Chemical Constitution and the Dissociation Constants of Monocarboxylic Acids. Part XIV.[*] *Monomethyl*cyclo*hexanecarboxylic Acids.*

By J. F. J. Dippy, S. R. C. Hughes, and J. W. Laxton.

[Reprint Order No. 5381.]

The thermodynamic dissociation constants of the seven monomethyl*cyclo*-hexanecarboxylic acids in water at 25° have been determined, together with those of *cyclo*hexanecarboxylic and α- and β-naphthylacetic acids. The results are in harmony with the other recorded physical constants of these acids, and examination of the conformations of the geometric isomers reveals that for each of the three pairs the higher strength is exhibited by the molecule capable of assuming a diequatorial conformation, notwithstanding whether the configuration is *cis* or *trans*.

It is noteworthy that the dissociation constant of the *trans*-2-methyl acid exceeds that of the unsubstituted acid. An explanation of this anomaly is difficult to find in terms of a spatial interaction of groups, because the distance separating the substituents here is the same as that in the *cis*-2-methyl acid whose strength is a half of that of the *trans*-acid.

The strengths of the naphthylacetic acids are consistent with expectation.

It has been claimed that *n*-butyric acid when compared with the homologous paraffinic acids displays an anomalous strength in water at 25° (Dippy, *J.*, 1938, 1222; Dippy and Jenkins, *J. Amer. Chem. Soc.*, 1940, **62**, 483; *Trans. Faraday Soc.*, 1941, **37**, 366; cf. also Magee, Ri, and Eyring, *J. Chem. Physics*, 1938, **6**, 499; Freri, *Gazzetta*, 1948, **78**, 286), and in this connection the strengths of the 2-methyl*cyclo*hexanecarboxylic acids have a special significance. Moreover, the strengths of the entire series of monomethyl*cyclo*hexanecarboxylic acids make an interesting comparison with the K_1 data for *cyclo*hexanedicarboxylic acids (Kuhn and Wassermann, *Helv. Chim. Acta*, 1928, **11**, 3) and the strengths of the monohydroxy*cyclo*hexanecarboxylic acids recently determined by Kilpatrick and Morse (*J. Amer. Chem. Soc.*, 1953, **75**, 1847) who have examined their results in terms of the likely conformations assumed by the three pairs of geometric isomers (cf. also Siegel and Morse, *J. Amer. Chem. Soc.*, 1953, **75**, 3857).

Table 1.

Acid	Λ_0 (acid)	10^5K	10^5K_{class}	10^5K (lit.)
*cyclo*Hexanecarboxylic	378·5	1·26	1·28	1·28,[1] 1·34,[2] 1·32[3] 1·25[4] [*]
1-Methyl*cyclo*hexanecarboxylic	377·8	0·739	0·749	0·69[2]
trans-2-Methyl*cyclo*hexanecarboxylic	377·4	1·84	1·87	2·05[2]
cis-2-Methyl*cyclo*hexanecarboxylic	377·5	0·921	0·936	1·64[2]
† *trans*-3-Methyl*cyclo*hexanecarboxylic	(377·9	*ca.* $0{\cdot}9_5$	—)	1·28[2] ‡
cis-3-Methyl*cyclo*hexanecarboxylic	378·3	1·31	1·33	—
trans-4-Methyl*cyclo*hexanecarboxylic	378·8	1·30	1·32	1·11[2]
cis-4-Methyl*cyclo*hexanecarboxylic	378·8	0·92	0·937	
α-Naphthylacetic	378·2	$5{\cdot}80_5$	5·92	—
β-Naphthylacetic	378·2	5·55	5·64	—

* A thermodynamic constant.

† Determinations of *K* for this acid were carried out on mixtures of the pair of geometric isomers, since attempts to isolate the pure *trans*-acid have been unsuccessful. The ratio of the isomers was *ca.* 1 : 1, and this has been assumed in arriving at the approximate value of *K* given above.

