

over platinum. The anion would be expected to exist preferentially in the zigzag form and to yield *anti*-material on hydrogenation.

As it is unlikely that the agreement of the results is purely due to coincidence, it appears that the "open-chain" derivatives of diphenic acid (the acid itself, its ester and its two hexahydrides) *all hydrogenate in the coiled or pseudo-tricyclic phase*. This would mean that this phase is the one which is most readily adsorbed on the catalyst. We can see no particular reason for this preference. Hydrogen bonding between the carboxyl groups could be invoked for the acid but not for its ester.

The hypotheses which are advanced in this paper are tentative and require additional experimental investigation from many points of view. This we hope to provide in due course. One aspect which has not yet been mentioned will have to be considered before these hypotheses could be applied generally. The present work has been almost completely confined to the ortho-substituted compounds. (This is to some extent inevitable in the study of polycyclic aromatic structures). It may be found that the behavior of compounds in which the orienting groups are further apart may be much less regular than those studied

in the present work. There are several indications in the literature that this may be true, for example, the considerable degree of *trans*-hydrogenation of terephthalic acid, as mentioned in Table I.

Summary

The stereochemistry of the hydrogenation of a number of derivatives of diphenic acid and of phenanthrene over a platinum catalyst is discussed. The nine compounds studied all hydrogenate *cis* and *syn*.

The results are explained on the basis of three hypotheses.

1. When one or more aromatic rings are hydrogenated during a single period of adsorption, the hydrogen atoms add to one side of the molecule.

2. The orientation of the adsorption of the aromatic molecule on the catalyst is affected by hindrance between the catalyst and the substrate.

3. The open-chain derivatives of diphenic acid are hydrogenated in the coiled phase.

Earlier work is discussed in the light of these views, and certain applications to related fields are indicated.

CONVERSE MEMORIAL LABORATORY

CAMBRIDGE, MASSACHUSETTS RECEIVED APRIL 30, 1942

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Stereochemistry of Catalytic Hydrogenation. II. The Preparation of the Six Inactive Perhydrodiphenic¹ Acids

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

Earlier work by Linstead and A. L. Walpole² on the hydrogenation of diphenic acid had revealed the following facts: (1) Catalytic hydrogenation of the free acid in acetic acid solution over platinum gave a perhydro acid of m. p. 273°. (2) Similar hydrogenation of dimethyl diphenate gave a solid perhydro ester, m. p. 73°, which on alkaline hydrolysis gave a perhydro acid of m. p. 220°. (3) Hydrogenation of dimethyl diphenate over Raney nickel by Adkins' procedure gave a mixture of the ester of m. p. 73° and a liquid ester which on alkaline hydrolysis gave a third perhydro acid of m. p. 244°. Other early work on the perhydro acids is reviewed later in the present paper.

(1) The common 2,2'-diphenic acid is referred to as diphenic acid for the sake of brevity throughout these papers. Its hydrogenated derivatives are correspondingly named without prefix.

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

We have now made a fuller study of the hydrogenation of diphenic acid and its derivatives over platinum, and of the stereochemical inversion of the products. This has led to the isolation of eleven distinct optically inactive hydrodiphenic acids. Six of these are dodecahydro- (perhydro-) derivatives; three are decahydro-, containing one double bond; and the remaining two are hexahydro-, and contain one intact benzene ring. This paper is concerned only with the perhydro acids.

As pointed out by Linstead and Walpole,² perhydrodiphenic acid can exist in six inactive modifications, four of which are resolvable. All the possible forms have therefore been obtained. Experiments on their resolution are described in the following paper.

The *syn*-Series

When diphenic acid is exhaustively hydrogenated in acetic acid solution over Adams catalyst, one main product and three by-products are obtained. The main product is a perhydro-acid, $C_{12}H_{20}(CO_2H)_2$, m. p. 289° . This is easily isolated and purified owing to its low solubility. Accompanying this, in low amounts, are two isomeric perhydro-acids melting at 198 and 200° , respectively. Usually also there is a certain amount of a hexahydro-acid $C_{12}H_{14}(CO_2H)_2$ of m. p. 242° , which occurs even when the uptake of hydrogen appears to have ceased completely. The proportions of the products appear to vary slightly with variations in the experimental procedure and in the catalyst, but the acid of m. p. 289° always constitutes the bulk of the product.

The acid of m. p. 289° is a slightly purer form of the material of m. p. 273° already reported by Linstead and Walpole² and by Hüchel.³ The m. p. varies with the rate of heating, and this fact may contribute to the lower m. p.'s previously recorded.

The same compound (accompanied by the same impurities) is formed when the hydrogenation of the acid is carried out in acetic acid containing 2% of hydrochloric acid. The hydrogenation also takes the same course in alcohol but in this case the reaction is much slower. When diphenic anhydride is hydrogenated over platinum and the product hydrolyzed, the perhydro acid of m. p. 289° is also obtained. Sodium diphenate resisted catalytic hydrogenation in aqueous solution. Dimethyl diphenate, however, was exhaustively hydrogenated over platinum without difficulty, and, in agreement with Linstead and Walpole,² the main product was a perhydro ester, m. p. 73° . It is proved below that this is the dimethyl ester of the 289° acid and that its alkaline hydrolysis is anomalous. There is, therefore, a general tendency for the diphenic acid system to be hydrogenated over platinum to the perhydro form corresponding with the acid of m. p. 289° .

Because of the complicated inversions which can occur in the chemistry of the 289° acid and its derivatives, it was necessary to establish conclusively its relationship with its anhydride and esters. This was done as follows.

The perhydrodiphenic acid of m. p. 289° on treatment with acetic anhydride yielded a mixed anhydride, $CH_3COOCC_{12}H_{20}COOCC_3H_7$, which

on sublimation gave the simple perhydrodiphenic anhydride, $C_{12}H_{20}(CO)_2O$, m. p. 146 – 147° . From this the parent acid could be regenerated. These results confirm those already reported.² Treatment of the anhydride with sodium methoxide yielded a monomethyl ester, m. p. 129° . When either the 289° acid or its monomethyl ester was treated with diazomethane, there was obtained a dimethyl ester of m. p. 73 – 74° . This was identical with the perhydro ester prepared by the direct hydrogenation of dimethyl diphenate. Fischer-Speier esterification of the 289° acid or of the 129° acid ester also yielded the 73° dimethyl ester, but the reaction was slow. The best preparative method for the esterification of the acid is to boil it for several days with methanol containing 2% of fuming sulfuric acid. Treatment of the anhydride with methanol and a trace of oleum gave a mixture of the 129° acid ester and the 73° dimethyl ester. When the 289° acid was treated with one equivalent of diazomethane, the main reaction was the formation of the dimethyl ester, an approximately equivalent amount of the acid remaining unchanged. A small amount (10%) of the 129° acid ester was also formed. It therefore appears that the acid ester reacts more readily with diazomethane than does the dicarboxylic acid. Acid hydrolysis of the 73° ester yielded a mixture of the 289° acid and the 129° acid ester. Acid hydrolysis of the 129° acid ester gave the 289° acid.

