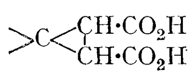
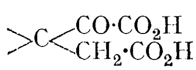
232. *The Dissociation Constants of Organic Acids. Part XVIII.* Some Cyclic 1 : 1-Diacetic Acids.*

By William L. German and Arthur I. Vogel.

Of the numerous methods that have been employed for the comparative study of the influence of substituents upon chemical properties with a view to the determination of qualitative values for valency-deflexion angles and also for throwing light upon the structure of ring systems, the two that have been applied to the largest number of substituents are those due to Thorpe and Ingold and their co-workers (J., 1915 *et seq.*) and to Vogel (J., 1928, 2014). The former depends *inter alia* upon (i) the stability of the *trans-spiro*-acid (I) towards hydrochloric acid of various concentrations at different temperatures, and (ii) the tautomeric change between keto-acids of the type (II) and their hydroxy-ring isomerides


(I.)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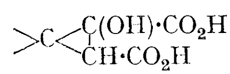
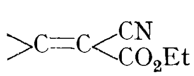
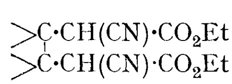

(III.)

(IV.)



(V.)

(III). The latter method utilises the yield of the bimolecular compound (V), obtained by the reduction of the unsaturated cyano-ester (IV) with aluminium amalgam in moist ethereal solution, as a basis of comparison. The yields of (V) (compare J., 1931, 1796) for the substituents *cyclo*pentane and 3-methyl*cyclo*pentane are 13% and 13% respectively, and for *cyclo*hexane, and 2-,† 3-, and 4-methyl*cyclo*hexane the corresponding yields are 6, 2,† 6, and 4% respectively. These figures would suggest that there is no essential difference in the configurations of the *cyclo*pentane and 3-methyl*cyclo*pentane rings or between the unsubstituted *cyclo*hexane and the 3- and 4-methyl*cyclo*hexane rings and possibly also the 2-methyl*cyclo*hexane ring. Desai (J., 1932, 1065), employing the Thorpe–Ingold method, has found a remarkable similarity between the behaviour of the *cyclo*pentane and 3-

* The paper entitled "A New Series of Buffer Mixtures Covering the p_H Range 1 to 6" (*Analyst*, 1937, **62**, 271) is regarded as Part XVII.

† Oommen, Ph.D. Thesis, London, 1929.

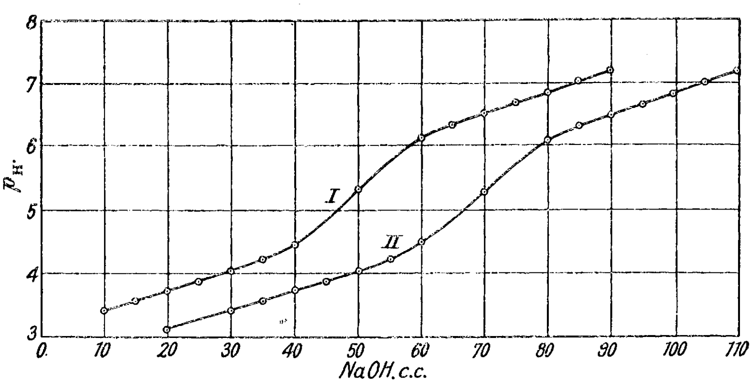
methyl*cyclo*pentane compounds, but serious differences were encountered between the *cyclo*hexane and the 3- and 4-methyl*cyclo*hexane compounds (J., 1932, 1053). Ives, Linstead, and Riley (J., 1932, 1093) suggest, as a result of their determinations of the *classical* primary dissociation constants of *cyclo*pentane-, *cyclo*hexane-, and 3- and 4-methyl*cyclo*hexane-1 : 1-diacetic acids, that the chemical tests employed by Desai are here " misleading if applied as a test for valency deflexion." The three authors state (*loc. cit.*) that their determinations of $K_{1\ \text{class.}}$ for these acids by conductivity " involve certain difficulties of calculation." A method for overcoming all these difficulties and which leads to values of the primary *thermodynamic* dissociation constants is described in Part XI of this series (J., 1935, 22). In view of the importance of the subject in connexion with the general question of the structure of simple and substituted *cyclo*pentane and *cyclo*hexane rings, measurements have been made of the *true* primary and secondary ionisation constants of the substituted 1 : 1-diacetic acids by potentiometric titration, and the distances between the carboxyl groups have been calculated by the methods of Bjerrum (*Z. physikal. Chem.*, 1923, **106**, 219) (B.) and of Gane and Ingold (J., 1931, 2153, 2160, 2180) (G. & I.). Our results, together with those of Gane and Ingold (J., 1931, 2158) and of Ives, Linstead, and Riley (I. L. & R.), are collected in the following table.

