was a partially inverted acid (24.6 mg., m. p. 192–234°). The mother liquor yielded 11.3 mg. of beautiful prismatic needles. This acid melted at 237–240° alone and in admixture with the authentic *trans-anti-trans* acid softened at 237° and finally melted at 246–248°.

The *dimethyl ester* of the *trans-anti-trans* acid was prepared by means of diazomethane in the usual way in 89% yield. It formed prisms, m. p. 84.5–86°.

Anal. Calcd. for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28. Found: C, 67.85; H, 9.19.

Summary

All the six optically inactive forms of perhydrodiphenic acid, which are theoretically possible, have been prepared.

One of these, m. p. 289°, is the main product of the catalytic hydrogenation of diphenic acid over platinum, and its derivatives are similarly formed from the corresponding derivatives of diphenic acid. The monomethyl ester of the 289° acid is capable of half-inversion to an isomeric acid of m. p. 200°, or its derivatives. The dimethyl ester of the 289° acid is capable of double inversion to an isomeric acid of m. p. 223°, or its derivatives. The acid of m. p. 200° has two monomethyl esters. One of these can be inverted and hydrolyzed to the 223° acid. These three acids form the *syn*-stereoisomeric series. The 200° acid is intermediate in configuration between the 289 and 223° acids.

The catalytic hydrogenation of diphenic acid gives as by-products the 200° acid and a fourth isomer of m. p. 198°. The 198° acid can be converted by half-inversion into the fifth isomer of m. p. 206°, and by double inversion into the sixth isomer of m. p. 247°. The 198, 206 and 247° acids thus represent the second (*anti-*) stereoisomeric series, the 206° acid being intermediate in configuration between the other two.

The formation of esters by diazomethane or by the Fischer–Speier procedure, the formation of anhydrides and the acid hydrolysis of esters proceed normally. The hydrolysis of esters with alcoholic alkali proceeds with inversion.

The results are correlated with previous investigations in the field. It is shown that the tricyclic ketones of Marvel cannot belong to the hydrophenanthrene series.

CONVERSE MEMORIAL LABORATORY
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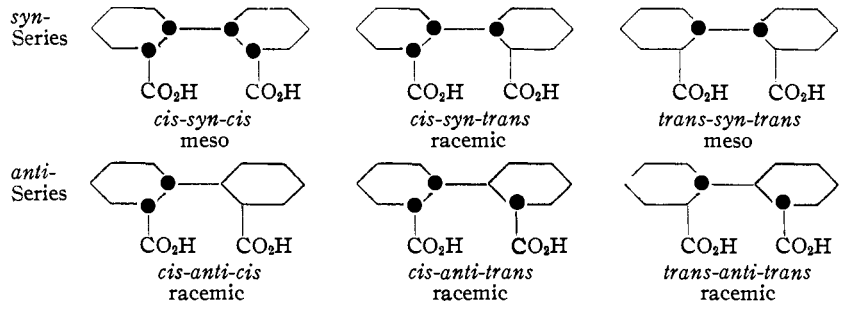
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Stereochemistry of Catalytic Hydrogenation. III. Optically Active Perhydrodiphenic Acids. A Proof of the Configuration of the Backbone

BY R. P. LINSTEAD AND W. E. DOERING

It has been shown in the preceding paper that the six perhydrodiphenic acids can be divided into two series of three members each. It has been found possible to interconvert the members within each series but not (as yet) to pass from one group to the other. These two series have the two possible backbone configurations, *syn-* and *anti-*. In order to assign the correct configuration to each of the six isomers, three questions must be answered: (1) Which series is *syn-* and which *anti-*? (2) In each series which member is the intermediate with the unlike (*cis-trans*) arrangement of the carboxyl groups? (3) In the terminal or symmetrical members of each series, which has the two *cis-* arrangements and which the two *trans-*? The first two of these questions are answered below. The third question is answered in Part V.

(1) **Backbone Configuration.**—As was pointed out by Linstead and Walpole,[1] of the six isomeric acids, four are capable of existence in optically active forms and two are internally compensated. This is shown below



The two symmetrical molecules are both in the *syn*-series. Two propositions therefore follow:

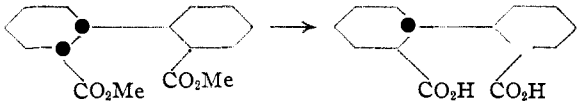
(1) Linstead and Walpole, *J. Chem. Soc.*, 850 (1939).

