85. *The Dissociation Constants and Stereochemistry of some Stereoisomeric Dibasic Acids.*

By J. C. SPEAKMAN.

Thermodynamic dissociation constants have been measured for some pairs of stereoisomeric dibasic acids, derived from *cyclo*pentane, *cyclo*hexane, tetrahydronaphthalene, and di*cyclo*hexyl. The results are discussed in relation to the stereochemistry of the acids, and with special reference to the consequences of the discovery that high potential barriers restrict " free rotation " about the single C–C bond. The hypothesis, generally accepted, that the barriers are so oriented as to favour the " staggered " configuration around each bond leads to a simple procedure for reckoning the average spatial separation of any two in a saturated and strainless system of carbon atoms.

PART I.

AN approximate equation expressing the inverse relationship between the intercarboxyl distance in a symmetrically dibasic acid and the ratio of its first to its second dissociation constant was first derived by Bjerrum (*Z. physikal. Chem.*, 1923, **106**, 219); his treatment has since been refined by various authors (*e.g.*, Ingold, J., 1931, 2179; Jones and Soper, J., 1936, 133; Kirkwood and Westheimer, *J. Chem. Physics*, 1938, **6**, 506, 513; for further references see Greenspan, *Chem. Rev.*, 1933, **12**, 339). Difficulties are met in the attempt to apply this relationship accurately, and especially when the carboxyl groups are close together; but there is no doubt that it can give valuable information of an approximate kind on stereochemical problems (cf. *e.g.*, Gane and Ingold, J., 1928, 1594; 1931, 2153). In the present paper the thermodynamic dissociation constants of some pairs of *cis-trans*-isomerides are given, and their implications are discussed.

EXPERIMENTAL.

The author is indebted to Prof. R. P. Linstead, F.R.S., for providing specimens of *cis*- and *trans-cyclo*pentane-1-carboxylic-2-acetic acids (J., 1934, 960), of *cis-cyclo*pentane-1 : 2-diacetic acid (J., 1934, 941), and of *trans-cyclo*hexane-1 : 2-diacetic acid (J., 1935, 441); to Prof. R. D. Haworth for specimens of *cis*- and *trans*-tetrahydronaphthalene-2 : 3-dicarboxylic acids (J., 1940, 1321); and to Dr. A. H. Cook for an analytically pure specimen of *trans-cyclo*pentane-1 : 2-diacetic acid (J., 1935, 440). The *cis-cyclo*hexane-1 : 2-diacetic acid (m. p. 160°) was prepared by a two-stage oxidation (Kandiah, J., 1931, 947) of *cis*-β-decalol (m. p. 100—105°). All the acids, except the analytically pure specimen, were recrystallised from water or from water and ethyl acetate.

Thermodynamic dissociation constants were measured at 20° by the method already described (J., 1940, 895). Results (averages of a number of determinations, and expressed as $p_K = -\log K$) are given in Table I, the estimated accuracy being $\pm$ 0·05 unit for p_K and $\pm$ 0·03 for Δp_K. For comparison, the data of Ingold and Mohrhenn (J., 1935, 949) and of Wassermann (*Helv. Chim. Acta*, 1930, **13**, 207, 223) for the *cyclo*pentane-1 : 2-dicarboxylic acids, and those of Kuhn and Wassermann (*ibid.*, 1928, **11**, 62) for the *cyclo*hexane-1 : 2-dicarboxylic acids are also included.

TABLE I.

Thermodynamic Dissociation Constants.

	cis-.			*trans*-.		
Acid.	p_{K_1}.	p_{K_2}.	Δp_K.	p_{K_1}.	p_{K_2}.	Δp_K.
*cyclo*Pentane-1 : 2-dicarboxylic (I. and M. at 25°)	4·43	6·57	2·14	3·96	5·85	1·89
,, ,, (W. at 19°)	4·37	6·51	2·14	3·89	5·91	2·02
*cyclo*Pentane-1-carboxylic-2-acetic acid	4·40	5·79	1·39	4·39	5·67	1·28
*cyclo*Pentane-1 : 2-diacetic	4·42	5·42	1·00	4·43	5·43	1·00
Tetrahydronaphthalene-2 : 3-dicarboxylic	3·98	6·47	2·49	4·00	5·70	1·70
*cyclo*Hexane-1 : 2-dicarboxylic (K. and W. at 19°)	4·34	6·74	2·40	4·18	5·93	1·75
*cyclo*Hexane-1 : 2-diacetic	4·42	5·45	1·03	4·38	5·42	1·04

DISCUSSION.