It was shown by Linstead and Walpole² that hydrolysis of the 73° dimethyl ester with alcoholic potash yielded an acid of m. p. 220° , identical with that formed by heating the 289° (273°) acid with hydrochloric acid at 200° . In the present work, this result was confirmed and the perhydro-acid produced was found to melt, in the pure state, at 223° . This hydrolysis involved an inversion of configuration at one or both of the carboxyl groups. It has frequently been observed⁴ that esters, in which the carbalkoxyl group is directly attached to a cyclic carbon atom which carried a hydrogen, can be inverted in configuration by treatment with sodium alkoxide. (This inversion normally proceeds in the direction *cis*→*trans*; however, it is the existence rather than the direction of the inversion which we wish to stress at the moment.) We therefore attempted to invert the 73° ester without hydrolysis by

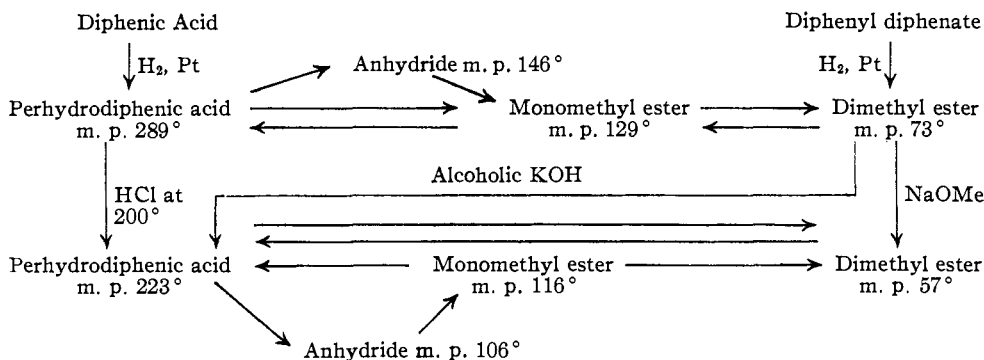
(4) Hüchel and Goth, *Ber.*, **58**, 447 (1925); Cook and Linstead, *J. Chem. Soc.*, 946 (1934).

(3) Hüchel, note in Vocke's paper, *Ann.*, **508**, 1 (1934)

heating it with sodium methoxide. This was successful; the ester was converted almost completely into an isomeride of m. p. 57°. A small amount of another isomeride, m. p. about 10°, also was formed. This is discussed later.

Acid hydrolysis of the 57° ester yielded the perhydrodiphenic acid of m. p. 223°. Esterification of the 223° acid with diazomethane yielded the ester, m. p. 57°. The acid was also characterized by conversion into the anhydride, m. p. 106° (in agreement with Linstead and Walpole²) and thence the monomethyl ester, m. p. 116°. Acid hydrolysis of the latter regenerated the 223° acid, while treatment with diazomethane formed the dimethyl ester, m. p. 57°.

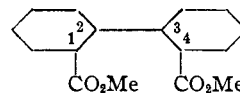
The inter-relationships between the substances so far mentioned are summarized.



A curious anomaly in the literature should be mentioned at this point. Hückel³ reported that his acid, m. p. 273°, on esterification with diazomethane gave an ester, m. p. 57°. There can be little doubt that Hückel's acid was substantially our 289° acid. We have performed this esterification many times with diazomethane, as well as by the other methods already mentioned. Our product has always melted at 73° and we are convinced that this material is the authentic dimethyl ester. It would appear most probable that Hückel's note contains a misprint. This is supported by the fact that our 73° ester crystallizes in beautiful long needles, and this is the form described by Hückel for his "57°" ester. On the other hand, our 57° ester has never crystallized in this form. From the agreement of the m. p. with that of the invert ester, an alternative explanation for Hückel's result is that an inversion due to some contamination by alkali may have occurred in his work.

The question now arises, what is the nature of the inversion of configuration which occurs when

the ester of m. p. 73° is converted into its isomeride of m. p. 57°? We are concerned only with the stereochemistry at carbons 1 and 4 (in the formula given below).



The configuration at C₂ and C₃—the "backbone configuration"^{4a}—is fixed in the catalytic hydrogenation and will not be affected by the experimental conditions of our inversions. As regards C₁ and C₄, there are three possibilities. (1) Either these both have the same configuration in the 289° acid (and 73° ester) and both centers are inverted (*e. g.*, *cis-cis* → *trans-trans*); or (2) both have the same initial configuration and only one

center is inverted, because the *cis-trans* is the alkali-stable form, (*e. g.*, *cis-cis* → *cis-trans*); or (3) they have different initial configurations and one center is inverted (*e. g.*, *cis-trans* → *trans-trans*). It is proved below that the first of these possibilities is correct.

It was first shown by direct experiment that the 289° acid was stable to hot aqueous alkali. The inversion of the ester during treatment with alcoholic alkali therefore occurs in the unhydrolyzed ester, and cannot be brought about at the carbon atom carrying the ionized carboxyl. (This is of course due to the difference in the ease of enolization of the two groups.) The half-ester of the 289° acid therefore contains *one* group which is capable of effecting an inversion. If possibility (1) is correct, treatment with alkali should yield either a new acid (inversion + hydrolysis) or a new half-ester (inversion) according to the experimental conditions. If possibility (2) is correct, then either there will be no inversion

(4a) See Linstead and Walpole² and the preceding paper for a general outline of the stereochemistry.

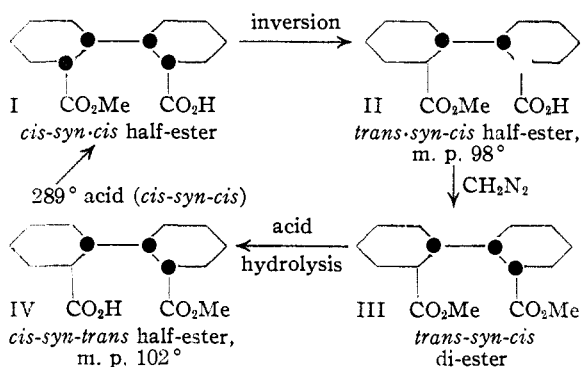
or inversion to the 223° acid series will occur; the same is true of possibility (3).

The monomethyl ester of the 289° acid (m. p. 129°) was accordingly refluxed first with sodium methoxide, and the solution was then diluted somewhat with water and the heating continued. The product was a new perhydrodiphenic acid, m. p. 200°. (When the same acid ester was hydrolyzed with boiling aqueous alkali it gave the parent acid, m. p. 289°. The small amount of alcohol formed in this hydrolysis was clearly insufficient to effect any appreciable inversion.) When the 129° monomethyl ester was refluxed with sodium methoxide in the absence of water, it was converted into an isomeride of m. p. 98°. Acid hydrolysis of the new monomethyl ester yielded the new acid, m. p. 200°. Esterification of both the 98° monomethyl ester and the 200° acid with diazomethane yielded a dimethyl perhydrodiphenate, m. p. 14°. This material was identical with the by-product obtained in the inversion of the 73° dimethyl ester into the 57° isomeride.

An interesting observation which shows the ease of inversion in alkaline medium is the following. The anhydride of the 289° acid was boiled with some methanol which had been freshly distilled from baryta. It yielded mainly the corresponding monomethyl ester, m. p. 129°, but also, in 14% yield, the acid ester (m. p. 98°) of the half-invert acid. The partial inversion was traced to the presence of a small amount of barium methoxide in the methanol.

When the dimethyl ester (m. p. 14°) of the new acid was hydrolyzed for a comparatively short time with hydrochloric and acetic acids, it gave a mixture of the parent acid (m. p. 200°) and an acid ester. The latter melted at 102° and was not identical with that (m. p. 98°) described above; it depressed its m. p. and behaved differently on alkaline hydrolysis. It is clear therefore that this is the second acid ester which is theoretically possible for the half-invert acid, owing to the non-equivalence of the two carboxyl groups. The carbomethoxyl group preferentially hydrolyzed by acid is that on the *inverted* side of the molecule. To make this clearer we shall anticipate the assignment of the configuration to the acids. The 200° acid has been conclusively proved to have the *cis-syn-trans* configuration (see Part III). To distinguish between its two acid esters we shall refer to the configuration *on the ester side* first.

Thus, in the *trans-syn-cis* half-ester, the hydrogen atom on the carbon which carries the carbomethoxyl group is orientated *trans-* to that on the neighboring backbone carbon; whereas that on the carbon which carries the free carboxyl group is orientated *cis-* (II). The preparation and naming of the two acid esters is shown in the following scheme.



The *cis-syn-trans* acid with acetic anhydride yields a distinct anhydride, m. p. 104°, from which it can be regenerated. The anhydride is not inverted by prolonged boiling with acetic anhydride.

