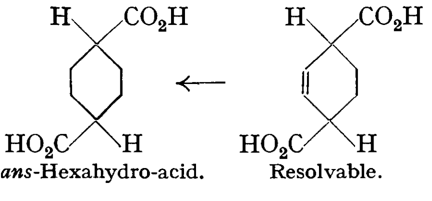
327. *The Configurations of the Δ^2-Tetrahydro- and the Hexahydro-terephthalic Acids.*

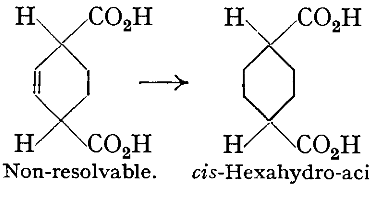
By W. H. Mills and G. H. Keats.

Until recently there has been no evidence to fix the configurations of the two geometrically isomeric forms of hexahydroterephthalic acid (*cyclo*hexane-1 : 4-dicarboxylic acid). In the latter part of last year, however, Malachowski and Jankiewiczowna (*Ber.*, 1934, **67**, 1783) succeeded in obtaining from this acid a normal unimolecular anhydride, and showed that when hydrolysed it gave in a state of purity the modification of hexahydroterephthalic acid which, from its greater solubility and lower melting point, Baeyer had named the *maleinoid* form. From this observation it is to be concluded that the *maleinoid* is the *cis*- and the *fumaroid* the *trans*-form of the acid.

When the work of Malachowski and Jankiewiczowna was published we had already been engaged for some time on an investigation also designed to fix the configurations of the two hexahydroterephthalic acids. Our plan was first to fix the configurations of the geometrically isomeric Δ^2-tetrahydroterephthalic acids by determining which of them was resolvable into optically active antimerides, and then to relate these tetrahydro-acids to the hexahydro-acids by catalytic reduction.



trans-Hexahydro-acid. Resolvable.



Non-resolvable. *cis*-Hexahydro-acid.

Since this gives an independent proof of the configurations of the hexahydro-acids and incidentally fixes that of the tetrahydro-acids, we proceeded with our investigation and have now brought it to completion.

Of the isomeric Δ^2-tetrahydroterephthalic acids, Baeyer's *fumaroid* modification (m. p. 228°) proved to be resolvable. The lævo-form of this acid was obtained optically pure with the aid of brucine, and showed the specific rotation $[\alpha]^{16°}_{5461}$ — 279°. The *maleinoid* modification could not be resolved. The *fumaroid* form has therefore the *trans*-configuration and the *maleinoid* form (m. p. 161°) has the *cis*-configuration.

The two tetrahydro-acids were then reduced with hydrogen and platinum-black in acetic acid solution : the *fumaroid* tetrahydro-acid gave the *fumaroid* hexahydro-acid, and the *maleinoid* the *maleinoid.* It is clear that reduction in this manner would not change the orientation of the $>CH{\cdot}CO_2H$ groups, and indeed experimental evidence that no such change occurs is given by the fact that each tetrahydro-acid yields one hexahydro-acid only. Our observations thus confirm the conclusions of Malachowski and Jankiewiczowna with regard to the relative configurations of the hexahydro-acids.

Although in each case the more soluble (" *maleinoid* ") modification proved to have the *cis*- and the less soluble (" *fumaroid* ") the *trans*-configuration, it is to be observed that a relationship of this kind does not invariably hold in geometrically isomeric dicarboxylic acids. Thus of the two hexahydro*iso*phthalic acids it is the modification of lower melting point which has the *trans*-configuration (Böeseken and Peek, *Rec. trav. chim.*, 1925, **44**, 841).