Important implications for stereochemistry follow from the recognition (*e.g.*, Kemp and Pitzer, *J. Amer. Chem. Soc.*, 1937, **59**, 276; Kistiakowsky and Nazmi, *J. Chem. Physics*, 1938, **6**, 18; Aston, *Chem. Rev.*, 1940, **27**, 63) of high potential barriers (of the order of 3—4 kg.-cals./mol. in so simple a molecule as ethane, and probably larger in substituted ethanes) hindering " free rotation " about the single C–C bond. The physical evidence for these barriers applies mainly to molecules in the gaseous state, but it appears certain that similarly high barriers will occur when the molecule is in the solid state or in solution (cf. Lewis and Smyth, *J. Chem. Physics*, 1939, **7**, 1085). It is not yet clear from the physical side whether the potential barriers in ethane are oriented so as to favour the azimuth corresponding to the " opposed " or " eclipsed " (I), or that corresponding to the " staggered " or " alternate " (II), configuration round the C–C bond; but general considerations strongly support the latter (see Schomaker and Stevenson, *J. Chem. Physics*, 1940, **8**, 637; Pitzer, *Chem. Rev.*, 1940, **27**, 44; Conn, Kistiakowsky, and Smith, *J. Amer. Chem. Soc.*, 1939, **61**, 1872; however, see also Gorin, Walter, and Eyring, *ibid.*, p. 1876; Eucken and Schäfer, *Naturwiss.*, 1939, **27**, 122), which certainly represents the more stable state in some substituted ethanes (*e.g.*, ethylene dihalides; see Beach and Palmer, *J. Chem. Physics*, 1938, **6**, 639). In this connexion importance attaches to the deduction, made by Gane and Ingold (*loc. cit.*, p. 2164) on the basis of their dissociation-constant measurements, that the carbon chain in the normal ω-dibasic acids is a flat zigzag (*i.e.*, in aqueous solution); for this state of the chain (III), occuring also in crystalline paraffin-chain compounds, requires the *staggered* (II) azimuth round each C–C bond. It is now suggested that the principal factor imposing this extended configuration is not a repulsion between the end groups (even when both are ionised, the coulombic potential will be relatively small when the distance apart of the groups exceeds $2\frac{1}{2}$—3 A.; cf. Moelwyn-Hughes and Sherman, J., 1936, 103), but is rather the hindering potential around each bond. In ethane itself the potential barrier will have triad symmetry; but in polymethylene chains there will presumably be an especially deep potential well favouring that azimuthal angle, at each C–C bond, corresponding to a flat zigzag (III) (cf. Pitzer, *loc. cit.*).

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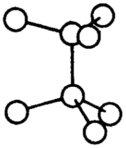

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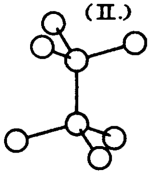

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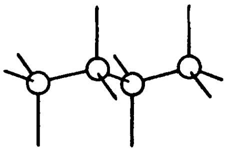

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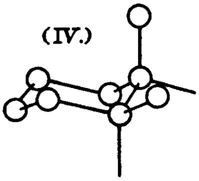

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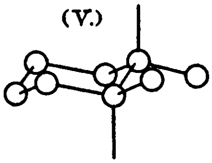

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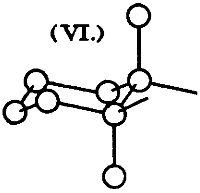

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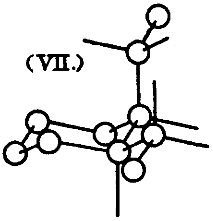

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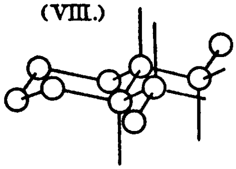

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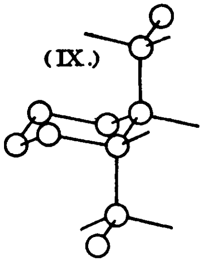
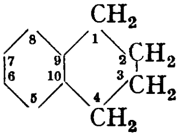