It was pointed out above that the *trans-syn-cis* half-ester (II) was prevented from inverting further because its configurationally unstable (*cis*) ring carried the carboxyl group which was unable to provide a path for the inversion under the experimental conditions used. This is not true of the second half-ester (IV), for this carries the carbomethoxyl group on the unstable ring. It was accordingly expected that this would invert on hydrolysis with alcoholic alkali and this was realized. The 102° half-ester yielded the fully inverted acid of m. p. 223°. This series of reactions makes it certain that the 200° acid is intermediate in configuration between its isomers of m. p. 289° and 223°. We can now answer the question raised at the beginning of this section explicitly by saying that the inversion of the 73° to the 57° ester is a *double inversion*. We are not concerned at the moment with the proof of the direction of this but it is shown in later papers that it is *cis* \rightarrow *trans*.

The acids of m. p. 289, 200 and 223° form one of the "backbone" series (*syn-* and *anti-*). It is proved later that this is the *syn*-series of perhydrodiphenic acids.

The *anti*-Series

The acids of this group are less accessible than their *syn*-isomers. This is particularly true of the

two members which contain configurationally unstable (*cis*-) arrangements.

It has already been stated that the catalytic hydrogenation of diphenic acid yields, besides the 289° acid, minor quantities of other hydrogenation products. The separation of these was laborious and difficult. Little or no benefit was achieved by converting the acids into their esters and carefully fractionating these. Direct fractional crystallization was useless in the early stages except for the isolation of the 289° acid. The following technique was of considerable assistance. The mixed acids were dissolved in sodium carbonate and the solution acidified in stages at the boiling point with dilute hydrochloric acid. Successive small crops of acids were so obtained. The method depends upon differences in acidity as well as in solubility. By its use the perhydro acids separate first and incompletely hydrogenated acids, which are aromatic and hence stronger, come down later. It was also possible by this means to separate a resinous ψ -acidic material (probably a lactone) which was sometimes present.

As an example, when the product of the hydrogenation of diphenic acid over platinum in alcohol was fractionated in the above manner, a succession of fractions were obtained, of which the principal components were

- Crops 1-4: Perhydro acid, m. p. 289° (*cis-syn-cis*)
 Crop 5: Perhydro acids, m. p. 289° and m. p. 198° (*cis-anti-cis*)
 Crop 6: Perhydro acid, m. p. 198°
 Crop 7: Perhydro acids, m. p. 198° and m. p. 200° (*cis-syn-trans*)
 Crop 8: Perhydro acid, m. p. 200°, and hexahydro acid, m. p. 242° (*cis*)
 Crops 9-10: Mainly diphenic acid

The various fractions could subsequently be further purified by direct crystallization. This enabled an estimate to be made of the relative amounts of the various products. In the above mixture these were approximately

- Perhydro acids: *cis-syn-cis*, 53%; *cis-anti-cis*, 10%; *cis-syn-trans*, 7%
 Hexahydro acid: 10%
 Diphenic acid: 20%

The method was found superior to that used by Vocke⁵ for the separation of perhydro and hexahydro diphenic acids, which involves the use of barium salts.

In material exhaustively hydrogenated over platinum in acetic acid solution, the amount of

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

unchanged or incompletely reduced acid was much lower. The proportion of *cis-syn-cis* material expressed as a percentage of the total perhydro acids was about the same, 70-80%, and the by-products were the same, namely, the *cis-anti-cis* acid, m. p. 198°, and the *cis-syn-trans* acid m. p. 200°. The isolation of these products is described in detail in the experimental section. The two acids were quite distinct and gave different series of derivatives. The *cis-syn-trans* (200°) acid was identical with that obtained by the half-inversion of the *cis-syn-cis* (289°) acid as described above. The final purification of the new acid (m. p. 198°) was conveniently achieved through the anhydride (m. p. 100°). The acid yielded crystalline di- and mono-methyl esters, melting at 44 and 99°, respectively. Acid hydrolysis of both these esters regenerated the parent acid.

It seemed reasonable to suppose that the new acid would have two configurationally unstable centers and would therefore be capable of half-inversion and of double inversion, as in the case of the 289° acid and its derivatives. The methods used in the *syn*-series were therefore applied to the new *anti*-acid. The monomethyl ester on hydrolysis with alcoholic potash yielded a new acid, m. p. 206°, which gave a distinct anhydride, m. p. 93°. The dimethyl ester (m. p. 44°) on similar hydrolysis gave the known acid m. p. 244° of Vocke⁵ and of Walpole and Linstead.² This is now found to melt at 246-248° and to yield a dimethyl ester, m. p. 86°. The fact that this acid has previously been obtained by the hydrolysis of perhydro esters with alcoholic alkali is understandable. It represents the final alkali-stable form of all the *anti*-material originally present in the ester.

The above results make it clear that the *anti*-series consists of the three acids of m. p. 198, 206 and 248°, and that the acid of m. p. 206° is intermediate in configuration between the other two.

The melting points (in round numbers) of the six inactive perhydrodiphenic acids and of their derivatives are summarized in the table. Un-

Acid, probable (or certain) configuration	Melting points, °C.			
	Anhydride	Mono-methyl ester(s)	Di-methyl ester	
<i>cis-syn-cis</i>	289	147	126	73
<i>cis-syn-trans</i>	200 (and 174)	104	98 and 102	14
<i>trans-syn-trans</i>	223	106	117	57
<i>cis-anti-cis</i>	198	100 (and 96)	99	44
<i>cis-anti-trans</i>	206	93
<i>trans-anti-trans</i>	247	242	..	86

stable dimorphous modifications are given in parentheses.

There is no doubt that these six isomers are distinct individuals. The three acids with very similar melting points (200°, 198°, 206°) depress each others' melting points, and have distinctive crystalline forms. Their derivatives are also different. All the six inactive forms, which are theoretically possible, have therefore been made and interrelated.

There were on record in the literature, however, two other substances to which the perhydrodiphenic acid structure has been assigned. These are the acid of m. p. 213°, described by Vocke,⁵ and that of m. p. 203°, prepared by Linstead and Walpole.² After the present work had been completed, Marvel and White⁶ described what appeared to be a further isomer, m. p. 174–175°. It became necessary, therefore, to consider the nature of these compounds.

Vocke Acid, m. p. 213°.—This acid was obtained by Vocke⁵ by alkaline hydrolysis of the product of the hydrogenation of dimethyl diphenate over nickel. It was separated from the *trans-anti-trans* (247°) acid, which was Vocke's main perhydro-product, by a tedious fractional crystallization. We have never obtained a substance with these properties. It seems most probable that Vocke's acid was an impure form of our *trans-syn-trans* acid (m. p. 223°). This would tally with the method of preparation, for all the *syn*-material would be expected to assume the *trans-trans* configuration during the alkaline hydrolysis. Moreover, there is no doubt that *syn*-material is formed in hydrogenations over nickel, because the solid *cis-syn-cis*-dimethyl ester can be isolated in quantity from the unhydrolyzed reaction product.² The m. p. of Vocke's anhydride (80°) does not agree with ours (106°) but his compound was not analyzed and it is possible that it was a mixed anhydride with acetic acid, similar to that which Linstead and Walpole isolated from the *cis-syn-cis* acid.² The other discrepancy lies in the ease of ketonization. Linstead and Walpole² were able to form a pyroketone from the 223° acid, whereas Vocke observed that his acid and anhydride sublimed practically undecomposed. An alternative possibility is that Vocke's 213° acid may have contained one double bond, *i. e.*, it may have been a decahydrodiphenic acid. We have isolated a

(6) Marvel and White, *THIS JOURNAL*, **62**, 2739 (1940).

decahydrodiphenic acid of m. p. 212° as a by-product in certain hydrogenations. Vocke's analytical figures, however, correspond with a perhydro product.

Linstead and Walpole Acid, m. p. 203°.—This differs from the six isomerides described above. The position with regard to it is more complicated. It was prepared² by the nitric acid oxidation of a ketone, m. p. 51°, itself obtained⁷ by the hydrogenation of two unsaturated ketones of m. p. 39 and 94°. These two unsaturated ketones were first prepared by Marvel and co-workers⁸ by cyclization of di- Δ^1 -cyclohexenylacetylene with formic acid, and were considered by them to have a hydrophenanthrene structure. Linstead and Walpole⁷ reduced the two unsaturated ketones to hydrocarbons which were dehydrogenated to phenanthrene. Moreover, treatment of the saturated ketone with methylmagnesium iodide followed by dehydrogenation yielded 9-methylphenanthrene.⁷ This provided definite evidence in support of Marvel's proposed skeletal structure. Further supporting evidence by the same method of attack has been reported by Marvel, Pearson and White.⁹ It appeared to follow that the saturated ketone was 9-keto-perhydrophenanthrene and the acid obtained from it by oxidation was a perhydrodiphenic acid.

