly are contributing factors to the interesting (large) ΔpK values observed for some 3,3-disubstituted cyclopropane-1,2-dicarboxylic acids [J. L. Haslam, E. M. Eyring, W. W. Epstein, G. A. Christiansen, and M. H. Miles, *ibid.*, **87**, 1 (1965)].

(17) J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); F. H. Westheimer and J. G. Kirkwood, *ibid.*, **6**, 513 (1938).

(18) Unless some effect can be invoked which would result in decreasing K_1/K_2, the results on substituted cyclopropane-*cis*-1,2-dicarboxylic acids suggest an upper limit of 200 to 300 for K_1/K_2 due solely to electrostatic effects in *cis*-1,2-diacids. It should be noted with these compounds that increasing alkyl substitution which presumably would increase the volume of hydrocarbon cavity and therefore according to theory[17] increase K_1/K_2 actually produces a decrease for K_1/K_2. An explanation for small decreases in the K_1/K_2 ratio for *cis*-1,2-diacids has been presented [L. L. McCoy, *J. Org. Chem.*, **30**, 3762 (1965)].