According to the Sachse theory, the *cyclo*hexane ring can exist in two " puckered " forms—the **Z** or " chair," and the **C** or " boat." If the above principles are accepted, it follows that the ring will be more stable in the **Z** form, in which all the C–C bonds possess the staggered configuration, than in the **C** form, in which two bonds possess the opposed configuration; the former should be the more stable by an energy difference of the order of 7 kg.-cals./mol. Thus, although the molecule when activated will be able to pass into the **C** form, and readily undergo the inversion of the **Z** form necessary to account for the non-occurrence of isomers of the 1 : 1-disubstituted *cyclo*hexanes (*e.g.*, Wightman, J., 1926, 2541), the normal state of *cyclo*hexane and its derivatives will be one in which the ring has the **Z** form. This consideration simplifies Kuhn and Wassermann's treatment (*loc. cit.*, p. 57) of the stereochemistry of the *cyclo*hexanedicarboxylic acids; for instance, instead of its being necessary to envisage three possible forms of the *cis*-1 : 2-isomer, one suffices (IV); and instead of five forms of the *trans*-isomer, only two (V and

VI), of which (V) can probably be eliminated because the additional effect of repulsion between the carboxyls favours (VI). If (IV) and (VI) are taken as the normal states of the *cis*- and *trans*-acids, the observed Δp_K values are adequately accommodated.

The stereochemistry of a tetramethylene chain fused on to a benzene ring in the ortho-positions (X) has been discussed by Mills and Nixon (J., 1930, 2515). They concluded that that arrangement of the atoms 1, 2, 3, 4 corresponding (nearly) to half of the *cyclo*hexane ring in its **Z** form is more stable than that corresponding to the **C** form (with the atoms 1, 2, 3,4, coplanar, but inclined to the plane of the benzene ring). In their calculations, the length of the bonds 9–1 and 10–4 was taken as 1·48 A.; if, instead, one uses 1·53 A., which appears more likely (see Brockway and Robertson, J., 1939, 1324), their argument is reinforced.* Their conclusion is further strengthened if the staggered is accepted as the more stable configuration round the C–C bond. The fact that the difference between the Δp_K values for the *cis*- and *trans*-2 : 3-dicarboxylic acids (Table I) is approximately equal to that for the *cyclo*hexane-1 : 2-dicarboxylic acids, and much larger than that for the *cyclo*pentane-1 : 2-dicarboxylic acids, supports their conclusion again; for, were the atoms 1, 2, 3, 4 co-planar, conditions would resemble those in the *cyclo*pentane, rather than those in the *cyclo*hexane, diacids.



(X.)

With the *cyclo*hexane-1 : 2-diacetic acids, on the other hand, the Δp_K values are equal within experimental error—a result which recalls the similar situation found by Kuhn and Wassermann for the 1 : 3- and 1 : 4-*cyclo*hexanedicarboxylic acids. It can be attributed to the occurrence of those orientations about the bonds between the $CH_2{\cdot}CO_2H$ groups and the ring shown at (VII) for the *cis*-isomer, and of those shown at (VIII) and (IX) (the latter more probable) for the *trans*-isomer. It is calculated (see Part II) that the distances between the carboxyl carbons are 5·8, 5·8, and 6·3 A., respectively. The distances between the effective charges on the ionised groups will be greater by some 2·0 A. (see Gane and Ingold, *loc. cit.*, p. 2163), so that the expected difference between Δp_K values is within experimental error.

In the *cyclo*pentane derivatives the situation differs in that this ring is probably planar, and consequently with opposed azimuths at each C–C bond. In the *cis*-1 : 2-disubstituted compound (but not in the *trans*-) it seems possible that steric repulsion may cause slight distortion of the ring, by a rotation about the included C–C bond so as to approach a staggered orientation there. This would account for the unexpectedly small difference between the Δp_K values found by Gane and Ingold. The still smaller difference indicated in Wassermann's data is more difficult to account for. A similar distortion effect may occur in the *cis*-1 : 2-diacetic acid; along with an orientation of the acetic acid residues approximately as shown at (VII), (VIII), and (IX), it would account for the Δp_K value's being practically the same as that for the *trans*-acid.