Marvel⁸ was originally led to assign the hydrophenanthrene structure to his ketones from the behavior of a hydrocarbon obtained from one of them. This yielded on selenium dehydrogenation a product very similar in properties to what was at the time believed to be *trans-as*-octahydrophenanthrene. Levitz, Perlman and Bogert¹⁰ have conclusively proved that this substance is a spirane. They therefore suggested that Marvel's ketones are also spiranes, a possibility earlier rejected by Marvel.¹¹

The evidence summarized above on the structure of Marvel's ketones is inconclusive. However, now that six distinct perhydrodiphenic acids have been prepared and interrelated, there are only two possibilities for the 203° acid. Either it has a different skeletal structure, or the perhydrodiphenic acid series contains more isomeric forms than are demanded by classical

(7) Linstead and Walpole, *J. Chem. Soc.*, 842 (1939).

(8) Marvel and co-workers, *THIS JOURNAL*, **58**, 972 (1936); **59**, 2666 (1937).

(9) Marvel, Pearson and White, *ibid.*, **62**, 2741 (1940).

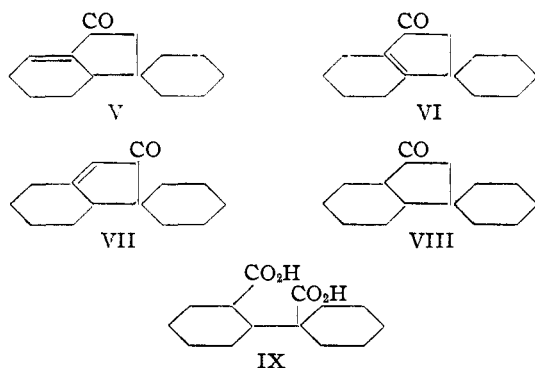
(10) Levitz, Perlman and Bogert, *J. Org. Chem.*, **6**, 105 (1941).

(11) Marvel, Mazingo and Kirkpatrick, *THIS JOURNAL*, **61**, 2003 (1939); *cf.* Marvel and Walton, *J. Org. Chem.*, **7**, 88 (1942).

stereochemical theory. In the latter connection, the least unreasonable suggestion would be that there was a restriction of free rotation about the inter-nuclear bond, as in the case of various substituted diphenic acids. Many arguments could be raised against this possibility. It will be sufficient to quote the following direct experimental evidence. We find that *all* the authentic perhydrodiphenic acids yield pyroketones, whereas the 203° acid does not. It is inconceivable that the delicate isomerism due to restricted rotation could survive the high temperatures (300°) involved in this reaction.

It is, therefore, concluded that the 203° acid cannot be a perhydrodiphenic acid. Hence the 51° ketone is not a perhydrophenanthrene derivative and the unsaturated ketones of Marvel cannot have a phenanthrene skeleton.

We, therefore, accept as probable the spirane skeleton proposed by Levitz, Perlman and Bogert,¹⁰ which is most easily reconciled with the dehydrogenation results. The following further suggestions as to the structure are made. It was shown by Linstead and Walpole⁷ that both the unsaturated ketones have $\alpha\beta$ -double bonds and give the same pair of saturated ketones on hydrogenation. The carbonyl group is now placed in the five-membered ring because of the consistent formation of 9-alkyl phenanthrenes after Grignard reaction and dehydrogenation, as noted above.^{7,9} Moreover, this offers a simple explanation for the fact that the 203° acid forms an anhydride but no pyroketone.² The three possible structures for the two unsaturated ketones which came up for consideration are (V), (VI) and (VII)



The structure corresponding to (VII) in the hydrophenanthrene series was eliminated by a stereochemical argument (Linstead and Walpole⁷),

which is not valid in the spirane series. However, (VII) can be ruled out because it cannot possibly give the same ketones on hydrogenation as either (V) or (VI). Structures (V) and (VI), therefore, are the most acceptable for the two unsaturated ketones. Woodward¹² has given spectrographic evidence which indicates that (VI) is to be preferred for the ketone of m. p. 94°, and (V) for the more common isomeride, m. p. 39°. Essentially the same spectrochemical deduction has independently been drawn by Evans and Gillam¹³ from Woodward's generalization. They placed the bonds in the equivalent positions in keto-decahydrophenanthrene molecules.

The two saturated ketones of Linstead and Walpole now become the *cis*- and *trans*-forms of (VIII). It is probable that the more stable modification (m. p. 51°) is the *cis*-form, judging from the relative stabilities of the α -hydrindanones. The acid of m. p. 203°, must have structure (IX) if the spirane skeleton is correct. It is therefore dicyclohexyl-1,2'-dicarboxylic acid.

Marvel and White Acid, m. p. 174°.—A sample of this material was kindly sent us by Professor Marvel. It was found to be essentially a dimorphic modification of the *cis-syn-trans* acid (m. p. 200°). When crystallized from dilute acetic acid it separated in the high melting form and was then identical with our material. Moreover, the melt of the 174° form soon solidified and then remelted at 198–200°.

Before the present work was completed, two "perhydrodiphenic acids" were known which apparently broke the Blanc rule regarding the pyrolysis of adipic acids. These were the 203 and 213° acids, which have been discussed above. It is now plain that the 203° acid is not a perhydrodiphenic acid at all, and the validity of the work on the 213° acid is doubtful. We propose to reserve further discussion on this general topic until our investigation of the pyrolysis of the new perhydrodiphenic acids is complete.

The optical resolution of the perhydrodiphenic acids is described in Part III, and the evidence for the assignment of configuration is given in Parts III and V. The bearing of the new result on the stereochemistry of perhydrophenanthrene derivatives is discussed in Parts VI and VII.

(12) Woodward, *THIS JOURNAL*, **64**, 76 (1942); *cf. ibid.*, **63**, 1123 (1941).

(13) Evans and Gillam, *J. Chem. Soc.*, 818 (1941).

Experimental¹⁴

Intermediates

The following procedures, based on those of Oyster and Adkins¹⁵ and Linstead and Walpole,² respectively, were found satisfactory for the routine preparation of pure diphenic acid from crude phenanthrene.

Potassium dichromate (300 g.) was dissolved in a mixture of 500 cc. of concentrated sulfuric acid and 1500 cc. of water contained in a 4-l. beaker. Without cooling, 100 g. of crude phenanthrene was added with vigorous stirring. This operation requires caution as much heat is evolved. After the reaction had quieted, a further 300 g. of potassium dichromate was added. The mixture was allowed to stand for one hour, and was then diluted with water (2 l.) and allowed to cool. The granular product was filtered off, washed thoroughly with water and dried; yield of crude phenanthraquinone, 89 to 94 g. (76–80%), m. p. 190–194°.

The quinone was oxidized in 100-g. lots in a 2-l. flask, fitted with stirrer and condenser, by means of a mixture of 120 cc. of 30% (100 vol.) hydrogen peroxide, 900 g. of 3% hydrogen peroxide and 300 cc. of glacial acetic acid. The mixture was boiled *very gently* for three hours. The product was filtered hot (steam funnel) from a little unreacted anthraquinone, and allowed to crystallize overnight in the ice-box. The crude diphenic acid was filtered off and dried (45 to 48.5 g.). To obtain material capable of being readily hydrogenated, the following procedure was used: 12 g. of the crude acid was dissolved in 1.5 l. of boiling water, the solution filtered and boiled for one-half hour with 2 g. of Norit. The solution was then filtered and the treatment repeated twice, using thirty minutes of boiling with 2 g. and 1 g. of Norit, respectively. The final filtrate deposited on cooling 6–7 g. of glistening plates of diphenic acid, m. p. 232–233°. The over-all yield from the crude phenanthrene varied between 18 and 21%.

