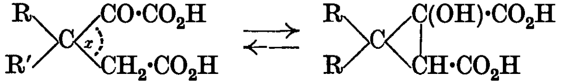
139. *The Primary Dissociation Constants of the Methyl*cyclo*hexane-*1 : 1*-diacetic Acids. An Anomaly between the Physical and Chemical Tests of the Valency-deflexion Hypothesis.*

By David James Gibbs Ives, Reginald Patrick Linstead, and Harry Lister Riley.

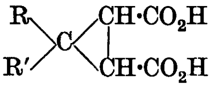
General experimental evidence for the valency-deflexion hypothesis of Thorpe and Ingold has been drawn from a wide field, but for its more rigid support, three methods, involving quantitative comparative work, have been mainly employed. In these, the effect has been examined of varying the group RR′ on the following processes : (*a*) The tautomeric change between the keto-acids of type (I) and their hydroxy-ring isomerides (II); (*b*) the stability of *spiro*-acids of type (III) towards fission of the *cyclo*propane ring by acids ; (*c*) the electrolytic dissociation of the ββ-disubstituted glutaric acids (IV).

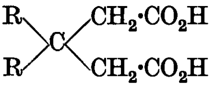
(I.)



(II.)

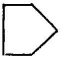
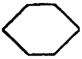
(III.)





(IV.)

As is well known, important facts in support of the hypothesis are provided by the similarity observed in all these tests between the *gem*-dimethyl compounds (RR′ = Me, Me) and their *cyclo*pentane analogues ; and further, by the dissimilarity between corresponding *cyclo*pentane and *cyclo*hexane derivatives. These chemical facts are summarised in the following table :

RR′ =	Me,Me		
% Keto-acid at equilibrium (I ⇌ II)	100	100	0
Resistance of (III) to 5% HCl at 200°	decomp.	decomp.	stable

This difference between the *cyclo*pentane and *cyclo*hexane rings is attributed by Thorpe and Ingold to the fact that, whilst the former is uniplanar and strainless, the average condition of the latter is between a strainless and a strained (uniplanar) form (J., 1928, 1318), with the corollary that the extracyclic angle (*x*, formula I) is smaller in the six-membered ring compounds.

Desai (this vol., p. 1047) has carried out parallel investigations of the substituted 3- and 4-methyl*cyclo*hexane compounds, with the result that, by both chemical tests (*a*) and (*b*), these simulated the *cyclo*pentane, not the *cyclo*hexane analogues. Two explanations alone seem possible : either the entry of the methyl groups has stabilised a multiplanar (strainless) form of the *cyclo*hexane ring, or the chemical methods of diagnosis of ring-strain have broken down.

In the present paper, the first possibility was tested by the physical method (*c*) involving a comparison of the dissociation constants of 3- and 4-methyl*cyclo*hexane-, *cyclo*pentane-, and *cyclo*hexane-1 : 1-diacetic acids. These determinations, which were carried out by the conductivity method, involved certain difficulties in calculation (see next section). Following Gane and Ingold, a more rigid comparison of the acids would have been possible had their secondary dissociation constants been available. There is no doubt, however, that for similarly constituted acids the primary dissociation constants provide *comparative* information as to the distance apart of the two carboxyl groups, the approach of which varies the constant (compare, *inter alia*, Spiers and Thorpe, J., 1925, **127**, 538; Gane and Ingold, J., 1929, 1696).

The mean values obtained for the primary dissociation constants, calculated from the simple dilution law, are shown below, previous determinations being given in parentheses :

Acid.	K_1 (at 25°) × 10^4.
*cyclo*Pentane-1 : 1-diacetic	1·76 (1·66,* 1·73†)
*cyclo*Hexane-1 : 1-diacetic	3·23 (3·34,* 3·37†)
3-Methyl*cyclo*hexane-1 : 1-diacetic	3·25
4-Methyl*cyclo*hexane-1 : 1-diacetic	3·21

* Gane and Ingold, J., 1928, 2267. † Spiers and Thorpe (*loc. cit.*).

It will be seen that the substituted *cyclo*hexane acids resemble the parent substance and not the *cyclo*pentane compound. On these grounds, the *cyclo*hexane rings of the substituted acids are in their normal condition, as is, indeed, to be expected on general grounds and from the fact that Desai (*loc. cit.*) observed no abnormal stereoisomerism.

