

### 293. *The Stereochemistry of Catalytic Hydrogenation. Part IX. Confirmatory Evidence of the Configurations of the Perhydrodiphenic Acids.*

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Optically active *cis-syn-trans*-perhydrodiphenic acid is racemised when converted into *syn*-perhydrofluorenone, but optically active *trans-anti-trans*-perhydrodiphenic acid gives an active pyroketone. These facts confirm the *syn*- and the *anti*-configurations assigned to the two series of perhydrodiphenic acids by Linstead and Doering.

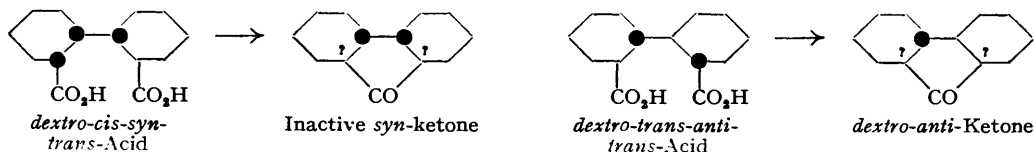
The hexahydrodiphenic acid of m. p. 221° yields *trans*-hexahydrophthalic acid on ozonisation. This confirms the *cis*- and the *trans*-configurations assigned to the terminal members of the *syn*-series of perhydrodiphenic acids.

*The syn- and anti-Configurations of the Backbone.*—In the third paper of this series, Linstead and Doering (*J. Amer. Chem. Soc.*, 1942, **64**, 2003) proved that, of the six known perhydrodiphenic acids (Linstead and Doering, *ibid.*, p. 1991), those of melting points 289°, 200°, and 223° formed the *syn*- and those of melting points 198°, 206°, and 247° formed the *anti*-series. The present communication presents confirmatory evidence of these configurations by a different method.

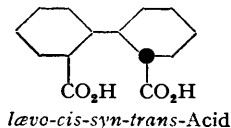
It was shown in the preceding paper (Davis, Doering, Levine, and Linstead) that all six perhydrodiphenic acids yield perhydrofluorenone on pyrolysis. The acids of the *syn*-series give a *syn*-ketone and those of the *anti*-series an *anti*-ketone. As the configuration of the backbone is preserved, there can be no migration of hydrogen from the  $\beta$ -carbon atoms. On the other hand, the  $\alpha$ -carbon atoms are so involved because, in each series, essentially the same mixture of ketones is obtained from all three acids.

Optically active perhydrodiphenic acids are now available in both the *syn*- and the *anti*-series (Linstead and Doering, *ibid.*, p. 2003). The molecular dissymmetry of the acids of the *anti*-series involves both the  $\alpha$ - and the  $\beta$ -carbon atoms, whereas that of the *cis-syn-trans*-acid (the only active isomeride of the *syn*-series) involves only the  $\alpha$ -carbon atoms. It follows that the optical activity of the acids of the *anti*-series should survive pyrolysis to tricyclic ketones,

whereas racemisation should occur during the pyrolysis of the active acid of the *syn*-series. This is illustrated in the diagram.



Formulae with dots, as shown above, actually represent only one enantiomorphous form of a dissymmetric molecule. The *laevo*-form of the *cis-syn-trans*-acid would be represented in terms of this convention by the formula :



We have studied the pyrolysis of the optically active forms of the perhydrodiphenic acids of m. p. 200° (*cis-syn-trans*) and 247° (*trans-anti-trans*) (Linstead and Doering, *loc. cit.*). The ketone obtained from the first acid was optically inactive and yielded an optically inactive mixture of oximes, identical with that obtained from the racemic *cis-syn-trans*-acid (Davis, Doering, Levine, and Linstead, preceding paper). On the other hand the ketone obtained from the active *trans-anti-trans*-acid, after removal of unchanged acid and anhydride, was strongly levorotatory ( $[\alpha]_D -130^\circ$ ) and yielded an optically active semicarbazone.

These results conclusively prove that the acid of m. p. 200° belongs to the *syn*-, and that of m. p. 247° to the *anti*-series, in agreement with the configurations assigned by Linstead and Doering (*loc. cit.*). The absence of racemisation of the *anti*-acid shows conclusively that the  $\beta$ -carbon atoms are not involved in pyrolyses of acids of the adipic acid series.