The acid (25 g.) was esterified by five days of refluxing with 250 cc. of absolute methanol (freshly distilled from magnesium methoxide) containing 14 g. of dry hydrogen chloride. The product was separated by means of sodium carbonate into neutral and acid fractions. The neutral product was crystallized once from methanol which yielded 25.4 g. (91%) of pure dimethyl diphenate, m. p. 73–74°. Acidification of the sodium carbonate extract yielded a small quantity of the *monomethyl ester* of diphenic acid, which does not appear to have been described previously. It crystallizes from dilute alcohol in delicate plates, m. p. 110–111°.

Anal. (material dried at 80° *in vacuo*). Calcd. for C₁₅H₁₂O₄: C, 70.30; H, 4.72. Found: C, 70.45, 70.34; H, 4.80, 4.64.

syn-Series

289° Acid (*cis-syn-cis*¹⁶).—All the hydrogenations described in this paper were carried out in a Parr apparatus using an initial gage pressure of hydrogen of about 60 lb./sq. in. The glacial acetic acid was refluxed over, and then

distilled from potassium permanganate. The Adams catalyst was prepared following Bruce.¹⁷

A solution of 20 g. of diphenic acid in 250 cc. of acetic acid was shaken under hydrogen with 1 g. of catalyst. Most hydrogenations went to completion in from one to four days without the addition of more catalyst. Occasionally a further gram of platinum oxide had to be added to complete the reduction. The bulk of the perhydro-acid separated from the solution during the reaction.

The catalyst and precipitate were filtered off from the product on a sintered-glass funnel and washed with 100 cc. of glacial acetic acid. The investigation of the filtrate (A) is described later. The solid acid was extracted from the catalyst by means of 5% aqueous alkali and was precipitated by dilute hydrochloric acid. The crude product weighed 11.2–12.7 g. (56–63%) and melted at 282–284°. Recrystallization from 500 cc. of glacial acetic acid yielded the pure *cis-syn-cis*-perhydrodiphenic acid, m. p. 287–289°.

The m. p. of this acid varies with the rate of heating owing to the formation of anhydride and to stereochemical inversion. For these reasons, also, very sharp values cannot be obtained. The above constant was obtained by immersing the capillary at 280° and raising the temperature 1° every six seconds. A mixture with a sample of the acid of Linstead and Walpole² (recorded m. p. 273–274°) melted under the same conditions at 285–287°.

Anal. (material dried at 110° *in vacuo*). Calcd. for C₁₄H₂₂O₄: C, 66.13; H, 8.72. Found: C, 66.21, 66.43; H, 8.83, 8.88.

The hydrogenation in alcohol solution was much slower and required frequent addition of fresh catalyst. The main product was the 289° acid. The separation of the products is more conveniently considered later under the 198° (*cis-anti-cis*) acid. The *cis-syn-cis* acid can also be prepared by catalytic hydrogenation of *cis*-hexahydrodiphenic acid. This is described in Part IV.

Derivatives of the 289° Acid

Anhydride.—Following Linstead and Walpole,² the acid (6 g.) was refluxed for twenty hours with 100 cc. of acetic anhydride. The excess of reagent was removed *in vacuo* and the solid residue sublimed onto a cold "finger" at 130° and 2 mm. After three sublimations, the acetic anhydride had been practically all eliminated and 4.0 g. (72%) of a crude anhydride m. p. 137–142° remained. Crystallization of this (1.6 g.) from 100 cc. of ligroin (b. p. 60–90°) gave 1.15 g. of the pure anhydride, shining plates, m. p. 146–147°; 1.5 g. of unsublimable material, probably polymeric anhydride, was also obtained.

Dimethyl Ester.—(1) The acid (5 g.) was refluxed for four days with 100 cc. of absolute methanol and 2 cc. of fuming sulfuric acid, containing 15% SO₃. The alcohol was boiled off and the residue was stirred with 100 cc. of hot 10% sodium carbonate solution. On cooling the ester crystallized, and was filtered off (m. p. 67–72°, yield, 5.3 g., 95%). One crystallization from dilute methanol gave 4.7 g. (85%) of long needles of pure *cis-syn-cis* dimethyl perhydrodiphenate, m. p. 73–74°. This material was identical with that prepared by Linstead and Walpole² by hydrogenation of dimethyl diphenate. Acidification of the sodium carbonate solution gave 0.13 g. (2.5%) of the

(14) All melting points are corrected.

(15) Oyster and Adkins, *THIS JOURNAL*, **43**, 208 (1921).

(16) The configurations assigned are discussed more fully in the following papers. They have been added for convenience in reference.

(17) Bruce, *THIS JOURNAL*, **68**, 687 (1936).

monomethyl ester, m. p. 124–126°, which is described more fully below.

(2) The acid (5.08 g.) dissolved in 150 cc. of dioxane was added to an ethereal solution of diazomethane, prepared from 10.3 g. of nitroso-methyl urethan. After two days at room temperature the product was treated with acetic acid, the solvent removed and the residue crystallized from methanol, yield 89%, m. p. and mixed m. p. 73–74°.

Monomethyl Ester.—The anhydride, m. p. 147° (3.22 g.) was treated with a solution of sodium methoxide from 1.26 g. (4 moles) of sodium in 60 cc. of methanol. After three hours at room temperature, the solvent was removed, the residue taken up in water and the solution filtered and acidified. The crude half-ester which separated was dried and recrystallized from ligroin, b. p. 60–90° (ca. 250 cc.). This yielded 2.80 g., 76.5%, of the pure monomethyl ester of *cis-syn-cis*-perhydrodiphenic acid, small plates, m. p. 128.5–129.5°.

Anal. (material dried *in vacuo* at 110°). Calcd. for $C_{18}H_{24}O_4$: C, 67.14; H, 9.02. Found: C, 67.32, 67.12; H, 9.09, 9.08.

An alcoholic solution of 2.54 g. of the 289° acid was treated with one equivalent of diazomethane (from 2.11 cc. of nitrosomethyl urethan). The solution was immediately decolorized. It was extracted with 5% aqueous sodium hydroxide. The ethereal layer yielded 1.07 g. (38%) of the dimethyl ester, m. p. 72–74°. The alkaline extract was acidified and the crystalline precipitate so obtained was extracted with boiling ligroin (b. p. 60–90°). The residue (1.12 g., 44%) was the unchanged acid (m. p. 270–277°). The ligroin extract yielded the acid ester (0.28 g., 11%) which melted at 127–129° after one crystallization from ligroin.

When the monomethyl ester (150 mg., m. p. 129°) was treated with diazomethane in ether, it yielded the dimethyl ester (150 mg., m. p. and mixed m. p. 73°).

The anhydride, m. p. 147° (470 mg.), was refluxed for sixty-four hours with 20 cc. of methanol containing a drop of fuming sulfuric acid (15% SO_3), moisture being excluded. The methanol was removed and the residue extracted with boiling ligroin (b. p. 70–90°). Fractional crystallization of the ligroin solution yielded 160 mg. (30%) of the acid ester (less soluble) and 280 mg. (50%) of the dimethyl ester, identical with material already described.

Hydrolyses.—The dimethyl ester, m. p. 74° (500 mg.), was refluxed for twenty hours with 5 cc. of glacial acetic acid and 2 cc. of concentrated hydrochloric acid. The product was diluted with water and the precipitate so obtained was extracted with aqueous sodium carbonate. The insoluble portion (170 mg.) was the unchanged dimethyl ester. The carbonate solution was heated to the boiling point and treated with hydrochloric acid in drops until crystals began to appear. The acid ester (150 mg., m. p. 126–127.5°) then separated. Completion of the acidification yielded the slightly impure dicarboxylic acid, m. p. 270–272°, mixed m. p. 275–285° (140 mg.).