We have also measured the primary and secondary electrolytic dissociation constants, K_1 and K_2, of the tetrahydro-acids (those of the hexahydro-acids were measured by Kuhn and Wassermann, *Helv. Chim. Acta,* 1928, **11**, 50). For the *cis*-Δ^2-acid at 22° we found $K_1 = 0{\cdot}82 \times 10^{-4}$, $K_2 = 0{\cdot}81 \times 10^{-5}$, and for the *trans*-isomeride $K_1 = 1{\cdot}18 \times 10^{-4}$, $K_2 = 1{\cdot}19 \times 10^{-5}$. Thus, whilst the *trans*-acid is slightly the stronger, the ratio K_1/K_2 is nearly the same for both acids. The values 10·1 and 9·9 for this ratio indicate, according to the formula deduced by Bjerrum (*Z. physikal. Chem.*, 1923, **106**, 219) and modified by Ingold (J., 1931, 2179), that the distance between the dissociating hydrogen atom and the negative charge on the ion $HO_2C{\cdot}C_6H_{10}{\cdot}C\bar{O}_2$ is approximately 8·2 Å. in both the *cis*- and the *trans*-acid.

This result is in agreement with the indications given by models of the acids. If the most favoured configuration of each acid is that in which the distance between the carboxyl groups is a maximum, the models take the forms represented in (1*a*) and (1*b*). In these the distance in question is almost exactly the same in each acid, 8·7 Å., and since this is a maximum distance, the mean distance under thermal agitation should be somewhat less.

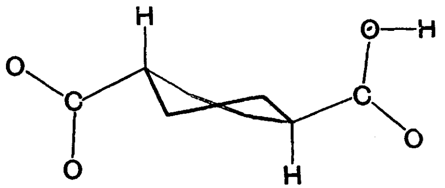


FIG. 1(*a*). trans-*Acid.*

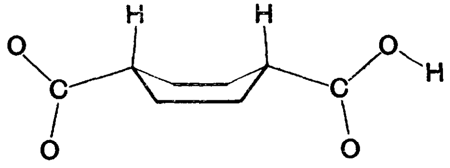


FIG. 1(*b*). cis-*Acid.*

EXPERIMENTAL.

cis- and *trans*-Δ^2-Tetrahydroterephthalic acids were prepared from terephthalic acid by Baeyer's method (*Annalen*, 1889, **251**, 278, 280, 306) with slight modifications. Terephthalic acid was reduced to $\Delta^{2:5}$-dihydroterephthalic acid in 40 g. portions, vigorous stirring being essential for success. The $\Delta^{1:5}$-acid was crystallised from alcohol before being further reduced. The *cis*- and the *trans*-Δ^2-acid were crystallised from water and had m. p.'s 161° and 228° respectively (Baeyer gives 150—155° and 220°). From 400 g. of terephthalic acid, 170 g. of *trans*-Δ^2- and 40 g. of *cis*-Δ^2-acid were obtained (Found : *cis*-Δ^2, C, 56·2; H, 5·8; *trans*-Δ^2, C, 56·3; H, 5·8. Calc. for $C_8H_{10}O_4$: C, 56·5; H, 5·9%). The dimethyl *trans*-Δ^2-ester had m. p. 11°, b. p. 152—154°/30 mm., and the *cis*-ester, b. p. 148°/30 mm.

l-trans-Δ^2-*Tetrahydroterephthalic Acid.*—30 G. of the *trans*-Δ^2-acid and 141 g. of brucine were dissolved in 1800 c.c. of hot water, and the salt allowed to crystallise (colourless prisms). The product was crystallised four times from water and the rotation of the brucine salt, dried in a vacuum at 100°, was tested after each crystallisation : $[\alpha]_{5461}^{16^\circ}$ (for 0·4 g. in 50 c.c. of chloroform) $-$ 92·5°, $-$ 112·0°, $-$ 116·0°, $-$ 117·0°, $-$ 117·0°. The last fraction (8 g.) was pure and the brucine was removed by treatment with ammonia, filtration, and extraction with chloroform. The ammonium salt was acidified, and the *trans*-Δ^2-acid extracted with ether. It was crystallised from water; m. p. 222° (Found : C, 56·3; H, 5·8%). 0·2 G. of the acid in 50 c.c. of ethyl alcohol at 16° had a rotation of $-$ 4·465° for the Hg green line in a 4 dm. tube. Hence $[\alpha]_{5461}^{16^\circ} = -279^\circ$. The brucine mother-liquors yielded a dextrorotatory acid, $[\alpha]_{5461}^{16^\circ} = +132^\circ$. Attempts to get the dextrorotatory acid pure failed. The strychnine salt can be crystallised to give the lævo-acid, but attempts with the acid and neutral salts of quinine, cinchonine, cinchonidine, morphine, and nor-ψ-ephedrine gave only slightly active acids.