*cis- and trans-Configurations in the syn-Series.*—Linstead, Davis, and Whetstone (*J. Amer. Chem. Soc.*, 1942, **64**, 2009) assigned the *cis-cis*-configuration to the *syn*-perhydrodiphenic acid of m. p. 289°. The evidence was in brief: (i) The acid was symmetrical, with similar configurations of the two carboxyl groups. (ii) It was formed by the catalytic hydrogenation of a hexahydrodiphenic acid of m. p. 242°; this hexahydro-acid had a *cis*-configuration because it could be ozonised to *cis*-hexahydrophthalic acid.

In view of the key position of this ozonisation in the general determination of configurations in this group, we thought it advisable to carry out a control series of experiments in the *trans*-series. The geometrical isomeride of the hexahydro-acid of m. p. 242° melts at 221° and gives *cis-syn-trans*-perhydrodiphenic acid on catalytic hydrogenation (Linstead and Davis, *ibid.*, p. 2006). We now find that ozonisation of the latter hexahydro-acid followed by treatment with hydrogen peroxide yields *trans*-hexahydrophthalic acid, identified by comparison with authentic material and by conversion into the known *trans*-dianilide. The ozonisation of the acid, m. p. 221°, thus yields results fully consistent with the previous findings and provides additional evidence for the configurations assigned to the two hexahydrodiphenic acids, m. p.s 242° (*cis*) and 221° (*trans*). These deductions are based on the assumption that, as we think highly probable, there is no inversion of configuration during ozonisation.

During the preparation of ( $\pm$ )-*trans*-hexahydrophthalic acid for comparison with the ozonisation product, it was observed that the melting point of this well-known compound is considerably depressed by the presence of small amounts of impurities, and that the values recorded in the literature are too low. For the inactive *trans*-acid, von Baeyer (*Annalen*, 1890, **258**, 145) gave m. p. 215—221°, Hüchel and Goth (*Ber.*, 1925, **58**, 447) 215—216°, and Vavon and Peignier (*Bull. Soc. chim.*, 1929, **45**, 293) 213—218°. An acid melting in this range is, indeed, easily obtained, but on further crystallisation from water it attains a constant melting point of 227—229° (corr.). The melting point is affected to some extent by the rate of heating, but this is less true of the pure acid.

#### EXPERIMENTAL.

(All m. p.s are corrected. Analyses are by Miss Eleanor Werble.)

*Ketonisation of laevo-cis-syn-trans-Perhydrodiphenic Acid.*—The acid used had been prepared by Dr. W. E. Doering (*J. Amer. Chem. Soc.*, 1942, **64**, 2003). It had m. p. 171—174°,  $[\alpha]_D^{25} -75^\circ$  (c, 1; in alcohol containing 5% of water). 250 Mg. were heated for 1 hour at 310° in nitrogen. The product was

removed from the reaction vessel with ether and the ether extracted with 5% aqueous sodium hydroxide to remove unchanged acid. The free acid obtained by acidification amounted to only 10 mg. of a sticky gum. The ethereal extract on evaporation gave 120 mg. of a pale yellow oil. Without removal of any anhydride present the oil was dissolved in 6 c.c. of alcohol. The solution gave no observable rotation in a 2-dm. tube. The main portion of the alcohol was removed and the ketone converted into the oxime in the manner described in the preceding paper. The oxime was optically inactive. After 2 crystallisations from methanol it formed fine needles, m. p. 159—165°,  $[\alpha]_D^{20}$  0° ± 1° (c, 1; in alcohol containing 5% of water), and was indistinguishable from the mixture of oximes prepared from the racemic *cis-syn-trans*-acid and similarly purified.

*Ketonisation of dextro-trans-anti-trans-Perhydrodiphenic Acid.*—The *dextro*-acid was prepared by resolution with ephedrine, following Slinger (Linstead and Doering, *loc. cit.*). It had m. p. 259—260°,  $[\alpha]_D^{25}$  78° ± 1° (c, 1; in 95% alcohol). 175 Mg. of it were heated in a slow stream of nitrogen for 45 minutes at 300—320°. The oily product was extracted with ether and the residue after removal of the ether was warmed for 15 minutes with 3 c.c. of 20% methyl-alcoholic potassium hydroxide. This served to hydrolyse any anhydride present. The solution was evaporated to dryness, and the residue suspended in a little water and extracted thrice with ether. The ethereal extract was dried (MgSO<sub>4</sub>) and the solvent removed. The residual *laevo-anti*-perhydrofluorenone (83 mg.),  $[\alpha]_D^{27}$  -130° ± 0.5° (c, 2; in 95% alcohol), was a pale yellow oil with the characteristic pleasant smell of ketones of the group.

