because the reagent is rather costly as compared with potassium sulfate and copper sulfate. We do, however, consider the use of hydrogen peroxide very desirable in preventing the troublesome foaming so common with substances high in carbohydrates and fats. The time is a very serious factor here. Frequently it is necessary to digest filter paper in biological analyses. We have been able to digest completely 2 sheets of 12.5cm. filter paper in 25 cc. of concd. sulfuric acid in 30 minutes by the addition of 30% hydrogen peroxide.

We have convinced ourselves that ammonia in the absence as well as in the presence of chloride is not lost in this digestion. We are also certain that the changes in alkalinity or in concentration of sulfate brought about by differences in lengths of time of digestion are negligible factors.

## Summary

1. The addition of 30% hydrogen peroxide to a solution of organic matter in concd. sulfuric acid causes a very rapid oxidation with complete retention of the nitrogen as ammonia.

2. A new micro-Kjeldahl method involving this action has been devised. It is the most rapid method yet reported.

3. The use of hydrogen peroxide is also recommended for the macro-Kjeldahl estimation on substances high in carbohydrates.

4. The results obtained by the application of this reagent to the micro- and macro-Kjeldahl estimations upon urine, milk, blood and pure substances are very satisfactory.

5. A modified Nessler-Folin reagent is described which does not cause the turbidity so frequently and easily obtained when the regular Folin reagent is used.

CHICAGO, ILLINOIS

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[CONTRIBUTION FROM THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY, LABORATORY OF ORGANIC CHEMISTRY]

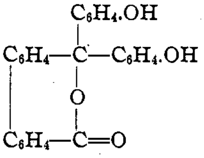
# STUDIES IN THE DIPHENIC ACID SERIES. II

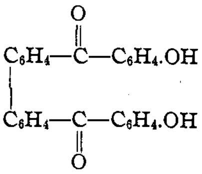
BY H. W. UNDERWOOD, JR. AND E. L. KOCHMANN

RECEIVED MARCH 31, 1924 PUBLISHED SEPTEMBER 5, 1924

In a previous paper[1] we pointed out that when phenol and diphenic anhydride are heated together in the presence of fuming stannic chloride, two isomeric condensation products are formed. One of these, phenoldiphenein (I), dissolves in sodium hydroxide solution with the development of a yellow color. If phenoldiphenein has a structural formula similar to that of phenolphthalein, the appearance of the solution of its sodium salt is anomalous.

[1] THIS JOURNAL, **45**, 3071 (1923).


I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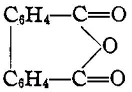
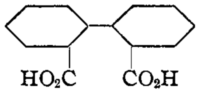

III

A consideration of the formula for diphenic anhydride (III) leads to a question as to whether two molecules of phenol might react with it in such a way as to eliminate the central oxygen atom and produce a symmetrical diketone (II). If the so-called phenoldiphenein has this structure, it seems likely that it would form a dioxime upon treatment with hydroxylamine, but in case it has two phenol rings attached to a single carbon atom it might be expected to behave like phenolphthalein and yield a monoxime. A part of this paper deals with an investigation of this point.

Since the transformation of diphenic acid (IV) or its anhydride into diphenyleneketone-4-carboxylic acid (V) involves the turning of one ring, it has an important bearing on the structure of compounds containing the biphenyl nucleus. We have treated a number of diphenic acid derivatives, including the dichloride, diamide, diethyl ester, dimethyl ester, monoethyl ester, monomethyl ester, mono-amide, imide and phenanthridone with sulfuric acid in order to ascertain whether this sort of transformation is general. From these experiments we also hoped to obtain information regarding the strength of the bonds which hold the various groups to the side-chain carbon atom which is directly attached to the ring. For example, a comparison of the results obtained in the cases of the diamide and the dimethyl ester might furnish a qualitative idea of the lability of the $—NH_2$ and the $—OCH_3$ groups. *p,p'*-Dinitro-diphenic acid was also studied on account of the fact that other investigators maintain that it forms no anhydride. In an attempt to change phenoldiphenein into an isomeric ketone acid derivative we have heated it alone and with fuming stannic chloride.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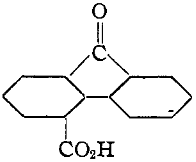
V