(1) That series which can be shown to contain *more than one* member capable of existing in optically active forms must have the *anti*-configuration of the backbone. (2) That series in which one (or more) member can be proved to have a meso configuration must be the *syn*-.

By both these tests it is proved below that the 289–200–223° acid series is *syn*-, and the 198–206–247° acid series is *anti*-.

The 247° (*trans-anti-trans*) acid was the first perhydrodiphenic acid to be resolved. The experimental work was carried out in 1939 by Dr. F. H. Slinger of the University of Sheffield, England. The resolution was effected by means of ephedrine. The *d*-acid[2] melted at 258° and had $[\alpha]_D$ +77.5°.

The 198° acid was resolved by means of cinchonidine into its enantiomorphs, which melted at 240° and had $[\alpha]_D$ ±44°. The *d*-enantiomorph was converted into the dimethyl ester by means of diazomethane. The ester had m. p. 27°, $[\alpha]_D$ +69°. When it was hydrolyzed by alcoholic potash it underwent a double inversion without racemization:



dextro-c.a.c. ester — *levo-t.a.t.* acid

The product was a levorotatory acid, m. p. 258°, $[\alpha]_D$ −79°. This was shown to be the enantiomorph corresponding to the *d*-acid obtained by the direct resolution of the 247° acid. A mixture of the two yielded the racemic *trans-anti-trans* acid, m. p. 247°.

This provides a refined confirmation of the corresponding experiment with the inactive materials, described in the previous paper.[3] The absence of racemization proves conclusively that the backbone carbon atoms are not involved in the reaction.

Attempts to resolve both the 289° and the 223° acids were fruitless. However, this does not prove the symmetry of their molecules, and to do this conclusively we made use of the principle used by Stoermer and Steinbeck[4] to prove the symmetry of the molecule of *cis*-hexahydrophthalic acid. According to this, an element of dissymmetry is first introduced by modifying one of the carboxyl groups, the compound is then resolved and the modifying group is removed by some mild reaction. If the resulting compound is inactive, then its molecule must be symmetrical.

The 289° acid was accordingly converted into its monomethyl ester. This was resolved by means of cinchonidine into two enantiomorphs of m. p. 134° and $[\alpha]_D$ ±10°. When the *l*-acid ester was hydrolyzed by acetic and hydrochloric acids it yielded the *inactive* parent acid, m. p. 289°. Even stronger evidence was provided by the fact that the *l*-acid ester on treatment with diazomethane yielded the *inactive* dimethyl ester, m. p. 73°, of the same acid. It will be recalled that the active form of the *cis-anti-cis* (198°) acid yielded the active ester on treatment with diazomethane. There is therefore nothing in the experimental conditions to cause racemization providing the molecule of the acid is unsymmetrical. These results prove that the 289° acid has a symmetrical structure. Hence the series to which it belongs has a *syn*-arrangement of the backbone.

We have also attempted to deduce the configuration of the backbone from a study of the formation of pyroketones from the acids. This work, which is still incomplete, will be the subject of a future communication.

(2) **Intermediate** (*cis-trans*) **Acids.**—In the preceding paper[3] it was shown by inversion experiments that the 200° acid was intermediate in configuration between the 289 and 223° acids. If this is so, it must be the *cis-syn-trans* acid, and be the only member of the *syn*-series capable of exhibiting optical activity. The following experiments confirm this view. The *l*-monomethyl ester of the 289° acid was inverted and hydrolyzed by treatment with sodium methoxide followed by the addition of a little water. This yielded a dextrorotatory acid, m. p. 173°, $[\alpha]_D$ +75°. A similar series of reactions performed with the *d*-monomethyl ester of the 289° acid gave the *levo*-enantiomorph, m. p. 173°, $[\alpha]_D$ −75°. A mixture of these acids gave the racemic acid of m. p. 200°, identical with that described in the preceding paper. This acid is thus conclusively proved to be *cis-syn-trans*-perhydrodiphenic acid. The existence of two acid esters[3] is in harmony with this conclusion.