1 : 1-Diacetic acid.	$K_{1\text{therm.}}$ × 10^4.	$K_{2\text{therm.}}$ × 10^8.	r (B.) × 10^8.	r (G. & I.) × 10^8.	G. & I. K_1 ($\mu = 0$) × 10^4.	G. & I. K_2 ($\mu = 0$) × 10^8.	I. L. & R. $K_{1\text{class.}}$ × 10^4.
*cyclo*Pentane	1·60	17·0	1·30	3·38	1·66	25·8	1·76
3-Methyl*cyclo*pentane...	1·61	18·2	1·32	3·40	—	—	—
*cyclo*Hexane *	3·27	8·26	1·03	3·12	3·34	9·9	3·23
2-Methyl*cyclo*hexane ...	2·96	13·00	1·16	3·25	—	—	—
3-Methyl*cyclo*hexane ...	3·23	8·34	1·04	3·15	—	—	3·25
4-Methyl*cyclo*hexane ...	3·23	8·02	1·03	3·13	—	—	3·21

* Jones and Soper (J., 1936, 135) give $K_{1\text{therm.}} = 3{\cdot}25 \times 10^{-4}$ and $K_{2\text{therm.}} = 10{\cdot}85 \times 10^{-8}$.

The potentiometric titration curves are shown in Figs. 1 and 2; the abscissæ have been displaced for the different acids in order to avoid overlapping and to emphasise the similarities in the curves. Our results support the view that the substituted acids closely resemble the parent substances, and provide definite evidence for the current accepted conception of the strainless structure of the *cyclo*pentane and *cyclo*hexane rings.

FIG. 1.



I. *cyclo*Pentane-1 : 1-diacetic acid. II. 3-Methyl*cyclo*pentane-1 : 1-diacetic acid.

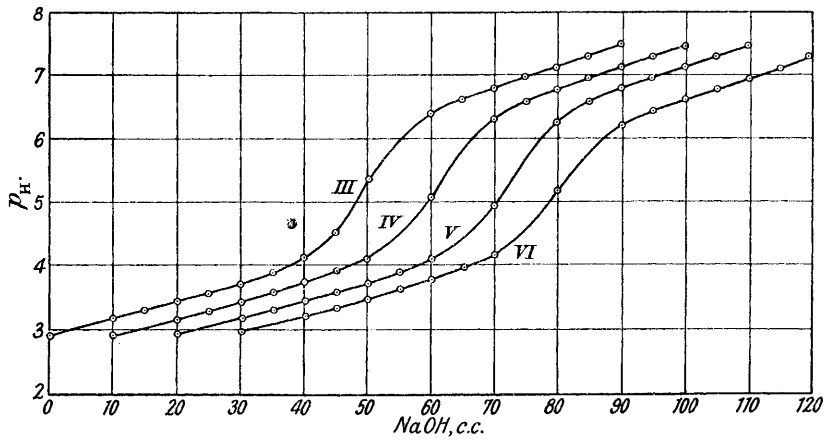
EXPERIMENTAL.

Preparation of Materials.—Full details of the preparation of all the acids, except 2-methyl*cyclo*hexane-1 : 1-diacetic acid, have been given by Vogel (J., 1934, 1760); only the methods of further purification are now indicated. All samples were dried in a vacuum desiccator over calcium chloride for several days before use.

cyclo*Pentane*-1 : 1-*diacetic acid.* Specimen I. A sample which had been recrystallised from dilute alcohol was crystallised from redistilled dioxan (b. p. 101—103·5°)–light petroleum

(b. p. 40—60°, AnalaR, sodium-dried), the separated solid well washed with sodium-dried light petroleum (b. p. 40—60°) to remove adhering dioxan, and then dried in a vacuum; m. p. 179°.

