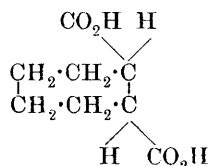


CCXLVII.—*Resolution of trans-cycloPentane-1 : 2-dicarboxylic Acid.*

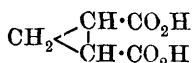
By LEONARD JAMES GOLDSWORTHY and WILLIAM HENRY PERKIN, jun.

IN accordance with the theory of Le Bel and van't Hoff, many of the dicarboxylic acids of the cyclic hydrocarbons should be capable of resolution into optically active modifications. Hitherto, only two acids of this type have been investigated in this respect, and the first to be resolved was *trans*-hexahydrophthalic acid :



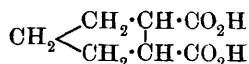
In 1899, Werner and Conrad (*Ber.*, **32**, 3050) showed that this externally compensated acid may be resolved into its active modifications by the fractional crystallisation of the quinine salts, and the active acids were found to have $\alpha_D + 18.2^\circ$ and -18.5° respectively. These investigators also showed that, whilst the externally compensated acid is almost insoluble in water and melts

at 215°, the *d*- and *l*-modifications melt at 179—183°, and are much more soluble; again, the anhydrides of the active acids melt at 164°, or considerably higher than that of the *dl*-acid, which melts at 140°. Furthermore, the conversion of the acids into their anhydrides is attended by a reversal and at the same time considerable increase of the rotation, since the *d*-acid ($\alpha_D + 18.2^\circ$) yields an anhydride with $\alpha_D - 76.7^\circ$; the dimethyl esters have the same sign as their acids and the rotations $\alpha_D + 28.6^\circ$ and -29.6° respectively. At a later date (*Ber.*, 1905, **38**, 3112), Buchner and von der Heide investigated *trans*-cyclopropane-1:2-dicarboxylic acid,



and showed that this acid can be resolved into its active components by the fractional crystallisation of the salts with brucine, quinine, or cinchonidine. The active acids melt at 175°, that is, at the same temperature as the *dl*-acid, and have $\alpha_D \pm 84.5^\circ$; all attempts to prepare the anhydrides of these acids have been unsuccessful, since they distil unchanged and are not acted on by acetyl chloride.

Some years ago, a series of experiments was commenced in the Laboratories of Manchester University by one of us in conjunction with Mr. H. D. Gardner with the object of effecting the resolution of *trans*-cyclopentane-1:2-dicarboxylic acid,



(Perkin, T., 1887, **51**, 244), but the investigation was not completed.

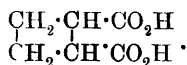
We have now taken up the subject again and find that resolution may be readily and completely brought about with the aid of brucine.

When the *dl*-acid is combined with brucine and the mixed salts are recrystallised from water, the salt of the *d*-acid separates first and is readily obtained pure by repeated recrystallisation. The *l*-acid may then be recovered from the mother liquors in the manner described on p. 2643. The observed rotations of the *d*- and *l*-modifications were $\alpha_D + 87.6$ and -85.9 respectively, and those of the corresponding ethyl esters, $\alpha_D + 70.31^\circ$ and -69.76° . The *d*- and *l*-modifications of cyclopentane-1:2-dicarboxylic acid melt at 181° or 21° higher than the melting point of the *dl*-modification (m. p. 160°). For the sake of ready comparison, the rotations and melting points of the *trans*-cyclopropane-, -pentane-, and -hexane-1:2-dicarboxylic acids are appended in tabular form:

TRANS-CYCLOPENTANE-1:2-DICARBOXYLIC ACID. 2641

	α_D , <i>d</i> -acid.	α_D , <i>l</i> -acid.	M. p. of <i>d</i> - and <i>l</i> - acids.	M. p. of inactive acid.
<i>trans</i> -cycloPropane- 1:2-dicarboxylic acid	+84.9°	--84.5°	175°	175°
<i>trans</i> -cycloPentane- 1:2-dicarboxylic acid	+87.6°	--85.9°	181°	160°
<i>trans</i> -cycloHexane- 1:2-dicarboxylic acid	+18.2°	--18.5°	178—183°	215°

It would be interesting to fill up the gap between *trans*-cyclopropane-1:2-dicarboxylic acid and the corresponding cyclopentane-dicarboxylic acid by the resolution of *trans*-cyclobutane-1:2-dicarboxylic acid,



but, unfortunately, the preparation of this acid (T., 1894, **65**, 585) in quantity sufficient for resolution is most troublesome and, although experiments with this object have been commenced, we have not yet been able to separate the active modifications in a pure state.

EXPERIMENTAL.

d-trans-cycloPentane-1:2-dicarboxylic Acid.

The *dl*-trans-cyclopentane-1:2-dicarboxylic acid employed in these experiments was prepared by the method described by Perkin (T., 1887, **51**, 240; compare T., 1894, **75**, 586). The pure acid, in quantities of 15 grams, dissolved in hot water, was mechanically stirred, and brucine (90 grams) gradually added, when the alkaloid readily dissolved. The excess of brucine was filtered off, well washed with hot water, and the filtrate and washings were concentrated on the water-bath until crystals just commenced to form on the surface. When the liquid was cooled and vigorously stirred, a copious crystallisation took place, and the whole became semi-solid; the crystals were then collected and repeatedly recrystallised from hot water. During this operation, the progress of the separation of the brucine salt of the *d*-acid from that of the *l*-modification was followed with the polarimeter, and the table given below shows that the separation is nearly complete after six crystallisations, since the difference between the rotation of this crop and of that obtained as the result of the twelfth crystallisation is very small.