We have not as yet had sufficient material to perform a similar partial asymmetric synthesis in the *anti*-series. As, however, the 206° acid has

(2) The prefixes *d*- and *l*- in this paper refer solely to the observed rotations and do not imply any relationships in configuration.

(3) Linstead and Doering, THIS JOURNAL, **64**, 1991 (1942).

(4) Stoermer and Steinbeck, *Ber.*, **65**, 413 (1932).

been shown to stand in precisely the same relation to the other *anti* acids as does the 200° acid in the *syn*-series, there can be no doubt that it has the *cis-anti-trans* configuration.

J. C. Speakman[5] has recently determined the first and second dissociation constants of two of the perhydrodiphenic acids (m. p.'s 222 and 247°), and has explored the possibility of estimating the inter-carboxyl distances from their ΔpK values, by the Bjerrum–Ingold method. This method has sometimes given significant results for cyclic dicarboxylic acids—a recent example is provided by Speakman's measurement of the *cis*- and *trans*-forms of tetralin 2,3-dicarboxylic acid.[5] However, each perhydrodiphenic acid has so many configurational possibilities that no safe deduction can be made from the results. It is nevertheless interesting that the 247° acid has a ΔpK of 1.1 and therefore behaves very like adipic acid, whereas the 222° acid has the high ΔpK of 1.7, which, from the usual calculation, would indicate that the mean intercarboxyl distance is unusually small.

The properties of the various forms of the acids are summarized in Table I.

TABLE I

OPTICALLY ISOMERIC PERHYDRODIPHENIC ACIDS

Configuration	dextro Form	levo Form	Inactive form, m. p., °C.
cis-syn-cis	Not possible		288–289 (meso)
cis-syn-trans	m. p. 170–174°, [α] +75°	m. p. 171–174°, [α] −75°	199–200 (rac.)
trans-syn-trans	Not possible		222–223 (meso)
cis-anti-cis	m. p. 238–240°, [α] +43°	m. p. 238–240°, [α] −45°	198–199 (rac.)
cis-anti-trans	Not yet prepared		206–207 (rac.)
trans-anti-trans	m. p. 257–259°, [α] +77.5°	m. p. 257–258.5°, [α] −79°	246–247 (rac.)

Experimental Part[6]

syn-Series

***cis-syn-cis* Acid (289°).**—The cinchonidine, brucine, quinine, ephedrine and ψ-ephedrine salts were also crystalline but no resolution was observed. (Experiments by Dr. F. H. Slinger.)

The monomethyl ester,[7] m. p. 130° (3.80 g.), and 4.17 g. of cinchonidine were dissolved in 160 cc. of methanol and the solution diluted with 100 cc. of distilled water at the boiling point. On cooling the solution deposited long fine needles, which were filtered and washed with 50 cc. of 60% aqueous methanol. The dry salt weighed 3.55 g. (45% of the theoretical yield from both enantiomorphs) and melted at 186–188°. The acid ester was regenerated from it by means of 5% hydrochloric acid and crystallized from ligroin (b. p. 70–90°). The heavy prismatic needles so obtained weighed 1.35 g. (36%) and had m. p. 134° and $[\alpha]^{27}D$ −9.1°. This *levo* **acid ester** after one more crystallization from ligroin had m. p. 133.5–134.5°, $[\alpha]^{27}D$ −10.7 ± 0.3° (1% solution in alcohol containing 5% water). Subsequent recrystallization failed to change the specific rotation.

The aqueous alcoholic mother liquor from the original precipitate, containing 190 cc. of methanol and 120 cc. of water, was diluted at the b. p. with 70 cc. of water. The solution then deposited 2.64 g. (33%) of heavy needles, m. p. 172–174°. From this there was regenerated 1.34 g. of *d*-acid ester, m. p. 134°. The alcoholic mother liquor when boiled free from alcohol yielded a further 230 mg. of the *d*-acid ester and 270 mg. of the original racemate. The total *dextro* **acid ester** was crystallized to constant rotation from ligroin. It had m. p. 133.5–134.5°, $[\alpha]^{27}D$ +10.3 ± 0.3° (1% solution in 95% alcohol). The *d*-acid ester was dried at 80° *in vacuo* and analyzed.