FIG. 2.



III. *cyclo*Hexane-1 : 1-diacetic acid. IV. 2-Methyl*cyclo*hexane-1 : 1-diacetic acid.
V. 3-Methyl*cyclo*hexane-1 : 1-diacetic acid. VI. 4-Methyl*cyclo*hexane-1 : 1-diacetic acid.

Specimen II. This was purified through the anhydride and recrystallised from hot water; m. p. 178°.

cyclo*Hexane*-1 : 1-*diacetic acid*. Recrystallised from 80% alcohol; m. p. 181°.

2-*Methyl*cyclo*hexane*-1 : 1-*diacetic acid*. 400 C.c. of absolute alcohol were saturated with dry ammonia at − 5° during 5 hours and added to a mixture of 112 g. (1 mol.) of pure 2-methyl*cyclo*hexanone, b. p. 164°/770 mm., and 226 g. (2 mols.) of ethyl cyanoacetate contained in a large (1500 c.c.) wide-mouthed glass-stoppered bottle. The whole was kept at 0° for 4 days and then at room temperature for 5 days. A small amount of solid (cyanoacetamide) separated; 2 litres of water were added (the separated solid dissolved), the whole extracted three times with ether, the aqueous layer acidified with hydrochloric acid (to methyl-red), and a further 200 c.c. of concentrated hydrochloric acid added. The separated dicyano-imide was collected after 24 hours and dried at 100° (29·3 g.). The crude substance had m. p. 243°, and m. p. 245° after recrystallisation from 50% alcohol (Kon and Thorpe, J., 1919, **115**, 694, give m. p. 245°). 58·4 G. of the finely-powdered dicyano-imide were dissolved in 120 c.c. of cold concentrated sulphuric acid, left for 24 hours, 112 c.c. of water cautiously added, and the whole boiled under reflux for 17 hours. The crude acid which had separated was filtered off after 48 hours, extracted with a saturated solution of sodium bicarbonate, the extract filtered, acidified with concentrated hydrochloric acid, and the solid collected after 24 hours (yield: 46·4 g. after drying at 100°). The acid was recrystallised successively from ether–benzene (2 : 1) and 50% alcohol; it had m. p. 152° (Kon and Thorpe, *loc. cit.*, give m. p. 148°).

3-*Methyl*cyclo*pentane*-1 : 1-*diacetic acid*. This was purified through the anhydride, and recrystallised from chloroform (AnalaR)–light petroleum (b. p. 40—60°, AnalaR, sodium-dried); m. p. 134—135°.

3-*Methyl*cyclo*hexane*-1 : 1-*diacetic acid*. Recrystallised from 50% alcohol; m. p. 142°.

4-*Methyl*cyclo*hexane*-1 : 1-*diacetic acid*. Recrystallised from 50% alcohol; m. p. 160°.

General Technique and Apparatus.—This has already been described (J., 1935, 912, 1628; *J. Amer. Chem. Soc.*, 1936, **58**, 1546; *Phil. Mag.*, 1936, **22**, 796). All measurements were carried out at 25° ± 0·01° with the quinhydrone electrode. Standardisation was effected before and after each titration against at least two independent 0·1*N*-calomel cells, and also against 0·05*M*-potassium hydrogen phthalate (the A.R. solid was specially purified for this purpose) and Walpole's standard acetate buffers (18°), appropriate allowance being made for the difference in temperature.

The results were computed as described for maleic acid (*Phil. Mag.*, *loc. cit.*), the large difference in magnitude between K_1 and K_2 permitting the independent evaluation of $K_{1\,\text{class.}}$ and $K_{2\,\text{class.}}$. All the results are collected in the following tables; the classical values are included to permit comparison with the data in the literature.

cyclo*Pentane*-1 : 1-*diacetic Acid* (M = 186·10).