The active *anti*-perhydrofluorenone (about 60 mg.) in 1 c.c. of 50% aqueous alcohol was heated on the steam-bath for 40 minutes with sodium acetate (150 mg.) and semicarbazide hydrochloride (100 mg.). The product was cooled in ice, but only a trace of semicarbazone separated. Further quantities of the reagents (half as much as before) were added and the reaction mixture was heated for a further 7 hours. Cooling in ice then precipitated 42 mg. of the semicarbazone of the *laevo*-ketone. Recrystallisation from a large volume of methanol gave the pure *semicarbazone*, irregular laminated plates, m. p. 200—202°,  $[\alpha]_D^{25}$  -20° ± 4° (c, 0.25; in 95% alcohol). The substance is sparingly soluble in cold 95% alcohol; a 0.5% solution could not be prepared at room temperature (Found: C, 67.8, 67.45; H, 9.0, 8.9. C<sub>14</sub>H<sub>23</sub>ON<sub>3</sub> requires C, 67.4; H, 9.3%). The *laevo*-semicarbazone in general resembles the corresponding racemate obtained by Vocke (*Annalen*, 1934, 508, 1) and by Linstead and Walpole (*J.*, 1939, 850), which melts at 216—217°.

*Ozonisation of trans-Hexahydrodiphenic Acid.*—A stream of ozonised oxygen was led for 4 hours through a solution of the acid (*J. Amer. Chem. Soc.*, 1942, 64, 2006) (1.00 g.; m. p. 220°) in 20 c.c. of warm glacial acetic acid. The product was left overnight with 50 c.c. of 3% hydrogen peroxide and then evaporated to dryness on the steam-bath in a current of air. The dry residue was taken up in 15 c.c. of 10% aqueous sodium carbonate, and the solution extracted with ether and submitted to fractional acidification by Linstead and Doering's method (*loc. cit.*). The first material to separate was unchanged *trans*-hexahydrodiphenic acid (274 mg.). Subsequent addition of a total of 6 c.c. of concentrated hydrochloric acid caused deposition only of a little tar. The aqueous solution was accordingly extracted with ether. This yielded 340 mg. of a mixture of acids which on crystallisation from aqueous acetic acid gave *trans*-hexahydrophthalic acid (71 mg.; 14% calc. on the hexahydrodiphenic acid consumed). The hexahydrophthalic acid so obtained was not quite pure: it melted at 210—214° alone and at 211—215° in admixture with authentic acid. For further identification it was converted into the dianilide. The acid (25 mg.) was dissolved in 2 c.c. of dry ether containing 63 mg. of phosphorus pentachloride. After 20 minutes the solvent was removed and the vessel evacuated. The residue was treated with aniline (60 mg.) in ether. The solvent was removed and the dianilide crystallised twice from glacial acetic acid, forming glistening needles (16 mg.) (Found: C, 74.4; H, 6.5. Calc. for C<sub>20</sub>H<sub>22</sub>O<sub>2</sub>N<sub>2</sub>: C, 74.5; H, 6.9%), m. p. 317—318° alone or admixed with authentic *trans*-dianilide. These m. p.s were obtained by the use of a block preheated to 260°. When the capillary was heated slowly from room temperature, the m. p. was 303—304°, in agreement with Stoermer and Steinbeck (*Ber.*, 1932, 65, 413).

(±)-*trans*-Hexahydrophthalic Acid.—The acid was prepared by the inversion and hydrolysis of methyl *cis*-hexahydrophthalate (cf. Hückel and Goth, *loc. cit.*). The ester was boiled for 5 hours with an excess of 20% methyl-alcoholic potassium hydroxide, and the acid isolated by acidification after the removal of methanol in the usual way. The overall yield of crude *trans*-acid, m. p. 195—214°, was 1.90 g. from 2.25 g. of *cis*-acid. Four successive crystallisations from the minimum amount of water gave the following products: 1.51 g., m. p. 200—217°; 1.23 g., m. p. 215—222°; 0.86 g., m. p. 227—229°; m. p. 227—229°. These m. p.s were obtained by the use of a bath preheated to 200°. Pure *trans*-hexahydrophthalic acid (m. p. 227—229°) forms bold, thick transparent prisms (Found: C, 56.0; H, 7.25. Calc. for C<sub>8</sub>H<sub>10</sub>O<sub>4</sub>: C, 55.8; H, 7.0%). The anhydride, made from the pure acid and acetyl chloride, melts at 142.5—144° (lit., 140°) and the dianilide at 317—318° (see above). The dianilide is practically unaffected by being refluxed (18 hours) with 80% acetic acid, in agreement with Stoermer and Steinbeck (*loc. cit.*).

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[Received, January 5th, 1950.]