## Discussion of Experiments and Interpretation of Results[2]

During the course of our investigations it was necessary to make large quantities of diphenic acid by the oxidation of phenanthraquinone, which in turn was obtained from phenanthrene. Sodium or potassium dichromate and sulfuric acid were used for this work. In the production of the quin-

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[2] All the temperatures given are uncorrected.

one we have secured data which show the differences in yields obtained by varying the amount of sodium dichromate used and by substituting potassium dichromate for the sodium salt. The same course was followed with regard to the preparation of diphenic acid, but here we have also determined the influence of solvents, glacial and 56% acetic acid, upon the oxidation.

**Oxidation of Phenanthrene.**—The crude phenanthrene used in the experiments contained about 80% of the hydrocarbon. For the preparation of the quinone the first step was the thorough mixing of the dichromate, water and sulfuric acid in a large evaporating dish. After the solution had been heated to 100°, it was stirred and the finely powdered phenanthrene added during the course of an hour. The contents of the evaporating dish were maintained at 110° for half an hour after the preliminary reaction had ceased. When the mixture had cooled somewhat, it was poured into ice water, filtered, and the solid washed until free from chromium salts and dried. In order to obtain the pure quinone the crude material was finely powdered, and placed in an evaporating dish containing a liter of a nearly saturated solution of sodium bisulfite. The mixture, stirred occasionally, was kept at 50–60° for approximately two hours. The residue obtained by filtration was repeatedly extracted (usually twice more) until all the quinone had been removed. A 50% solution of sulfuric acid to which a little sodium dichromate had been added was used to acidify the combined extract liquors. After the phenanthraquinone had been completely precipitated, it was collected on a filter, washed with water until free from sulfuric acid, and dried in a hot closet.

Eight 100g. lots of phenanthrene (80%) were oxidized with sodium dichromate in quantities which varied from 2.7 to 6.3 times the calculated amount. In each experiment 1.53 g. of 96% sulfuric acid and 2.5 g. of water were employed for 1 g. of dichromate. The maximum yield (45%) of phenanthraquinone (m. p., 201–204°) was obtained when a 350% excess of the oxidizing agent was used. An equivalent amount of potassium dichromate gave better results (56% yield).

**Oxidation of Phenanthraquinone.**—Phenanthraquinone (pure or crude) was placed in a round-bottom flask containing acetic acid (glacial or 56%) and provided with a reflux water condenser. After the contents of the flask had been heated to 125° by means of an oil-bath, the mixture of dichromate, sulfuric acid and water was carefully added through a dropping funnel placed at the top of the condenser. This required about two hours. When pure quinone in glacial acetic acid was treated with sodium or potassium dichromate the total time of heating was about three hours. In the cases where 56% acetic acid was employed as a solvent for the pure quinone, or glacial acid for the crude quinone, the total time of heating was approximately six hours. After the reaction mixture was cold, it was filtered, and the solid material was washed with water until free from chromium salts. The combined solutions of sodium diphenate, obtained by repeated extractions of the washed reaction product with a 25% solution of sodium carbonate, were acidified with hydrochloric acid, and the diphenic acid thereby precipitated was collected on a filter, washed, dried and weighed. In those experiments where crude phenanthraquinone was oxidized it was found advisable to treat the sodium carbonate extract liquor with sodium chloride, let it stand for several hours, and then collect the precipitated material. This procedure removed tarry impurities which had been dissolved by the sodium carbonate.

Ten 25g. lots of pure phenanthraquinone were oxidized with potassium dichromate in quantities which varied from 2.1 to 8.5 times the calculated amount. The proportions of sulfuric acid and water used were the same as those mentioned in connection with the preparation of the quinone. When glacial acetic acid acted as a solvent (5 g. for 1 g. of quinone) a maximum yield of 70% was secured by the use of a 750% excess of dichromate. Substitution of 56% acetic acid for glacial increased the yield of diphenic acid to 74%. When an amount (70.5 g.) of crude quinone (not purified by treatment with sodium bisulfite) equivalent to 25 g. of pure material was oxidized with a 750% excess of sodium dichromate in the presence of glacial acetic acid (125 g.) a 76% yield of diphenic acid was obtained. The melting points of the diphenic acid in the various lots produced in the oxidations varied between 223° and 227°.