‡ This value was related to no particular configuration.

[1] Lumsden, *J.*, 1905, **87**, 90. [2] Zelinsky and Izgarysev, *J. Russ. Phys. Chem. Soc.*, 1908, **40**, 1379. [3] Spiers and Thorpe, *J.*, 1925, **127**, 538. [4] Kilpatrick and Morse, *loc. cit.*

Thermodynamic dissociation constants (*K*) and Λ_0 data for nine acids at 25° in water are set out in Table 1. Results for two of these compounds, *viz.*, α- and β-naphthylacetic acids, are supplementary to those contained in Part XIII (*loc., cit.*). All earlier values of dissociation constants were classical data (with one exception) and are given in the last column of Table 1.

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[*] Part XIII, *J.*, 1954, 1470.

EXPERIMENTAL

Materials and Procedure.—1-Methyl-, *cis*- and *trans*-2-methyl-, and *cis*- and *trans*-4-methyl-*cyclo*hexanecarboxylic acids were provided by Professor H. A. Smith and Dr. J. A. Stansfield whose generosity is warmly acknowledged. *cis*-3-Methyl- and *cis*- and *trans*-2-methyl-*cyclo*-hexanecarboxylic acids were kindly provided by Professor Killen Macbeth, to whom we are also grateful for the gift of the mixed amide of *cis*- and *trans*-3-methyl*cyclo*hexanecarboxylic acids from which a sample of mixed acids was prepared. *cyclo*Hexanecarboxylic acid and α- and β-naphthylacetic acids were purchased.

All solid acids were recrystallised from conductivity water and dried for several weeks in desiccators. The liquid acids were first dried by azeotropic distillation with pure benzene, and then distilled at 0·4 mm. so as to give two fractions. Measurements of K were then made upon each fraction, and in every instance the results were found to agree within the range of experimental error. Table 2 sets out the physical criteria of purity which compare with the best to be found in the literature (Macbeth *et al.*, *J.*, 1929, 1245; 1949, 1011; 1953, 1364); equivalents were checked in the making of the sodium salt solutions.

The experimental determinations upon acid and salt solutions, and the calculations of the acid strengths contained in Table 3 (where C is given in g.-equiv./l and K is $K_{\text{therm.}}$), were along the lines described in Part XIII (*loc. cit.*). No weight dilutions were made in this series of determinations; each solution was made up directly from the pure acid. In the case of liquid

TABLE 2.

*cyclo*Hexanecarboxylic acid	M. p. (corr.)	n_D^{20}	*cyclo*Hexanecarboxylic acid	M. p. (corr.)
(Unsubstd.)	30·4—30·9°	—	*cis*-4-Methyl-	12—13°
1-Methyl-	37—38	—	*trans*-4-Methyl-	110—111
cis-2-Methyl-	—	1·4642		
trans-2-Methyl-	50·5—51·5	—	Acid	M. p. (corr.)
cis-3-Methyl-	—	1·4576	α-Naphthylacetic	131·4°
cis- and *trans*-3-Methyl-	—	1·4592—1·4596	β-Naphthylacetic	140·5—141

TABLE 3. (Cell-constant data : $a = 0{\cdot}09146$; $b = 0{\cdot}03764$.)