The *cyclo*pentane-1-carboxylic-2-acetic acids occupy an intermediate position. Because their molecules do not possess the requisite symmetry, the Bjerrum principle is not strictly applicable to them; but, in fact, the small difference between the Δp_K values accords well with the estimated distances between the carboxyl carbon atoms, *viz.*, 4·4 A. for the *cis*-, 5·4 A. for the *trans*-isomer.

PART II.

EXPERIMENTAL.

Apart from the possibility of isomerism due to restricted rotation about the central C–C bond, 2 : 2′-perhydrodiphenic acid is expected to exist in six stereoisomeric forms (Linstead and Walpole, J., 1939, 851; see also *Chem. and Ind.*, 1937, **56**, 510, for nomenclature). Through the kindness of Prof. Linstead, three acids (m. p.'s 289°, 244°, and 220°) were available for the present work. The first proved much too insoluble for measurements to be made on it. The other two had low solubilities in water (or aqueous alcohol); but, by boiling the solids with water in a Pyrex beaker for 10 mins., and filtering off the supernatant liquid at once, solutions (presumably supersaturated) were obtained of molar concentrations 0·002—0·0004. These

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* There are discrepancies between the lettering of Fig. 2 and that sometimes used in the text.

solutions were titrated potentiometrically at 20° in the manner described previously (J., 1940, 895), and the resulting data led to intelligible and reproducible values for K_1 and K_2.

Two objections might be raised to this procedure: (1) that traces of any acidic impurities in the solids would be preferentially extracted; (2) that the boiling might cause chemical changes in the acids. The first appears to be answered by the fact that consistent values for K_1 and K_2 resulted when the same portion of solid was used repeatedly; the second (which the chemical stability of these acids renders improbable anyhow), by the fact that solid material with essentially unchanged m. p. could be recovered from the solutions.

Results (means of six determinations) are given in Table II. The accuracy, lower than that attainable with less insoluble acids, is estimated at ± 0·2 for p_K, and somewhat better in Δp_K. The Δp_K values suggest unequivocally that the carboxyl groups are effectively closer together in the 220° than in the 244° acid, and that in the latter they are about as far apart as those in unsubstituted adipic acid (Δp_K = 1·00).

TABLE II.

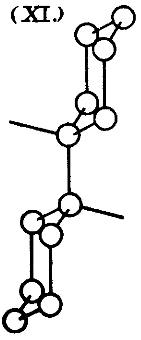
Thermodynamic Dissociation Constants at 20°.

	p_{K_1}.	p_{K_2}.	Δp_K.
Perhydrodiphenic acid, m. p. 220°	5·0	6·7	1·7
,, ,, ,, 244°	$4{\cdot}8_5$	$5{\cdot}9_5$	1·1

DISCUSSION.

If we apply the principles outlined in Part I, the ring system of the perhydrodiphenic acids should be capable of existing in two fundamental forms, (XI) and (XIV), with the possibility of an intermediate form. Of the two, (XIV) may be expected to be less stable because less extended. The potential barrier hindering rotation about the central C–C bond is likely to be considerably higher than that in ethane, and, if we postulate only staggered orientations, (XI) would give two other forms, (XII) and (XIII). Forms produced by the corresponding internal rotation of (XIV) appear to be improbable for steric reasons.

(XI.)



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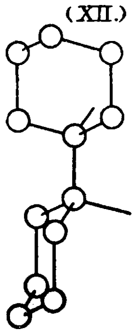

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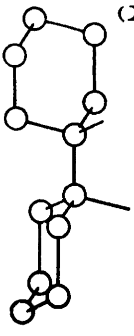

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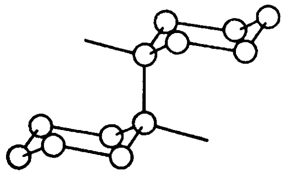

It must be emphasised that oscillations about these positions will certainly occur. Moreover, by surmounting the intervening energy barrier a molecule will be able to pass from one form to another. In addition, various activated forms, with the six-membered rings in the C form for example, would be similarly accessible, and must be attained as a prelude to certain chemical decompositions. Nevertheless, it is suggested that, allowance being made for the possible occurrence of *slight* distortions due to steric influences, the above forms, and especially (XI), (XII), and (XIII), include the most stable average positions of the atoms.