Anal. Calcd. for $C_{15}H_{24}O_4$: C, 67.14; H, 9.02. Found: C, 67.27, 67.21; H, 9.09, 9.03.

Esterification of the *levo*-monomethyl ester (160 mg.) with diazomethane in the usual manner gave 102 mg. of long prismatic needles of the meso dimethyl ester, m. p. and mixed m. p. 73–74°. A solution in alcohol showed no activity.

The *levo*-monomethyl ester (450 mg.) was boiled with 3 cc. of concentrated hydrochloric acid and 10 cc. of glacial acetic acid for twenty hours. The acid product was isolated by dilution and freed from starting material (160 mg.) by extraction with hot ligroin. The insoluble residue (220 mg.) on crystallization from 15 cc. of 95% alcohol yielded 170 mg. of inactive *cis-syn-cis* acid, m. p. 286–288.5°. The m. p. was not depressed by admixture with the authentic inactive acid and the solution showed no optical activity.

***cis-syn-trans* Acid (200°).**—The *l*-acid ester of the *cis-syn-cis* acid (1.11 g., m. p. 134°, $[\alpha]^{27}D$ −10.5°) was refluxed with sodium methoxide from 2 g. of sodium and 20 cc. of absolute methanol. After forty-eight, seventy-two and ninety-six hours 1 cc. of water was added. After five days the solvent was evaporated, and the residue acidified and extracted with ether. Evaporation of the ether left an oil which solidified when boiled with 40 cc. of ligroin. Recrystallization of the powder (980 mg.) from acetic acid failed to remove a small amount of the *cis-syn-cis* acid which was present. The impure acid was accordingly extracted with several small quantities of boiling benzene. This removed the *cis-syn-trans* acid and left the *cis-syn-cis*. After several further crystallizations from dilute acetic acid and from alcohol the pure *dextro-cis-syn-trans* **acid** crystallized in needles, m. p. 170–174°, $[\alpha]^{29}D$ +75° (1% in alcohol).

A similar inversion and hydrolysis was carried out on the *dextro*-acid ester of the *cis-syn-cis* acid (780 mg.). The crude acid product weighed 760 mg. Extraction with hot benzene removed 530 mg. of *levo-cis-syn-trans* **acid** which was crystallized to constant rotation, m. p. 171–174°, $[\alpha]^{28}D$ −75° (1% in 95% alcohol).

***trans-syn-trans* Acid (223°).**—The cinchonidine, quinine, ephedrine, ψ-ephedrine and strychnine salts could not be obtained crystalline. The brucine salt crystallized well from alcohol but showed no sign of resolution (experiment by Dr. Slinger).

(5) J. C. Speakman, *J. Chem. Soc.*, 490 (1941).

(6) All melting points are corrected.

(7) Linstead and Doering, THIS JOURNAL, **64**, 1991 (1942).

The half methyl ester of this acid should be capable of resolution but we have been unable as yet to find a suitable salt. The cinchonidine, cinchonine, ephedrine, brucine, quinine and strychnine salts could not be obtained crystalline (experiments by Miss E. J. Cook, Radcliffe College).

anti-Series

cis-anti-cis **Acid (198°).**—To a solution of 454.1 mg. of the acid and 1.051 g. of cinchonidine in 10 cc. of methanol there was added at the boiling point, 2.5 cc. of water. The solution deposited 1.03 g. of light needles, m. p. 194–200°, on cooling (A). The mother liquor was evaporated to dryness, the residue treated with acid and extracted with ether. The residue from the ether was crystallized from acetic acid. This yielded 100 mg. of the *dextro*-acid in heavy prisms, m. p. 235–239°. Recrystallization to constant rotation yielded material with m. p. 238.5–240.5°, $[\alpha]^{27}D$ +43 ± 1° (1% in 95% alcohol).

The salt (A) was recrystallized from 15 cc. of methanol and 2 cc. of water. This yielded 670 mg. of well-formed needles, m. p. 204.5–205.5°. Regeneration of the acid in the usual way gave the *levo*-acid which after two crystallizations from acetic acid formed prisms, m. p. 239–241° (132.8 mg.). This material was submitted to a second treatment with cinchonidine but its properties were unaltered (m. p. 238.5–240.5°). The specific rotation $[\alpha]^{26}D$ of a 1% solution in 95% alcohol was −45 ± 1°.