Cell	10^3C	Λ	10^5K	Cell	10^3C	Λ	10^5K	Cell	10^3C	Λ	10^5K
					cyclo*Hexanecarboxylic acid*						
(*a*)	4·496	19·78	1·26$_5$	(*b*)	2·214	27·73	1·26	(*b*)	0·8877	42·81	1·26
	3·651	21·84	1·26		1·429	34·16	1·26		0·5267	54·46	1·26
	2·727	25·10	1·26		1·268	36·04	1·25$_5$		0·2397	77·34	(1·24$_5$)
	2·584	25·71	1·26	(*a*) (*b*)	1·161	37·71 37·72	1·26				
					1-*Methyl*cyclo*hexanecarboxylic acid*						
(*a*)	2·260	21·33	0·750	(*b*)	1·053	30·48	0·735	(*b*)	0·7545	35·76	0·738
	1·436	26·36	0·741		1·045	30·61	0·736		0·6276	38·94	0·735
	1·392	26·93	0·749		0·8975	32·89	0·735		0·4842	43·80	(0·732)
					trans-2-*Methyl*cyclo*hexanecarboxylic acid*						
(*a*)	2·754	29·90	1·84	(*b*)	1·126	45·56	1·83	(*b*)	0·8496	52·00	1·84
	2·120	33·89	1·84		0·9150	50·18	1·83$_5$		0·6463	58·77	1·83
	2·055	34·42	1·84		0·8773	51·11	1·84		0·5145	64·77	(1·80)
(*a*) (*b*)	1·469	40·25 40·26	1·84								
					cis-2-*Methyl*cyclo*hexanecarboxylic acid*						
(*a*)	3·824	18·31	0·927	(*a*) (*b*)	1·106	33·30 32·32	(0·930)	(*b*)	0·7490	39·81	0·919
	1·898	25·69	0·926					(*a*) (*b*)	0·4828	48·98 48·99	0·924
	1·323	30·42	0·919	(*b*)	0·9447	35·65	0·917				
(*b*)	1·139	32·80	0·927		0·9240	36·01	0·916	(*b*)	0·4733	49·32	0·919
					3-*Methyl*cyclo*hexanecarboxylic acid* (*mixture of* cis- *and* trans-*isomers*)						
	1st Fraction				2nd Fraction				3rd Fraction		
(*b*)	1·330	33·91	1·16	(*b*)	0·4306	56·98	1·14	(*b*)	1·041	36·66	1·07
	0·5681	50·49	1·16		0·3024	66·53	1·13		0·2342	73·00	1·07
	0·5984	53·51	1·15						0·1970	79·36	1·09

The constants determined on the first distillation fraction are higher than those on the last fraction, indicating that the *trans*-acid possesses the higher boiling point.

TABLE 3. (*Continued.*)

Cell	10^3C	Λ	10^5K	Cell	10^3C	Λ	10^5K	Cell	10^3C	Λ	10^5K
cis-3-*Methyl*cyclo*hexanecarboxylic acid*											
(*a*)	1·699	32·12	1·31	(*a*)	0·9197	42·81	1·31	(*b*)	0·2181	82·44	1·31
	1·095	39·62	1·32		0·6017	52·20	1·31		0·1587	94·53	1·31
	0·9765	41·57	1·31		0·2839	73·39	1·31				
trans-4-*Methyl*cyclo*hexanecarboxylic acid*											
(*b*)	2·855	24·98	1·30$_5$	(*b*)	0·7910	45·87	1·30$_5$	(*b*)	0·4881	57·28	1·30
	1·440	34·56	1·30		0·5311	55·05	1·30		0·4040	62·19	(1·29)
	1·029	40·47	1·30		0·5257	55·14	(1·29)		0·3875	63·47	1·30
	0·7926	45·83	1·30$_5$								
cis-4-*Methyl*cyclo*hexanecarboxylic acid*											
(*b*)	1·913	25·82	0·926	(*b*)	0·5781	44·90	(0·907)	(*b*)	0·3266	58·09	0·924
	0·9067	36·50	0·918		0·5192	47·43	0·917		0·2740	63·62	0·919
	0·6952	41·50	0·925		0·4281	52·09	0·927				
α-*Naphthylacetic acid*											
(*a*)	1·879	61·63	5·80$_5$	(*a*)	1·181	75·84	5·81	(*b*)	0·4920	110·2	5·80$_5$
	1·813	62·59	5·80		0·9545	83·19	5·79		0·3044	133·6	5·80
	1·464	69·04	5·81		0·7397	92·40	(5·73)		0·2166	152·2	5·80$_5$
	1·362	71·07	5·80$_5$	(*a*) (*b*)	0·6203	100·2 100·2	5·81				
β-*Naphthylacetic acid*											
(*a*)	1·249	72·65	5·58	(*b*)	0·5140	106·3	5·55	(*b*)	0·2747	136·2	(5·51)
(*b*)	0·6742	94·77	5·55		0·4651	110·6	5·53		0·2484	142·0	5·54
	0·6734	94·95	5·57		0·4414	113·2	5·57				