A similar acid hydrolysis of the monomethyl ester also yielded the *cis-syn-cis* acid (m. p. 282–285°, mixed m. p. 284–287°). The acid ester (10.3 mg.) was refluxed for fifty-two hours in a soft-glass apparatus with 2 cc. of 20% aqueous sodium hydroxide. The acidic product, crystal-

lized from acetic acid, yielded 6.5 mg. (67%) of pure *cis-syn-cis* acid, m. p. and mixed m. p. 287–290°. No appreciable inversion had therefore occurred. On the other hand, hydrolyses of both the dimethyl and monomethyl esters with alcoholic potash led to inversions. These are described below under the headings of the appropriate acids.

200° Acid (*cis-syn-trans*)

The monomethyl ester of *cis-syn-cis*-perhydrodiphenic acid (1 g., m. p. 129°) was refluxed for seventeen hours with a solution of 2.0 g. of sodium in 20 cc. of absolute methanol. Water (2.5 cc.) was then added and the refluxing continued for a further fifty-seven hours. The solution was diluted, acidified and extracted with ether. Removal of the ether left a solid residue which was extracted with three 20-cc. portions of boiling benzene. The united extracts, on cooling, deposited a crust of *cis-syn-trans* acid. One crystallization from dilute alcohol gave 430 mg. (46%) of the pure acid in small needles, m. p. 198–200°. A second crop (420 mg.) of less pure acid was isolated from the benzene mother liquors. For analysis the acid was crystallized from acetic acid containing a trace of water, and was dried *in vacuo* at 110°, m. p. 199–200°.

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.13; H, 8.72. Found: C, 66.26, 66.22; H, 8.79, 8.72. Equivalent (dibasic); Calcd., 127.2. Found, 124.6.

The isolation of the same acid as a by-product in the hydrogenation of diphenic acid is described below under the *cis-anti-cis* (198°) acid. The acid has also been prepared by catalytic hydrogenation of *trans*-hexahydrodiphenic acid (see Part IV).

A sample of the material of Marvel and White⁶ was supplied by Dr. Marvel. It was a white powder, melting at 173–175° alone and at 198–200° in admixture with the *cis-syn-trans* acid, m. p. 199–200°. This material (3 mg.) was dissolved in 0.2 cc. of acetic acid and the solution was diluted to 0.5 cc. with water. The acid then separated in needles, m. p. 197–199°, identical with our *cis-syn-trans* acid. We have had occasional examples of the separation of this low-melting dimorphous modification. When this material has melted (at about 174°) it will resolidify and then melt at 198–200°.

Derivatives of the 200° Acid

***trans-syn-cis* Monomethyl Ester.**—The acid ester of the *cis-syn-cis* acid (m. p. 129°, 540 mg.) was treated with sodium methoxide made from 460 mg. of sodium and 20 cc. of freshly dried methanol. The solution was refluxed for sixteen hours in a soft-glass apparatus. Some of the methanol was removed and the product acidified, diluted and extracted with ether. Evaporation of the ether left an oil which was taken up in 5 cc. of ligroin (b. p. 70–90°) and the solution left to crystallize. A mixture of *trans-syn-cis* and unchanged *cis-syn-cis* half esters crystallized, the former in large prisms, the latter in small plates. They were separated partly manually, and partly by fractional crystallization.

Yield of crude *cis-syn-cis* half-ester: 230 mg., (44%), m. p. 118–125°

Yield of purified *cis-syn-cis* half-ester: 140 mg., m. p. 125–127.5°

Yield of crude *trans-syn-cis* half-ester: 180 mg., (33%), m. p. 90–93°

Yield of purified *trans-syn-cis* half-ester: 130 mg., m. p. 97–99°

For analysis, the *trans-syn-cis*-monomethyl perhydrodiphenate was dried *in vacuo* at 56°. Calcd. for $C_{16}H_{24}O_4$: C, 6.14; H, 9.02. Found: C, 67.37, 67.21; H, 9.14, 9.02.

The following experiment illustrates the ease of inversion of the *cis-syn-cis* configuration. The *cis-syn-cis* anhydride, m. p. 145° (5 g.) was refluxed for seventy hours with 200 cc. of methanol which had been freshly distilled from barium oxide. (Subsequent examination showed that this methanol contained a trace of barium methoxide.) Removal of the solvent gave a residue, which on one crystallization from dilute alcohol gave 2.87 g. of the *cis-syn-cis*-monomethyl ester (m. p. 127–129°). The mother liquors were freed from solvent and the residue crystallized from ligroin in the manner described above. In this way there was separated 220 mg. more of the *cis-syn-cis* half-ester and 810 mg. of the *trans-syn-cis* half-ester. The latter after two more crystallizations from dilute alcohol melted at 97–99°, alone, or in admixture with that described above.

Acid hydrolysis of the 98° half-ester (13.3 mg.) with hydrochloric and acetic acids (1:2) yielded the *cis-syn-trans* acid (6 mg.) identified by m. p. and mixed m. p.

Dimethyl Ester.—Esterification of the acid (360 mg., m. p. 196–198°) was carried out with an excess of diazomethane in the usual way. The neutral product, an oil, was dissolved in a little petroleum ether and left at –70° to crystallize. After two days, prismatic clumps of the dimethyl ester separated. These melted at 12.5–14.5° alone and below 5° in admixture with the dimethyl ester (m. p. 57°) of the *trans-syn-trans* acid (see below). The same material was formed by diazomethane esterification of the *trans-syn-cis*-monomethyl ester, yield 86%; m. p. 12.5–14.5°. This dimethyl ester was also obtained as a by-product in the inversion of the *cis-syn-cis* dimethyl ester (*q. v.*).

***cis-syn-trans*-Monomethyl Ester.**—The dimethyl ester (250 mg., m. p. 12–14°) was refluxed for eleven hours with 2 cc. of concentrated hydrochloric acid and 3 cc. of glacial acetic acid. The product was evaporated to dryness and the acidic material extracted with hot 10% aqueous sodium carbonate solution. The extract was filtered through a layer of Norit, diluted to 30 cc. with water, and heated to boiling. The solution was then treated at the b. p. with 10% hydrochloric acid, 2 drops at a time. The solution was cooled after each addition and any precipitate was filtered off. The first material to separate in this way was a new acid ester (60 mg.) which melted at 100–102.5° alone and at 80–90° in admixture with the acid ester (*trans-syn-cis*), m. p. 98°, described above. Three further crops separated on further acidification. These were united and separated into fractions soluble and insoluble in boiling hexane. The hexane-soluble fraction gave a further 80 mg. of the new acid ester. The hexane-insoluble fraction was essentially the *cis-syn-trans* acid. After two crystallizations from dilute acetic acid, 40 mg. was obtained which melted at 194–196° alone and at 195–198° in admixture with a pure sample.

The pure *cis-syn-trans*-monomethyl ester formed small

prismatic crystals from ligroin, m. p. 101.5–102.5°. The analytical sample was dried at 80° *in vacuo*. Calcd. for $C_{16}H_{24}O_4$: C, 67.14; H, 9.02. Found: C, 67.30, 67.20; H, 9.20, 9.08.

The *cis-syn-trans* acid (300 mg., m. p. 196–198°) was refluxed for an hour with 3 cc. of acetic anhydride. The **anhydride**, obtained by removal of the reagent, crystallized from petroleum ether (b. p. 35–60°) in glistening prisms, m. p. 104–104.5°.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.44; H, 8.29.

An oily product, probably a polymeric anhydride, was also formed. Both the crystalline anhydride and the oil, when boiled with aqueous alkali, regenerated the parent acid, m. p. and mixed m. p. 198.5–199.5°.

The crystalline *cis-syn-trans* anhydride was refluxed for twenty-four hours with 30 parts of acetic anhydride. The reagent was removed, the product treated with alkali and the acid fractionally precipitated by careful addition of dilute hydrochloric acid. Only *cis-syn-trans* acid was isolated. The absence of *cis-syn-cis* and *trans-syn-trans* acid was confirmed by the fact that neither of these could be obtained by seeding the mother liquor with authentic samples. (Experiments by Mr. Selby Davis; analysis by Miss E. Werble.)

Marvel and White⁶ had described an anhydride, m. p. 104°, made from their acid of m. p. 174°. This was undoubtedly identical with our anhydride, although we were unable to make a direct comparison as a sample provided by Dr. Marvel had already largely hydrated back to the acid.