The *dextro-cis-anti-cis* acid was esterified in the usual manner with diazomethane, yield 75.1 mg. from 84.5 mg. The *d*-dimethyl ester crystallizes from light petroleum at −70° in large prisms, m. p. 26–28°. $[\alpha]^{25}D$ +69 ± 1° (1% in 95% alcohol).

trans-anti-trans **Acid (247°).**—The above *d*-dimethyl ester (140 mg.) of the *cis-anti-cis* acid was refluxed for 112 hours with 0.5 g. of potassium hydroxide in 2 cc. of methanol. A little water was added from time to time. The acidic product was isolated by means of ether in the usual way. After two crystallizations from dilute acetic acid, the *levo-trans-anti-trans* acid was isolated with m. p. 257–258.5°, $[\alpha]^{26}D$ −79.5 ± 5° (1% in 95% alcohol).

Resolution of the 247° Acid (Experiments by Dr. Slinger).—The acid (3.0 g.) and ephedrine (1.98 g.) were dissolved in 60 cc. of alcohol, 90 cc. of water was added and the mixture heated to effect solution. Slow cooling precipitated needles of a salt from which 950 mg. of a crude dextrorotatory acid was regenerated. This material was submitted to a second resolution with ephedrine. The product melted at 257.5–259° and had $[\alpha]^{20}D$ +77.5° (1% in alcohol). A further resolution failed to alter the m. p. or specific rotation.

An equal mixture of the *d*- and *l*-acids (4 mg. of each) was dissolved in dilute acetic acid. The solution deposited needles, m. p. 237–239°, of the *dl-trans-anti-trans* acid. After resolidifying, these melted at 245–247° and did not depress a sample of authentic *dl*-acid, m. p. 245–247°.

Summary

The perhydrodiphenic acid of m. p. 289° gives an acid methyl ester which can be resolved into *d*- and *l*-forms. Conversion of these into the acid or the dimethyl ester gives inactive material. The acid therefore has a symmetrical molecule and must belong to the *syn*-series.

The perhydrodiphenic acid of m. p. 198° (*cis-anti-cis*) can be resolved by means of cinchonidine. The dimethyl ester of the active ester on hydrolysis and double inversion with alcoholic alkali gives the *levo*-enantiomorph of the *trans-anti-trans* acid (m. p. 247°). The latter acid has been resolved to give the other enantiomorph. As two acids in this series can be resolved, it must be the *anti*-series.

The three acids of m. p.'s 289, 200 and 223°, therefore, constitute the *syn*-series and the acids of m. p.'s 198, 206 and 247°, the *anti*-series.

The acids of m. p.'s 200 and 206° are proved to be *cis-syn-trans* and *cis-anti-trans*, respectively.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Stereochemistry of Catalytic Hydrogenation. IV. Hexahydrodiphenic Acids

BY R. P. LINSTEAD AND SELBY B. DAVIS

Vocke[1] reported that the hydrogenation of diphenic ester over Raney nickel yielded a mixture of perhydro- and hexahydro-diphenic esters. From the hydrolysis product of this he isolated two hexahydrodiphenic acids of m. p. 242 and 220°. It was shown that the 242° acid could be converted into the 220° isomer, and the acids were assigned the structures of *cis*- and *trans*- modifications of the hexahydrodiphenic acid with one intact aromatic ring.

We have investigated the partial hydrogenation of diphenic acid in acetic acid solution over a platinum catalyst. If hydrogenation is stopped arbitrarily at the half-way stage, there is obtained a mixture consisting substantially of *cis-syn-cis*-perhydrodiphenic acid, m. p. 289°,[2] a hexahydrodiphenic acid and unchanged diphenic acid. The hexahydro acid melts at 242° and has other properties which show its identity with Vocke's acid of similar m. p. The presence of an

(1) Vocke, *Ann.*, **508**, 1 (1934).

(2) Linstead and Doering, THIS JOURNAL, **64**, 1991 (1942).