There seems little doubt that the chemical evidence of reactions (*a*) and (*b*) is here misleading if applied as a test for valency deflexion. It may be recalled that Lanfear and Thorpe (J., 1923, **123**, 1683) showed that the *cis*-form of the hydroxy-ring acid (II) of the *cyclo*pentane series took no part in the keto-cyclol change. The abnormal results obtained by Desai can also be attributed, not to a one-sidedness of equilibrium, but to the operation of some factor inhibiting the tautomeric change (I $\rightleftharpoons$ II). In short, the reaction can only fairly be applied when both tautomeric individuals can be isolated and shown to yield the same equilibrium. It is not desired at present to enter upon a discussion of validity of these chemical tests, but it is clear that, in spite of their previous successful application, they are not sufficiently simple to provide in all cases unambiguous data on the deflexion of valency.

Measurement of Conductivity.—Measurement of the specific conductivity of the aqueous solutions of the acids and their sodium salts was carried out in an exactly similar manner to that already described (Ives and Riley, J., 1931, 1998), the same bridge and amplifier, conductivity cells, procedure, etc., being employed. The two methyl*cyclo*hexanediacetic acids were kindly supplied by Dr. Desai. The other acids were prepared by the method of Kon and Thorpe (J., 1919, **115**, 686). All were carefully purified by repeated crystallisation, both from non-aqueous solvents and from water. The sodium salts of the acids were made by adding an exactly equivalent quantity of carefully standardised, carbon dioxide-free sodium hydroxide solution, prepared from "A.R." caustic soda. The resulting solution was evaporated over the steam in a platinum basin, and when the salt commenced to separate, the solution was cooled and an excess of absolute alcohol added, the sodium salt being precipitated. This procedure was repeated three times, the salt was then dried at 120°, and its sodium content determined accurately. In each case the result was in excellent agreement with the theoretical.

For reasons already stated (*loc. cit.*), no correction for the conductivity of the water used was applied in the case of the acids, but the full correction was subtracted in the case of the sodium salts. The conductivity of the various samples of water used varied between 0·4 and 1·0 gemmho.

Some Observations on the Interpretation of the Conductivity Measurements of Organic Dicarboxylic Acids.—The agreement between the results obtained for the primary dissociation constants of certain malonic acids by the conductivity method (Vogel, J., 1929, 1476) and those obtained by the potentiometric method (Gane and Ingold, *loc. cit.*) indicated that Vogel's method of calculation, although open to criticism [on the grounds that (i) certain of the sodium salts employed are appreciably hydrolysed (compare Riley, J., 1930, 1642), and (ii) the assumption that the mobility of the HX′ ion is 0·5 (or 0·6; Chandler, *J. Amer. Chem. Soc.*, 1908, **30**, 694) times that of the X″ ion is not strictly accurate], gave results which cannot be very far from the correct ones. In view of the hydrolysis occurring with the sodium malonates, the sodium salts of the acids under consideration were tested and found to be appreciably alkaline to phenolphthalein. The existence of this hydrolysis introduces a very difficult problem, for it is, at present, impossible to measure this, with anything like the same degree of accuracy as that which can be attained in the measurement of the conductivity of solutions. Neither can it be calculated from the conductivity data without an accurate knowledge of the mobilities of acid and normal ions.

The possibility of determining the mobility of the HX′ ion by extrapolation methods was next considered, for there appeared to be a distinct possibility that where the secondary dissociation constant was very small compared with the primary, the secondary dissociation would not interfere sufficiently to reduce to any appreciable extent the accuracy of the results obtained. It is possible to determine, with a knowledge of the mobilities of the ions concerned, how K_1 should vary for given correct values of K_1 and K_2 if the secondary dissociation of the acid is neglected in the calculation of K_1 from conductivity data. Consider an acid with $K_1 = 3 \times 10^{-4}$ and $K_2 = 1 \times 10^{-7}$. (Gane and Ingold, J., 1931, 2153, record values of K_1 and K_2 for *cyclo*hexane-1 : 1-diacetic acid as $3{\cdot}34 \times 10^{-4}$ and $0{\cdot}99 \times 10^{-7}$ respectively; the above rounded values have been chosen in order to determine the behaviour of K_1 for an acid of this type.) The following relationships exist:

$$[\mathrm{H}^{\cdot}][\mathrm{HX}'] = K_1[\mathrm{H_2X}]\,;\ [\mathrm{H}^{\cdot}][\mathrm{X}'] = K_2[\mathrm{HX}']$$

$$[\mathrm{H}^{\cdot}] + [\mathrm{HX}'] + 2[\mathrm{H_2X}] = 2M,$$

and

$$[\mathrm{X}''] + [\mathrm{HX}'] + [\mathrm{H_2X}] = M$$

where M is the molarity and the other symbols have their usual significance. [For the solution of the above, compare the rather more complex case of the cadmium halides (Riley and Gallafent, this vol., p. 514).] The mobilities of the various ions being assumed to be $l_{\mathrm{H}} = 349$, $l_{\mathrm{HX}} = 21$, and $l_{\mathrm{X}} = 42$ (these values again must be considered as hypothetical and approximating to an acid of the type of *cyclo*hexane-1 : 1-diacetic acid; the experimental values found for these ions from the conductivity of the sodium salt should be compared), it is possible, by solving the above equations for various dilutions, to calculate K_1 at various dilutions when the secondary dissociation of the acid is neglected. The following results were obtained:

c (mol./litre).	$K_1 \times 10^4$.	c (mol./litre).	$K_1 \times 10^4$.
0·005	3·00065	0·0005	3·00351
0·002	3·00120	0·0001	3·02210
0·001	3·00194	0·00005	3·06185

These results indicate the possibility of obtaining accurate values for the mobility of the HX′ ion in acids of the above type by extrapolation methods. The experimental results are in excellent agreement with the above views.

Vogel (*loc. cit.*) ascribes the fall in the values of K_1 obtained for the malonic acids to the use of glass conductivity cells, the acid hydrogen ions, reacting with the glass, being replaced by sodium ions. It can be shown in a similar manner to the above that an acid (malonic) with $K_1 = 15 \times 10^{-4}$, $K_2 = 20 \times 10^{-7}$, $l_{\mathrm{HX}^{\cdot}} = 25$, and $l_{\mathrm{X}^{\cdot\cdot}} = 50$ (these values are those of Gane and Ingold for the dissociation constants and of Vogel for the mobilities, rounded to the nearest whole numbers) will give the following values for K_1 should the secondary dissociation be neglected in calculating this constant:

c (mol./litre).	$K_1 \times 10^4$.	c (mol./litre).	$K_1 \times 10^4$.
0·005	15·0398	0·0005	15·4448
0·002	15·0874	0·0001	23·1651
0·001	15·1833	(At greater dilutions a rapid increase.)	

In order to explain the different trend of Vogel's experimental values from those calculated above, it can be shown that a replacement of hydrogen ions by sodium ions to an extent of 7—9% is necessary. This, of course, is unlikely. A more likely explanation of the initial constancy of Vogel's experimental results is that considerable polarisation occurred during the measurements, since readings down to 20 ohms were made, indicating the employment of much heavier alternating currents than are desirable. This is believed to be the case from the fact that " perfect minima " were obtained, no current amplifier being used.

In view of the above, it appears to be necessary to compare the values of the primary dissociation constants of the acids at present under consideration, calculated by using the value of the mobility of the HX′ ion, obtained (1) from the conductivity of the sodium salt, and (2) by extrapolating the acid conductivity results.

The following methods of extrapolation have been used :

(*a*) The Ostwald dilution formula can be written $\lambda = \lambda_0 - \lambda^2 c/K\lambda_0$. By plotting λ against λc^2, a straight line is obtained, the intercept at $c = 0$ giving λ_0, and the slope giving $1/K\lambda_0$.

(*b*) The Kraus method, according to which the Ostwald dilution formula is written as $1/\lambda = 1/\lambda_0 - c\lambda/K\lambda_0^2$, and $1/\lambda$ is plotted against $c\lambda$, giving a straight line of intercept $1/\lambda_0$ and slope $1/K\lambda_0^2$. This method is not so good as (*a*), in that experimental errors are much less apparent and any error in drawing the best straight line through the points has a much greater effect upon the results.