acids, very small weighing bottles were used which could be inserted into the flasks in which the solutions were prepared. Conductivity experiments satisfied us that the presence of a weighing bottle had no adverse effect on the acid solution. The water employed had κ in the range 0·5—0·7 gemmho. No account of optical isomerism has been taken in this work, since it is accepted that enantiomorphs exert the same acid strengths. With the exception of two acids, the upper and the lower limits of K in each case differed by less than 1%.

DISCUSSION

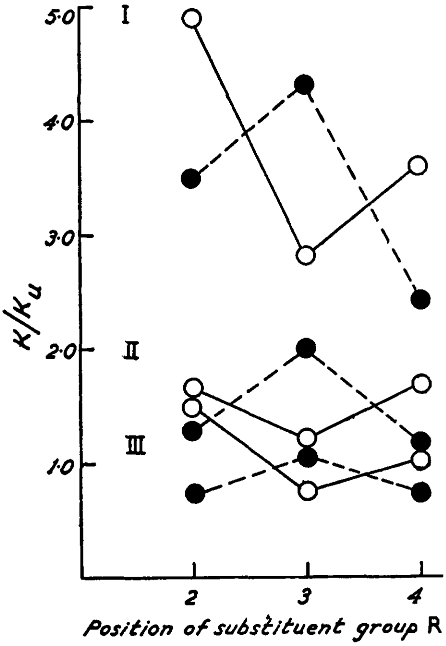
The strengths of *cyclo*hexanecarboxylic acid and its 1-methyl homologue (10^5K, 1·26 and 0·739) follow very closely the trend of strengths in the paraffinic acids [cf. 10^5K data : $CH_3{\cdot}CH_2{\cdot}CO_2H$, 1·33; $CHMe_2{\cdot}CO_2H$, 1·38; $CMe_3{\cdot}CO_2H$, 0·891 (Dippy, *J.*, 1938, 1222)]. That is to say the introduction of methyl progressively at the α-carbon atom has its most marked effect when replacing the last hydrogen. When the 2-, 3-, and 4-methyl*cyclo*hexanecarboxylic acids are considered, it is seen that the strength of the *trans*-2-methyl acid is twice that of its *cis*-isomer, and, is moreover, distinctly stronger than that of the parent *cyclo*hexanecarboxylic acid. The other methyl-substituted acids approximate to the parent in strength, or else are weaker, as might reasonably be expected.

Critical examination of the configurations assigned to disubstituted *cyclo*hexanes (Haggis and Owen, *J.*, 1953, 408; Darling, Macbeth, and Mills, *ibid.*, p. 1364; Kilpatrick and Morse, *loc. cit.*) has disclosed that, whereas the classical rules of Auwers and Skita hold for the 1 : 2- and 1 : 4-disubstituted compounds (containing the pairs of groups : Me, CO_2H; Me, Me; Me, HO; HO, HO; HO, CO_2H; CO_2H, CO_2H), they must be applied in reverse when dealing with the geometric isomers of the 1 : 3-compounds. Such conclusions, in so far as they affect the monomethyl*cyclo*hexanecarboxylic acids (Darling, Macbeth, and Mills, *loc. cit.*), have been reinforced by the present dissociation constant data for aqueous solution, since the sequence of acid strengths for the 1 : 3-isomers is the reverse of the sequences for the 1 : 2- and 1 : 4-acids. Moreover, comparison of these data with the respective values of K_1 and K for the *cyclo*hexanedicarboxylic acids and the monohydroxy*cyclo*hexanecarboxylic acids (Kuhn and Wassermann; Kilpatrick and Morse, *locc. cit.*) reveals a striking similarity of pattern, as the Figure shows.