223° Acid (*trans-syn-trans*)

(1) **Double inversion and hydrolysis of *cis-syn-cis* ester.**—*cis-syn-cis*-Dimethyl perhydrodiphenate, m. p. 73–74°, (1 g.) was refluxed for fifty hours with a solution of 7 g. of potassium hydroxide in 20 cc. of commercial methanol. The product was diluted, freed from neutral material with ether, acidified and again extracted with ether. The second extract was freed from solvent and the sticky residue dissolved in benzene. On standing, the solution deposited three successive crops (0.43 g., 48%) of almost pure *trans-syn-trans*-perhydrodiphenic acid, m. p. 221–223° (Linstead and Walpole,³ give 220°).

Derivatives.—Esterification of this acid with an excess of diazomethane in the usual way gave, in practically quantitative yield, the **dimethyl ester**. This crystallized from light petroleum in small opaque rosets, m. p. 56–57.5°. For analysis the material was dried *in vacuo* at 25°.

Anal. Calcd. for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28. Found: C, 68.28, 68.36; H, 9.26, 9.35.

Acid hydrolysis of this ester (300 mg.) was carried out in the usual way (2 cc. acetic acid, 1 cc. hydrochloric acid, nineteen hours of refluxing). The product was evaporated to dryness and the residue dissolved in aqueous sodium carbonate. The solution was boiled with charcoal, filtered and fractionally acidified at the boiling point by the method already described. The first product to separate was an oil from which no crystalline material was isolated. Further acidification yielded 3 crops of crystalline *trans-syn-trans* acid, a total of 190 mg. (70%) melting above 216°. One recrystallization of this gave the pure acid, m. p. and mixed m. p. 220–222°.

The anhydride, prepared by means of acetic anhydride, crystallized from ligroin (b. p. 70–90°) in flat rhombic prisms, m. p. 105–106.5°, in agreement with Linstead and Walpole.³ The anhydride (250 mg.) was refluxed for nineteen hours with 5 cc. of pure methanol, moisture being excluded. The product was evaporated to dryness, the residual oil taken up in ligroin and the solution filtered through a layer of charcoal. Removal of the solvent left an oil, which was dissolved in 4 cc. of petroleum ether (b. p. 20–40°) and the solution allowed to crystallize at 4°. Two types of crystals were obtained, which were separated by hand. The rarer type (20 mg., 7%) melted at 105–107° and was identified as unchanged anhydride. The common type (200 mg., 70%) melted at 109–114° and after three crystallizations from ligroin, formed hard prisms, m. p. 115.5–117.5°, of the pure monomethyl ester of the *trans-syn-trans* acid. For analysis it was dried at 80° *in vacuo*.

Anal. Calcd. for C₁₅H₂₄O₄: C, 67.14; H, 9.02. Found: C, 67.26, 67.17; H, 9.04, 9.14.

Acid hydrolysis of this material (10 mg.) gave in 84% yield the parent acid, m. p. and mixed m. p. 221–223°. The same result was obtained by alkaline hydrolysis but the reaction was more difficult and the purity low.

Esterification of the acid ester (13.4 mg.) with diazomethane yielded the dimethyl ester (11.6 mg., 82%). This crystallized from petroleum ether at –70° in white rosetts, m. p. and mixed m. p. 55.5–57°.

(2) **Inversion without Hydrolysis of *cis-syn-cis* Ester.**—*cis-syn-cis*-Perhydrodiphenic dimethyl ester (m. p. 74°, 1 g.) was refluxed for one hour with a solution of 0.1 g. of sodium in 4 cc. of dry methanol. The product was diluted and extracted twice with ether. The united extracts were washed with water, dried and evaporated to dryness. The oily residue was dissolved in 8 cc. of petroleum ether and the solution allowed to crystallize at –70°. The first two crops weighed 480 mg. (m. p. 51–56°) and 110 mg. (m. p. 47–51°), respectively. Recrystallization yielded 400 mg. of pure *trans-syn-trans* dimethyl ester, m. p. and mixed m. p. 56–57.5°. The mother liquor from the second crop was cooled to –70° and seeded with the dimethyl ester (m. p. 14°) of the *cis-syn-trans* acid. The solution then deposited 70 mg. of this ester, separating in the characteristic clumps, m. p. 8–11°.

(3) **Half-inversion and Hydrolysis of *cis-syn-trans* Half-ester.**—A solution of 10.6 mg. of *cis-syn-trans*-monomethyl ester (m. p. 102°) and 400 mg. of potassium hydroxide in 2 cc. of methanol was refluxed in soft glass for four days. The product was acidified, filtered from inorganic matter and the solvent removed. The residue was dissolved in ether and the solution washed with water. Removal of the ether left a crystalline solid which was crystallized from dilute acetic acid (charcoal). After the separation of a little oil, the solution deposited 3.6 mg. (36%) of *trans-syn-trans* acid crystallizing in prismatic needles, m. p. and mixed m. p. 220–223°.

anti Series—198° Acid (*cis-anti-cis*)

By-products in the Hydrogenation of Diphenic Acid.—

(a) Diphenic acid (5 g.) was catalytically hydrogenated in absolute alcohol (200 cc.) at 60 lb. pressure. In all, 7.6 g. of Adams catalyst, added in 7 portions, was required.

The precipitated acid was dissolved by heating and the catalyst was then filtered off. The first four crops which separated on concentrating the solution were the *cis-syn-cis* acid, m. p. 289° (see later), and no further crystalline material separated. The mother liquor on concentration gave a glass, which was dissolved in aqueous sodium carbonate and treated with charcoal. The filtrate was treated at the boiling point with 10% hydrochloric acid in drops until a faint permanent cloudiness could be seen. It was then left for fourteen days and the fifth crop of crystals was removed. The process of "fractional acidification" was then continued and five further crops were obtained. It was necessary to allow the solution to stand for several days after each acidification. The amounts, melting points and main components of the various fractions are summarized.

Crop	Wt., mg.	M. p., °C.	Main components
1	500	282–286	<i>c.s.c.</i> perhydro
2	850	274–284	<i>c.s.c.</i> perhydro
3	450	258–278	<i>c.s.c.</i> perhydro
4	400	250–270	<i>c.s.c.</i> perhydro
5	320	200–240	<i>c.s.c.</i> and <i>c.a.c.</i> perhydro
6	160	180–185	<i>c.a.c.</i> perhydro
7	240	90–130	<i>c.a.c.</i> and <i>c.s.t.</i> perhydro
8	600	165–205	<i>c.s.t.</i> perhydro and <i>cis</i> -hexahydro
9	320	185–222	Diphenic acid
10	520	188–210	Diphenic acid

The total recovery of acid was 4.36 g. or 87%, by weight. Fraction 5 was separated by benzene into a soluble and insoluble portion. The insoluble portion (100 mg.), together with fractions 1–4, on crystallization from acetic acid yielded 1.35 g. of pure *cis-syn-cis*-perhydro acid, m. p. 287–289° (26%). The benzene-soluble portion of fraction 5, together with fraction 6 and a small sample, obtained from fraction 7 by crystallization, were fractionally crystallized from dilute acetic acid. Eventually there was isolated a new perhydrodiphenic acid of m. p. 196–198° (120 mg., 2.3%). The mode of crystallization was characteristic. On rapid separation from dilute acetic acid the acid came out in fine feathery needles. After three weeks of standing in contact with the mother liquor these changed into a stable dimorphic form, which was also obtained by slow crystallization. The stable variety formed small clear prismatic parallelepipeds, m. p. 197–198.5°. A mixture with the *cis-syn-trans* acid m. p. 200°, melted at 162–182°. The analytical sample was dried at 110° *in vacuo*.

Anal. Calcd. for C₁₄H₂₂O₄: C, 66.13; H, 8.72. Found: C, 66.21, 66.36; H, 8.74, 9.03.

The derivatives of this acid and another method of preparation are described later.

Fractional crystallizations of the remainder of fraction 7 and of fraction 8, yielded 110 mg. (2.1%) of *cis-syn-trans*-perhydrodiphenic acid, m. p. 197–199°, which was identified by a mixed melting point determination.