(*c*) Derick's method consists in solving a number of simultaneous " dilution-law " equations for λ_0 and is extremely sensitive to experimental error, necessitating taking a mean of a large number of solutions.

(*d*) The value of λ_0 has been calculated from the number of carbon atoms in the molecule, as done by Spiers and Thorpe (*loc. cit.*) ; this method can only be considered approximate.

Methods (*a*), (*b*), and (*c*) give results in good agreement with each other. It is notable that *cyclo*pentane-1 : 1-diacetic acid appears to have a value of λ_0 *less* than that of *cyclo*hexane-1 : 1-diacetic acid by an amount quite outside the experimental error, although the methyl*cyclo*hexane acids give values for λ_0 slightly less than *cyclo*hexane-1 : 1-diacetic acid itself, as would be expected. It will be noted also that the values of K_1 obtained all show a slight decrease as the dilution increases. This decrease, over the dilution range studied, is not sufficiently large to vitiate the theoretical calculations, which indicate that there ought to be a slight increase in the value of K_1. Many disturbing factors are at work, which, although small in dilute solutions, are of sufficient magnitude to cause this small trend downwards in the value of K_1.

The results obtained for the sodium salts are shown in Table I.

There can be little doubt that the divergence between the values obtained for K_1 is due to the hydrolysis of the sodium salts in aqueous

TABLE I.

Conductivities of the Sodium Salts.

*cyclo*Hexane-1 : 1-diacetic acid.		3-Methyl*cyclo*hexane-1 : 1-diacetic acid.		*cyclo*Pentane-1 : 1-diacetic acid.	
10^3 *c* (mols./l.).	μ.	10^3 *c* (mols./l.).	μ.	10^3 *c* (mols./l.).	μ.
3·2280	168·0	3·0232	160·3	3·6386	169·8
2·6105	169·7	2·9193	166·3	2·2689	173·8
1·6136	173·2	1·9769	169·9	2·1812	174·3
1·3799	174·7	1·4285	172·5	1·4601	177·4
1·1135	175·8	0·8456	175·8	0·7663	181·6
0·7600	177·9	0·6576	177·0	0·7315	181·9
0·6156	178·3	0·4481	179·4	0·3989	184·4
0·4161	180·0	0·3002	180·1	0·2639	186·2
0·3348	180·1	0·2244	181·3	0·2115	186·5
0·2306	181·7	0·1523	182·4	0·1072	187·9
0·0000	187·8	0·0000	187·0	0·0000	192·4

$l_{X''} = 187{\cdot}8 - 102{\cdot}8$
$= 85{\cdot}0$
$l_{HX'} = 42{\cdot}5$
$\therefore \mu_{0\,H_2X} = 349{\cdot}05 + 42{\cdot}5$
$\therefore \lambda_0 = 391{\cdot}55$

$l_{X''} = 187{\cdot}0 - 102{\cdot}8$
$= 84{\cdot}2$
$l_{HX'} = 42{\cdot}1$
$\mu_{0\,H_2X} = 349{\cdot}05 + 42{\cdot}1$
$\lambda_{0\,H_2X} = 391{\cdot}15$

$l_{X''} = 192{\cdot}4 - 102{\cdot}8$
$= 89{\cdot}6$
$l_{HX'} = 44{\cdot}8$
$\mu_{0\,H_2X} = 349{\cdot}05 + 44{\cdot}8$
$\lambda_0 = 393{\cdot}85$

(The conductivities of solutions of the sodium salt of 4-methyl*cyclo*hexane-1 : 1-diacetic acid were not measured, for the acids themselves gave almost identical results. The values obtained for the 3-methyl sodium salt have been employed in the case of the 4-methyl acid.)