If the barriers separating (XI), (XII), and (XIII) were much higher than 15 kg.-cals./mol., the possibility of isolating the forms would arise. Claims to the isolation of stereoisomeric forms of di*cyclo*hexyl have indeed been made (Schrauth and Görig, *Ber.*, 1923, **56**, 1900; Zelinski, Schuikin, and Fatejev, *J. Gen. Chem. Russia*, 1932, **2**, 671; Levina, Juriev, and Loschkomoinikov, *ibid.*, 1937, **7**, 341), but probably on inadequate evidence (cf. Hückel and Neunhoeffer, *Annalen*, 1930, **477**, 99). Should such isomerism in fact occur, it appears more likely to arise through restricted rotation about the central bond than through fixation of the rings in C or Z forms, as supposed by the above authors. As, however, there is no evidence for the occurrence of this type of isomerism in the perhydrodiphenic acids, its occurrence in di*cyclo*hexyl is *a fortiori* improbable.

The distances between two carbon atoms substituted in the 2 : 2′-positions have been worked out for each form of each isomer, and are shown in Table III. All valency angles have been taken as tetrahedral, and all C–C bond lengths as 1·54 A. It is true that the position of the charge on the carboxylate ion is about 1·0 A. beyond the carbon atom (Gane and Ingold, *loc. cit.*, p. 2153), but for this sufficient allowance can easily be made later if required.

TABLE III.

Calculated Inter-carboxyl Distances (A.) *in Isomeric Perhydrodiphenic Acids.*

		Form.			
	Isomer.	I.	II.	III.	IV.
syn-Series.	*cis–cis-*	5·25 (*0*)	2·95 (*1*)	2·95 (*1*)	5·25 (*2*)
	cis–trans-	4·62 (*1*)	4·62 (*1*)	1·54 —	5·25 (*1*)
	trans–trans-	5·25 (*2*)	2·95 (*1*)	2·95 (*1*)	6·36 (*0*)
anti-Series.	*cis–cis-*	4·62 (*0*)	1·54 —	4·62 (*2*)	1·54 —
	cis–trans-	2·95 (*1*)	2·95 (*2*)	5·25 (*1*)	3·88 (*1*)
	trans–trans-	1·54 —	4·62 (*2*)	4·62 (*0*)	5·82 (*0*)

A notable simplification can be introduced into this calculation when it is realised that, according to the postulates made in the present paper, all inter-carbon distances must equal one or another of the inter-carbon distances in the diamond lattice, which belongs to the cubic system with lattice-complex *Fd3m* (*a*) (" International Tables for the Determination of Crystal Structure," p. 369), and $d_{100} = 1{\cdot}54/\sqrt{3}$ A., and may be regarded as a three-dimensional net-work of Z-form six-membered rings. When (as in the present example) the two carbon atoms whose spatial separation is required are connected by an even number of intervening atoms, the separation will equal some value of the expression $\sqrt{h^2 + k^2 + l^2}(1{\cdot}54/\sqrt{3})$, where the indices h, k, and l must be odd integers; when, on the other hand, the number of intervening atoms is odd, h, k, and l must be even and their sum divisible by 4. These simple relationships should apply to any saturated, strainless system of carbon atoms, so long as the staggered azimuth (II) is preserved at each C–C bond.

Were the orientations (XI), (XII), and (XIII) equally stable, and the contribution of (XIV) negligible, then the mean separation of carboxyl carbons would be the same (3·6 A.) for all six isomers. The data in Table II suffice to show that this is not so. Those forms with the intercarboxyl distance 1·54 A. can hardly occur, unless as a result of co-ordination between the groups. In some of the other forms one carboxyl, or both, are brought as near as 2·52 A. to the 2, or 6, carbon atom of the other ring; the numbers of such close approaches are added in parentheses in Table III. They may be expected to render the form less stable (cf. Pitzer, *loc. cit.*).

In relation to the experimental data, the possible configurations are clearly too numerous to warrant any detailed discussion of the actual form assumed by the molecule of any particular isomeride. The dissociation constants given do not enable any safe conclusion to be drawn regarding the structure of the acids. If, however, the acid of m. p. 220° is the *trans-syn-trans-*, and the 244° acid the *cis-anti-trans*-isomer (as, according to a private communication from Prof. Linstead, seems likely at present), the above scheme enables an accommodation between dissociation constants and structures to be attained.

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