The conformations of monosubstituted *cyclo*hexanecarboxylic acids have been discussed by Kilpatrick and Morse (*loc. cit.*) (cf. Barton, *J.*, 1953, 1027), whence it follows that, of the preferred conformations, three are those in which both substituents are attached by equatorial bonds (e–e) and three are those in which equatorial-axial (e–a) bonding of the substituents occurs, thus :

	cis	*trans*
1 : 2-Disubstituted *cyclo*hexane	e–a	e–e
1 : 3-Disubstituted *cyclo*hexane	e–e	e–a
1 : 4-Disubstituted *cyclo*hexane	e–a	e–e

It is particularly noteworthy that for every pair of geometric isomers, the molecule which is capable of permitting the substituents to assume the diequatorial conformation is the one which provides the higher dissociation constant, or, in other words, favours greater anion stability. It seems, therefore, that the relative strengths of the components of any pair of geometric isomers in these series is determined by considerations of conformation rather than by classical configuration.



Strengths of substituted cyclo*hexanecarboxylic acids* $R{\cdot}C_6H_{10}{\cdot}CO_2H$ *relative to that of unsubstituted* cyclo*hexanecarboxylic acid.*

I, R = CO_2H; *II*, R = OH; *III*, R = Me.

○ trans-*Acids*; ● cis-*acids*.

As already indicated, the large *K* of the *trans*-2-methyl acid might be described as anomalous, and in this it is comparable to *n*-butyric acid and *iso*valeric acid, whose terminal methyl groups are also separated from the carboxyl group by two saturated carbon atoms. It is noted that in water the *trans*-2-acid is stronger than the *cis*-2-acid in both the monohydroxy*cyclo*hexanecarboxylic acids and the *cyclo*hexanedicarboxylic acids and, moreover, in the latter series the *trans*-2-acid is the strongest of the six isomers.

It is seen, however, from models (possessing the foregoing conformations) that in *trans*-2-methyl*cyclo*hexanecarboxylic acid the methyl and the carboxyl substituent are separated by a distance in space which is the same as that in the model of the *cis*-isomeride. Thus the apparent anomaly in the strength of the *trans*-2-methyl acid is difficult to explain in terms of a specific spatial interaction of the substituents.

Kilpatrick and Morse also determined the strengths of the monohydroxy-acids in solvents of lower dielectric constant, and found that here the values of *K* for the *cis*- and *trans*-2-acids gave an inverted sequence. They suggest that this might be due to a change in the favoured conformation for the *trans*-2-hydroxy-acid (from diequatorial to diaxial). In seeking to explain this experimental observation, however, it should not be overlooked that *if* the relatively high value of *K* in water is due to some anomalous, specific steric interaction, the relative enhancement might well diminish as the dielectric constant of the solvent falls; this is already an established feature of most *ortho*-substituted benzoic acids.

The K data for the naphthylacetic acids make an interesting comparison with the strengths of several acids recorded earlier in this series. It appears that the naphthyl group has a greater inductive attraction for electrons than phenyl has in phenylacetic acid [10^5K : 4·88 (*J.*, 1934, 161)], and the effect is rather more pronounced where attachment is at the α-carbon atom. Moreover, the abnormality (steric effect) noticed in α-naphthoic acid disappears where carboxyl is separated from the aromatic ring by methylene. It is, also, noteworthy that the ratio of the strength of β-naphthylacetic acid to that of β-naphthoic acid (0·807) is in good agreement with the ratio of the strength of phenylacetic acid to that of benzoic acid (0·778), indicating a close correspondence of the mesomeric effects to be associated with phenyl and β-naphthyl substituents.

Department of Chemistry,
Chelsea Polytechnic, London, S.W.3.

[*Received, May* 12*th*, 1954.]