**Phenoldiphenein and Hydroxylamine.**—Two g. of phenoldiphenein, 0.8 g. of hydroxylamine hydrochloride (calcd. amt. times 1.1) and 2.16 g. of potassium hydroxide were added to 22 g. of water, and the mixture was heated at 80° for 15 hours. After the reaction mixture had cooled, 4 cc. of 95% ethyl alcohol was introduced, and then acetic acid was carefully added until the liquid was practically neutral to litmus paper. A white precipitate was obtained; this weighed nearly 2 g. when dry, and melted at 250° after crystallization from acetic acid. The material was identified as phenoldiphenein.

The results of our experiment show clearly that phenoldiphenein does not form an oxime under the conditions employed for the production of such a derivative from phenolphthalein. This fact might be interpreted as evidence against Formula I, but it is not necessarily inconsistent with the latter. It is possible that the oxygen atom in phenolphthalein which is connected to two carbon atoms that are in turn attached to a single benzene ring might react differently with hydroxylamine from the corresponding oxygen atom in a compound having the structure indicated in Formula I. Also the latter receives support from experimental work described elsewhere in our paper. At present we are engaged in attempts to prepare an oxime of phenoldiphenein under conditions different from those already described.

**Dichloride of Diphenic Acid.**[3]—A mixture of 15 g. of diphenic acid and 27.1 g. of phosphorus pentachloride (calcd. amt. times 1.05) were heated in an oil-bath at 190–195° for 20 minutes, whereupon the mass became liquid. Then the temperature was allowed to fall to 150°, and air was drawn through the neck of the flask for half an hour to remove phosphorus oxychloride. The flask was removed from the oil-bath; its contents were allowed to cool and subsequently removed by treatment with benzene. After being recrystallized from this solvent and dried, the reaction product weighed 13.9 g. (an 80.8% yield), and melted at 94–97°.

**Diphenamic Acid.**—When 30 g. of diphenic anhydride was heated with 30 g. of ammonium hydroxide (d., 0.90) and 35 g. of water at 110° for about an hour, the solid material gradually dissolved. Upon cooling and acidifying the reaction mixture with 20% sulfuric acid, diphenamic acid was precipitated. This has a tendency to form a pasty solid, but becomes granular on standing in a cool place. After being ground with water, it was collected and dried. The yield of this acid, m. p., 185–186°, was 31.02 g. (96.1%). Crystallization from alcohol raised the melting-point to 187–187.5°.

**Diphenimide.**—In an Erlenmeyer flask 15 g. of diphenamic acid (the mono-amide of diphenic acid), 15 g. of glacial acetic acid (solvent) and 25 g. of acetic anhydride were heated for seven hours at 130–140°. As the reaction product cooled it deposited crystals which weighed 8.9 g. and melted at 219° after they had been washed with water and with sodium carbonate solution and dried. About three-fourths of the acetic acid-anhydride

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[3] This compound and other derivatives of diphenic acid which we have described are listed in Beilstein.

liquor was distilled, and the residue poured into water. The precipitate obtained was treated with a 10% solution of sodium carbonate; the material undissolved (apparently impure diphenimide) weighed 0.6 g., and melted at 199° when washed and dried. One and seven-tenths g. of impure diphenamic acid (m. p., 163°) was secured from the carbonate extract. This procedure represents an apparently new method for preparing diphenimide, and is much more convenient than heating dry diphenamic acid as described in Beilstein.

**Diamide of Diphenic Acid.**—About 50 cc. of 6 *N* ammonium hydroxide was poured over 8 g. of diphenimide, and the mixture carefully warmed over a free flame until the solid material dissolved. The precipitate which formed as the solution cooled was collected on a filter, washed with a 10% solution of sodium hydroxide and with water and dried. It weighed 5.7 g. and melted at 209°. Acidification of the alkaline filtrate yielded 1.5 g. of diphenamic acid. If allowance be made for this unchanged material, the yield of imide is 80.3%.