No. of crystallisation.	Weight of substance. Gram.	Observed rotation.	Specific rotation.
1st crop	0.5250	—1.68°	—32.1°
3rd "	0.4566	—1.14°	—25.0°
6th "	0.5050	—1.15°	—22.8°
12th "	0.2612	—0.51°	—19.9°

A specimen of the pure brucine salt was subsequently prepared by adding excess of brucine to the hot dilute aqueous solution of the pure *d*-acid (see below), and, after filtering, the solution was allowed to crystallise slowly over sulphuric acid, when large, brilliant, tabular crystals separated. As these crystals effloresce in a vacuum desiccator, they were dried by exposure to air, and then analysed:

0.1314 gave 0.2782 CO₂ and 0.0859 H₂O. C=57.7; H=7.3.

0.5079 „ 22.6 c.c. N₂ at 19.8° and 753 mm. N=5.1.

2C₂₃H₂₆O₄N₂·C₇H₁₀O₄·9H₂O requires C=57.4; H=7.2; N=5.1 per cent.

That the salt has this composition was confirmed by the fact that 0.2316 gram, heated for one hour at 125°, lost 0.0336 H₂O, whereas the calculated loss for 9H₂O is 0.0339 gram.

In order to obtain the pure *d*-acid, the brucine salt from the twelfth crystallisation was dissolved in hot water, the brucine precipitated by ammonia and, after filtering and washing, the solution of the ammonium salt was concentrated and acidified with hydrochloric acid when, on cooling, the *d*-acid separated in plates, and melted at 178—180°. After completely decolorising with the aid of animal charcoal, and twice crystallising from water, the acid melted at 181°, and 0.1752 dissolved in water (20 c.c.) gave, in a 2-dcm. tube, a rotation of +1.535°, whence $\alpha_D + 87.6^\circ$. On titration, 0.1778 required 0.0898 NaOH for neutralisation, whereas this amount of an acid, C₅H₈(CO₂H)₂, should neutralise 0.0900 NaOH.

The *d*-ethyl ester, C₅H₈(CO₂Et)₂, was prepared by boiling the *d*-acid with five times its weight of 10 per cent. alcoholic sulphuric acid for six hours; water was then added, the ester extracted with ether, and, after washing with water and dilute sodium carbonate, the ethereal solution was dried, evaporated, and the ester distilled under diminished pressure.

It boiled constantly at 170°/100 mm., and 0.2596, dissolved in acetone (20 c.c.), gave, in a 2-dcm. tube, a rotation of +1.825°, whence $\alpha_D + 70.31^\circ$.

The d-Anilide, C₅H₈(CO·NH·C₆H₅)₂.—In order to prepare this derivative, the *d*-acid was heated with thionyl chloride in a sealed tube in boiling water for an hour, the clear liquid evaporated on the water-bath, and the residual acid chloride dissolved in benzene and mixed with excess of aniline. The benzene was removed by evaporation, the residue stirred with dilute hydrochloric acid, and the crystalline precipitate collected and recrystallised twice from

methyl alcohol, in which it is sparingly soluble, separating as a voluminous mass of needles melting at 245—247° (uncorr.):

0.2756 gave 21.7 c.c. N₂ at 18.4° and 762 mm. N=9.1.

C₁₉H₂₀O₂N₂ requires N=9.1 per cent.

0.1708, dissolved in acetone (20 c.c.), gave, in a 2-dcm. tube, the rotation +1.880°, whence $\alpha_D + 110.1^\circ$.

Attempts which were made with the object of preparing the anhydride of the *d-trans*-acid were not successful and the results obtained seem to throw some doubt on the existence of this anhydride. Since, however, *trans-cyclohexane-1:2-dicarboxylic acid* (*trans-hexahydrophthalic acid*) yields an anhydride without difficulty (Baeyer, *Annalen*, 1890, **258**, 179), there is every reason to suppose that the anhydride of *trans-cyclopentane-1:2-dicarboxylic acid* should also be capable of existence, but it is doubtful whether the substance described by Haworth and Perkin (T., 1894, **65**, 985) can be accepted as this anhydride.

1-*trans-cyclopentane-1:2-dicarboxylic Acid*.

In order to obtain this acid, the mother liquors from the first six crystallisations of the brucine salt of the *dl*-acid (p. 2641) were concentrated until crystals began to appear on the surface of the brown liquid. The salt, which separated in quantity on cooling, was dissolved in hot water, the solution decolorised with animal charcoal, and the crude *l*-acid isolated in the manner described in the case of the *d*-acid.

This acid is readily obtained pure simply by recrystallising four times from water, it then melted sharply at 180—181°, and 0.2363, dissolved in water (20 c.c.), gave, in a 2-dcm. tube, a rotation of -2.03°, whence $\alpha_D - 85.9^\circ$. On titration, 0.3110 required 0.1568 NaOH for neutralisation, whereas this amount of an acid, C₅H₈(CO₂H)₂, should neutralise 0.1575 NaOH.

The *l-ethyl ester*, C₅H₈(CO₂Et)₂, obtained in the manner described in detail in the case of the ester of the *d*-acid, distilled at 170°/100 mm., and 0.3326, dissolved in acetone (20 c.c.), gave, in a 2-dcm. tube, a rotation of -2.32°, whence $\alpha_D - 69.76^\circ$.

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