Potentiometric titration of 100·00 *c.c. of* 0·005M-*acid against* 0·009950M-*sodium hydroxide solution.*

NaOH, c.c.	p_H.	$K_{1\,class.}$ $\times 10^4$.	$\mu \times 10^3$.	$K_{1\,therm.}$ $\times 10^4$.	NaOH, c.c.	p_H.	$K_{2\,class.}$ $\times 10^7$.	$\mu \times 10^3$.	$K_{2\,therm.}$ $\times 10^7$.
0·00	3·085	—	—	—	50·00	5·281	—	—	—
10·00	3·382	1·70	1·32	1·63	60·00	6·083	—	—	—
15·00	3·531	1·70	1·59	1·62	65·00	6·296	2·10	4·81	1·65
20·00	3·680	1·69	1·87	1·61	70·00	6·479	2·15	5·25	1·67
25·00	3·832	1·69	2·14	1·60	75·00	6·638	2·24	5·67	1·72
30·00	4·000	1·65	2·40	1·56	80·00	6·811	2·25	6·08	1·71
35·00	4·142	1·65	2·65	1·56	85·00	6·990	2·29	6·42	1·73
40·00	4·401	—	—	—	90·00	7·162	2·60	6·78	(1·95)
				Mean 1·60					Mean 1·70

3-*Methyl*cyclo*pentane*-1 : 1-*diacetic Acid* (M = 200·24).

Potentiometric titration of 100·00 *c.c. of* 0·005M-*acid against* 0·009950M-*sodium hydroxide solution.*

NaOH, c.c.	p_H.	$K_{1\,class.}$ $\times 10^4$.	$\mu \times 10^3$.	$K_{1\,therm.}$ $\times 10^4$.	NaOH, c.c.	p_H.	$K_{2\,class.}$ $\times 10^7$.	$\mu \times 10^3$.	$K_{2\,therm.}$ $\times 10^7$.
0·00	3·078	—	—	—	50·00	5·240	—	—	—
10·00	3·382	1·70	1·32	1·63	60·00	6·068	—	—	—
15·00	3·531	1·70	1·59	1·62	65·00	6·266	2·25	4·81	1·77
20·00	3·680	1·70	1·87	1·61	70·00	6·447	2·31	5·25	1·80
25·00	3·833	1·69	2·14	1·60	75·00	6·607	2·40	5·67	1·84
30·00	4·000	1·65	2·40	1·56	80·00	6·780	2·41	6·08	1·84
35·00	4·160	1·74	2·65	1·64	85·00	6·964	2·44	6·42	1·84
40·00	4·451	—	—	—	90·00	7·156	2·65	6·78	(1·99)
				Mean 1·61					Mean 1·82

cyclo*Hexane*-1 : 1-*diacetic Acid* (M = 200·24).

Potentiometric titration of 100·00 *c.c. of* 0·005M-*acid against* 0·009919M-*sodium hydroxide solution.*

NaOH, c.c.	p_H.	$K_{1\,class.}$ $\times 10^4$.	$\mu \times 10^3$.	$K_{1\,therm.}$ $\times 10^4$.	NaOH, c.c.	p_H.	$K_{2\,class.}$ $\times 10^7$.	$\mu \times 10^3$.	$K_{2\,therm.}$ $\times 10^7$.
0·00	2·914	—	—	—	50·00	5·377	—	—	—
10·00	3·178	3·49	1·57	3·34	60·00	6·376	—	—	—
15·00	3·306	3·45	1·79	3·29	65·00	6·600	1·036	4·79	0·814
20·00	3·437	3·44	2·02	3·27	70·00	6·787	1·040	5·23	0·808
25·00	3·553	3·45	2·25	3·27	75·00	6·939	1·097	5·65	0·844
30·00	3·721	3·45	2·48	3·26	80·00	7·108	1·109	6·04	0·834
35·00	3·890	3·41	2·65	3·21	85·00	7·301	1·094	6·41	0·828
40·00	4·129	3·26	2·91	(3·07)	90·00	7·482	—	—	—
				Mean 3·27					Mean 0·826

2-*Methyl*cyclo*hexane*-1 : 1-*diacetic Acid* (M = 214·25).