Hydrogenation of cis- *and* trans-Δ^2-*Tetrahydroterephthalic Acids*.—The platinum oxide catalyst was prepared as described in "Organic Syntheses," **8**, 92. 1 G. of the acid, 0·1 g. of the catalyst, and 40 c.c. of glacial acetic acid were shaken at room temperature for 10 minutes, the calculated volume of hydrogen being absorbed. The product was filtered warm, the acetic acid removed under reduced pressure, and the residue crystallised from water. The *cis*-Δ^2-acid gave a hexahydro-acid, m. p. 167°; the *trans*-Δ^2-acid gave a hexahydro-acid, m. p. 309°. Malachowski gives the m. p.'s of *cis*- and *trans*-hexahydroterephthalic acids as 166—167° and 312—313° respectively. This method forms the most convenient way of preparing *cis*- and *trans*-hexahydroterephthalic acids.

Dissociation Constants of cis- *and* trans-Δ^2-*Tetrahydroterephthalic Acids*.—The measurements were made at 22°. 50 C.c. of a 0·009412M-solution of the acid were titrated against 0·0247N-sodium hydroxide (free from carbon dioxide), the p_H being measured when 7·0, 8·0, 9·0, 10·0, 11·0, 12·0 and 26·0, 27·0, 28·0, 29·0, 30·0, 31·0 c.c. of the hydroxide had been added. A quinhydrone electrode of the type recommended by Auerbach (*Z. physikal. Chem.*, 1924, **110**, 65) was used, in conjunction with a N-calomel electrode. A hydrogen electrode was found to be useless, owing presumably to reduction of the Δ^2-acid. Saturated potassium chloride bridges were used, being kept closed by taps. Two resistance boxes in series were used instead of a potentiometer wire, and the sum of the resistances in them was kept at 11,110 ohms. A standard cadmium cell was used as a source of known *P.D.* Four titrations of both acids were done and the procedure was repeated with the solutions diluted to three-quarters, one-half, and one-quarter of their original concentrations. The pairs of readings taken in calculating the dissociation constants corresponded to 7·0, 26·0; 8·0, 27·0, etc., c.c. of the sodium hydroxide solution. Following Gane and Ingold's procedure (J., 1931, 2153), the values of K_1 and K_2 were plotted against the concentration of acid, and the values at infinite dilution found by extrapolation of the straight lines.

	trans-Δ^2-Acid.		*cis*-Δ^2-Acid.	
Original conc. of acid, g./l.	10^4K_1.	10^5K_2.	10^4K_1.	10^5K_2.
1·6	1·18	1·35	0·883	1·03
1·2	1·18	1·30	0·883	0·971
0·8	1·18	1·28	0·858	0·917
0·4	1·10 *	1·10 *	0·841	0·862
Extrapolated values	1·18	1·19	0·82	0·81

* These values are not concordant with the rest and are neglected.

From Ingold's formula this gives values of r for the *cis*- and the *trans*-Δ^2-acid of 8·14 and 8·26 Å. respectively.

We are indebted to Mr. R. J. Thomas for carrying out some preliminary experiments on this problem. Our thanks are due to Mr. W. G. Palmer for advice concerning the electrical measurements, and to Pembroke College, Cambridge, and to the Board of Education for grants to one of us (G. K.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, July 12th*, 1935.]