Fraction 8 gave as its main component 400 mg. (7.8%) of an acid, m. p. 241–242° (bath initially at 235°). Analysis showed that this was a hexahydrodiphenic acid. It was identical with material prepared by Mr. Selby Davis and described more fully in a later paper (Part IV), and is

presumably identical with Vocke's hexahydro acid of the same m. p.⁶ The analytical sample was crystallized from acetic acid and dried *in vacuo* at 110°.

Anal. Calcd. for C₁₄H₁₆O₄: C, 67.72; H, 6.50. Found: C, 67.43, 67.68; H, 6.63, 6.65.

Fractions 9 and 10 yielded mainly impure starting material, melting at 222–227° alone and at 223–230° in admixture with diphenic acid (m. p. 232–233°). Even after a tedious series of crystallizations we were unable to separate the impurity which was obviously contaminating this.

Anal. Calcd. for C₁₄H₁₀O₄: C, 69.42; H, 4.16. Found: C, 69.24; H, 4.50.

(b) For preparative purposes the new (198°) acid was more easily obtained from the by-product of the catalytic hydrogenation of diphenic acid in acetic acid. Thus, 20 g. of diphenic acid was hydrogenated in the manner described under the *cis-syn-cis* acid; this substance (12 g.) was filtered off and the mother liquor was evaporated *in vacuo*. The colorless glass so obtained was dissolved in 15 cc. of acetic acid, and the sirup was allowed to crystallize. The first crop separated spontaneously, weighed 420 mg. and was essentially the perhydro acid of m. p. 289°. The mother liquor was then seeded twice with the 200° acid (*cis-syn-trans*) and two crops mainly composed of this acid were removed. These weighed 800 and 230 mg., and melted at 200–218° and 187–199°, respectively. The mother liquor was concentrated to 10 cc., seeded with the desired 198° acid (*cis-anti-cis*) and allowed to stand. A hard crust (3.25 g.) separated. An arduous series of fractional crystallizations from acetic acid yielded the acid in a state of moderate purity (prisms, m. p. about 190°), but it was found that final purification was best effected through the anhydride. In a typical experiment, 150 mg. of acid of m. p. 187–192° was refluxed with 2 cc. of acetic anhydride for thirty minutes. The excess of reagent was blown off in a stream of dry air and the residue crystallized from 2 cc. of ligroin (b. p. 60–90°), which yielded 57.3 mg. of the *cis-anti-cis* anhydride, m. p. 94.5–96°. Boiling 10% aqueous alkali regenerated the acid from this, m. p. 195–197°. In this manner a total quantity of 1.01 g. of the acid was prepared (4.8%).

Derivatives.—The pure acid, m. p. 198° (200.6 mg.), was refluxed for four hours with 3 cc. of acetic anhydride and the anhydride isolated and purified as described above, yield 156.1 mg., 83%. The **anhydride** is dimorphous; it separates in light needles, m. p. 95–96° and in prismatic needles, m. p. 99–100°. The melt of the lower melting form solidifies and the solid then remelts at 99–100°.

Anal. Calcd. for C₁₄H₂₀O₃: C, 71.16; H, 8.52. Found: C, 71.19; H, 8.77.

When boiled with methanol for forty-eight hours, the anhydride yielded the **monomethyl ester** in 87% yield. This first crystallized when its solution in petroleum ether was scratched and subsequently separated in heavy prisms, m. p. 97.5–99°. The analytical sample was dried *in vacuo* at 56°.

Anal. Calcd. for C₁₆H₂₄O₄: C, 67.14; H, 9.02. Found: C, 66.89; H, 9.09.

When the 198° acid (200 mg.) was esterified in the usual manner with diazomethane it gave an oil which soon crys-

tallized. The pure **dimethyl ester** (94% yield) separated from dilute alcohol in prismatic plates, m. p. 43–44.5°. The same dimethyl ester was obtained by treating the monomethyl ester with diazomethane (m. p. and mixed m. p. 42–44°).

Anal. Calcd. for C₁₆H₂₆O₄: C, 68.05; H, 9.28. Found: C, 68.13; H, 9.30.

Hydrolysis both of the monomethyl ester, m. p. 98° and of the dimethyl ester, m. p. 44°, with hydrochloric and acetic acids, in the manner already described for isomeric compounds, yielded the parent *cis-anti-cis* acid, m. p. and mixed m. p. 196–198°.

206° Acid (*cis-anti-trans*)

This was prepared by a similar method to that used for the *cis-trans* acid of the *syn*-series, namely, by the half-inversion and hydrolysis of the acid-ester of the *cis-cis*-acid. 25.0 mg. of the monomethyl ester of *cis-anti-cis* perhydrodiphenate (m. p. 99°) was refluxed for 150 hours with 500 mg. of potassium hydroxide dissolved in 2.5 cc. of methanol. The product was acidified and evaporated to dryness. The residue was diluted with water and extracted with ether. Removal of the ether left a solid which was crystallized from dilute acetic acid, yield 14.2 mg., 60%, irregular prisms, m. p. 200–204°. Two recrystallizations from acetic acid gave 7.3 mg. of prisms, m. p. 205.5–206.5°. The *cis-anti-trans* acid was also obtained in the form of needles. For analysis it was dried *in vacuo* at 110°.

Anal. Calcd. for C₁₄H₂₀O₄: C, 66.13; H, 8.72. Found: C, 66.28, 66.26; H, 8.87, 8.94.

The **anhydride** was prepared in the usual way, by refluxing the acid (80 mg.) for two and one-half hours with 2 cc. of acetic anhydride. It separated from ligroin in heavy prisms, m. p. 91.5–93° (yield, 53.7 mg.). A mixture with the *cis-anti-cis* anhydride (m. p. 99–100°) melted between 70 and 87°. For analysis it was dried *in vacuo* at 56°.

Anal. Calcd. for C₁₄H₂₀O₃: C, 71.16; H, 8.52. Found: C, 71.16; H, 8.53.

The anhydride dissolved slowly in boiling 10% aqueous sodium hydroxide. Acidification of the solution regenerated the *cis-anti-trans* acid, m. p. and mixed m. p. 205.5–206.5°.

Acid, m. p. 247° (*trans-anti-trans*)

The racemic form of this acid has been described by Linstead and Walpole² and by Vocke.⁶ It had been prepared by alkaline hydrolysis of a perhydro-ester obtained by hydrogenation of diphenic ester over Raney nickel, and also by the oxidation of a 9-keto-perhydrophenanthrene.² It has now been observed that the pure acid melts at 246–248° after a preliminary sintering at 237°. The following preparative method involves a double inversion and hydrolysis.

Dimethyl *cis-anti-cis*-perhydrodiphenate (50 mg., m. p. 42–44°) was refluxed for four days with a solution of 400 mg. of potassium hydroxide in 2 cc. of commercial methanol. The product was partly neutralized and evaporated to dryness. The solid was then shaken with dilute hydrochloric acid and ether. The ether layer was separated, washed, dried and evaporated to dryness. The residue was crystallized from dilute acetic acid. The first crop

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.

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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

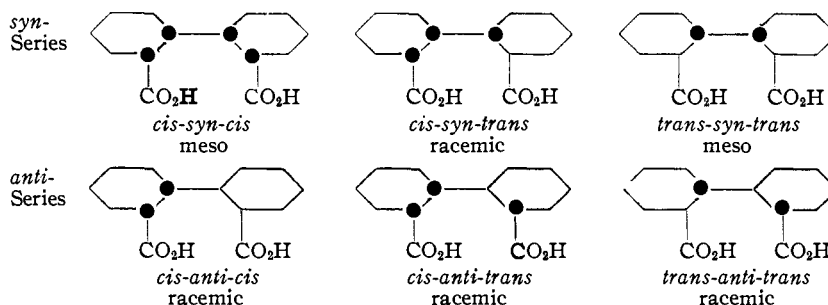
It has been shown in the preceding paper that the six perhydrodiphenic acids can be divided into two series of three members each. It has been found possible to interconvert the members within each series but not (as yet) to pass from one group to the other. These two series have the two possible backbone 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).