Potentiometric titration of 100·00 *c.c. of* 0·005M-*acid against* 0·009915M-*sodium hydroxide solution.*

NaOH, c.c.	p_H.	$K_{1\,class.}$ $\times 10^4$.	$\mu \times 10^3$.	$K_{1\,therm.}$ $\times 10^4$.	NaOH, c.c.	p_H.	$K_{2\,class.}$ $\times 10^7$.	$\mu \times 10^3$.	$K_{2\,therm.}$ $\times 10^7$.
0·00	2·970	—	—	—	50·00	5·176	—	—	—
10·00	3·208	3·11	1·52	2·98	60·00	6·183	—	—	—
15·00	3·338	3·10	1·76	2·96	65·00	6·415	1·60	4·79	1·26
20·00	3·467	3·13	1·99	2·98	70·00	6·596	1·64	5·24	1·28
25·00	3·606	3·13	2·23	2·96	75·00	6·761	1·68	5·65	1·29
30·00	3·758	3·12	2·47	2·95	80·00	6·926	1·72	6·06	1·31
35·00	3·927	3·14	2·69	2·96	85·00	7·093	1·81	6·40	1·36
40·00	4·134	—	—	—	90·00	7·288	1·95	6·76	(1·46)
				Mean 2·96					Mean 1·30

3-*Methyl*cyclo*hexane*-1 : 1-*diacetic Acid* (M = 214·25).

Potentiometric titration of 100·00 *c.c. of* 0·005M-*acid against* 0·009850M-*sodium hydroxide solution.*

NaOH, c.c.	p_H.	$K_{1\,class.}$ $\times 10^4$.	$\mu \times 10^3$.	$K_{1\,therm.}$ $\times 10^4$.	NaOH, c.c.	p_H.	$K_{2\,class.}$ $\times 10^7$.	$\mu \times 10^3$.	$K_{2\,therm.}$ $\times 10^7$.
0·00	2·931	—	—	—	50·00	5·058	—	—	—
10·00	3·168	(3·61)	—	—	60·00	6·313	—	—	—
15·00	3·300	3·49	1·79	3·32	65·00	6·562	1·07	4·73	0·845
20·00	3·438	3·39	2·01	3·22	70·00	6·756	1·07	5·23	0·832
25·00	3·574	3·39	2·24	3·20	75·00	6·932	1·07	5·59	0·824
30·00	3·719	3·40	2·47	3·22	80·00	7·100	1·08	5·98	0·825
35·00	3·890	3·38	2·68	3·19	85·00	7·271	1·11	6·35	0·843
40·00	4·090	3·48	2·90	3·28	90·00	7·435	—	—	—
				Mean 3·23					Mean 0·834

4-*Methyl*cyclo*hexane*-1 : 1-*diacetic Acid* (M = 214·25).

Potentiometric titration of 100·00 *c.c. of* 0·005M-*acid against* 0·009850M-*sodium hydroxide solution.*

NaOH, c.c.	p_H.	$K_{1\,class.}$ $\times 10^4$.	$\mu \times 10^3$.	$K_{1\,therm.}$ $\times 10^4$.	NaOH, c.c.	p_H.	$K_{2\,class.}$ $\times 10^7$.	$\mu \times 10^3$.	$K_{2\,therm.}$ $\times 10^7$.
0·00	2·941	—	—	—	50·00	4·937	—	—	—
10·00	3·184	3·38	1·55	3·23	60·00	6·257	1·23	4·20	(0·983)
15·00	3·213	3·34	1·77	3·19	65·00	6·584	1·11	4·73	0·801
20·00	3·438	3·38	2·01	3·21	70·00	6·772	1·04	5·23	0·805
25·00	3·577	3·36	2·24	3·18	75·00	6·946	1·04	5·59	0·799
30·00	3·715	3·45	2·47	3·26	80·00	7·113	1·05	5·98	0·800
35·00	3·884	3·44	2·68	3·24	85·00	7·291	1·06	6·35	0·804
40·00	4·078	3·60	2·90	(3·39)	90·00	7·492	—	—	—
				Mean 3·23					Mean 0·802

SUMMARY.

(1) The thermodynamic primary and secondary dissociation constants of *cyclo*pentane-, 3-methyl*cyclo*pentane-, *cyclo*hexane-, 2-methyl*cyclo*hexane-, 3-methyl*cyclo*hexane- and 4-methyl*cyclo*hexane-1 : 1-diacetic acids have been determined by potentiometric titration with the quinhydrone electrode at 25°.

(2) The intercarboxylic distances have been evaluated by the methods of Bjerrum and of Gane and Ingold. The results support the view that the *cyclo*pentane and *cyclo*hexane rings in these compounds are all strainless.

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