TABLE II.

cyclo*Hexane*-1 : 1-*diacetic Acid.*

10^3 *c* (mols./l.).	λ.	$K_1 \times 10^4$ as obtained by various methods (see p. 1098). (Na salt).	(*a*).	(*b*).	(*c*).	(*d*).
4·724	85·55	2·89	3·20	3·22	3·29	3·21
3·109	102·4	2·88	3·21	3·23	3·30	3·21
2·050	121·3	2·85	3·19	3·21	3·29	3·19
1·598	134·1	2·85	3·20	3·22	3·30	3·20
1·485	137·6	2·83	3·18	3·20	3·27	3·18
1·085	155·5	2·84	3·20	3·23	3·31	3·21
0·7504	176·3	2·77	3·15	3·18	3·26	3·15
0·6122	189·3	2·77	3·17	3·20	3·29	3·18
0·5279	198·2	2·74	3·15	3·18	3·27	3·15
0·2496	247·0	2·69	3·20	3·24	3·35	3·21
0·1753	266·6	2·55	3·09	3·13	3·26	3·10
0·1108	294·0	2·51	3·19	3·25	3·42	3·20
0·0808	308·4	2·36	3·12	3·18	3·38	3·13
0·0538	326·0	2·23	3·17	3·25	3·53	3·19
0·0220	355·0	1·94	3·86	4·11	5·07	3·90
Values of λ_0 obtained by extrapolation		391·55	374·2	373·1	369·8	374

solution. The agreement of the values obtained by the conductivity method with those from the potentiometric method, in the case of *cyclo*hexane-1 : 1-diacetic acid, indicates that the values of λ_0 obtained by extrapolation of the acid conductivity results are nearer the truth. These, however, cannot be considered strictly accurate,

TABLE III.

3-Methyl*cyclo*hexane-1 : 1-diacetic acid.				4-Methyl*cyclo*hexane-1 : 1-diacetic acid.				*cyclo*Pentane-1 : 1-diacetic acid.			
		$K_1 \times 10^4$.				$K_1 \times 10^4$.				$K_1 \times 10^4$.	
$10^3 c$.	λ.	(Na).	(*a*).	$10^3 c$.	λ.	(Na).	(*a*).	$10^3 c$.	λ.	(Na).	(*a*).
2·5553	109·1	2·76	3·26	2·7908	105·1	2·76	3·23	5·6641	58·0	1·44	1·77
1·6515	130·1	2·74	3·26	1·5007	134·8	2·72	3·23	2·5 84	82·4	1·43	1·76
1·0550	153·7	2·68	3·24	0·9896	157·8	2·70	3·24	1·6770	98·9	1·41	1·76
0·8755	164·9	2·69	3·26	0·8422	167·0	2·69	3·23	0·9308	125·4	1·38	1·75
0·4683	202·9	2·62	3·26	0·4763	201·6	2·61	3·22	0·6840	141·8	1·39	1·77
0·3672	217·7	2·57	3·24	0·2945	232·6	2·57	3·27	0·3360	182·3	1·34	1·76
0·1674	265·4	2·40	3·25	0·1542	271·6	2·43	3·30	0·2692	196·4	1·34	1·78
0·1303	280·2	2·36	3·31	0·0872	299·6	2·19	3·23	0·1644	226·5	1·28	1·78
0·0775	302·2	2·03	2·93	0·0488	321·4	1·85	3·10	0·1021	254·9	1·21	1·78
0·0476	317·2	1·66	2·83	0·0305	333·2	1·49	2·83	0·0818	268·0	1·19	1·80
0·0339	329·0	1·51	2·81	0·0228	342·2	1·29	3·07	0·0557	288·9	1·12	1·85
	λ_0	391·15	364·8			391·15	365·8			393·85	358·8

as no corrections for interionic forces have been applied and there is some uncertainty with regard to the solvent correction. These corrections would, however, be very similar for all the acids studied, so the results obtained serve accurately as a basis for comparison.

Table II gives the results obtained with *cyclo*hexane-1 : 1-diacetic acid, and compares the values of K_1 obtained by the different methods. The suffix to K_1 at the head of each column represents the method of extrapolation used, given in the above lettered paragraphs. Table III gives the results for the other acids studied. The values of K_1 given are those obtained by method (*a*) of extrapolation. These values of K_1 have been compared with those obtained by the other methods, but as Table II is characteristic, these comparisons (save that from the sodium salt) have not been included.

The authors express their thanks to Professor J. F. Thorpe for his interest in this research.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W. 7. [*Received, February* 15*th*, 1932.]