**Diethyl Ester of Diphenic Acid.**—When a mixture of 10 g. of diphenic acid in 75 cc. of absolute ethyl alcohol (saturated with dry hydrogen chloride) was refluxed for six hours on a water-bath, the acid gradually dissolved. After the alcohol had been removed by distillation a viscous liquid was left in the flask. This was treated with ether, the solution placed in a separatory funnel and shaken with a 10% solution of sodium carbonate. Next, the ether solution of the ester was filtered, and the solvent removed by distillation. By cooling the pasty residue with a mixture of ice and hydrochloric acid and scratching the walls of the container, the ester was obtained in the form of a crystalline mass. After drying in a vacuum desiccator the product, m. p. 41–42°, weighed 9.3 g. (a 75.6% yield).

**Dimethyl Ester of Diphenic Acid.**—The procedure in the preparation of this compound was similar to that described in the account of the previous experiment, except that the time of heating was ten hours. Ten g. of diphenic acid and 50 cc. of absolute methyl alcohol were used. After about one-half of the alcohol had been removed by distillation, crystals were deposited as the liquid cooled. When these were collected on a filter, washed with a 15% solution of sodium carbonate and with water, dried and weighed, there was obtained 7.4 g. of the dimethyl ester; m. p., 73–74°. By acidification of the sodium carbonate wash liquid 2.25 g. of diphenic acid was recovered. If allowance be made for this, the yield of dimethyl ester is 86.4%.

**Mono-ethyl Ester of Diphenic Acid.**—Ten g. of diphenic anhydride was dissolved in 50 cc. of absolute ethyl alcohol by refluxing the mixture for one hour on the water-bath. Removal of the alcohol produced a sirupy liquid. This was transformed into a semicrystalline solid by cooling it with a mixture of ice and hydrochloric acid. Subsequently the product was dried in a vacuum desiccator. The yield of the mono-ethyl ester, m. p. 91–92°, was 11.6 g. (92.8%).

**Monomethyl Ester of Diphenic Acid.**—After a solution of 10 g. of diphenic anhydride in 50 cc. of absolute methyl alcohol had been refluxed on a water-bath for six hours, most of the methanol was distilled and the reaction product transferred to a beaker which was left in a vacuum desiccator for a day. The crystalline monomethyl ester, m. p. 106–108°, was thus secured with a practically quantitative yield.

**Phenanthridone.**—To a solution of 50 g. of diphenamic acid in 500 cc. of dil. (15%) aqueous sodium hydroxide, 600 cc. of a 6% solution of sodium hypobromite was added, and the mixture then heated at 70–80° for 3.5 hours. During the final stages of the heating, phenanthridone appeared in the liquid. After the latter had been allowed to cool, the precipitate was collected on a filter, and the filtrate was acidified with a 20% solution of sulfuric acid. The precipitate formed was extracted with a 20% solution of sodium carbonate. It was found that the material left undissolved was phenanthridone and that the substance removed by the carbonate solution was unchanged diphenamic acid. In the experiment 34.15 g. of the latter was recovered. The total yield of phenanthridone, m. p. 283° (after two crystallizations from glacial acetic acid) was 9.8 g., 65.5% of that calculated for the diphenamic acid used.

***p,p'*-Dinitro-diphenic Acid.**[4]—A mixture of 5 g. of 2,7-dinitro-phenanthraquinone (m. p., 303°) and 25 g. of 50% acetic acid was heated to 125°. Then a solution of 6.5 g. of potassium dichromate (calcd. amt. times 4) in 40 cc. of water and 10.2 g. of 95% sulfuric acid were added during the course of an hour. After being heated at 140° for six and a half hours, the reaction mixture was allowed to cool. The crystals deposited were collected on a filter, washed with water, and taken up in a 20% solution of sodium carbonate; all the material dissolved. Acidification of the carbonate solution yielded 5.3 g. of *p,p'*-dinitro-diphenic acid, m. p., 253° (a 95.1% yield). The 2,7-dinitro-phenanthraquinone used in this experiment was prepared by another investigator. Details of the procedure employed in making it are not available.

***p,p'*-Dinitro-diphenic Acid and Acetic Anhydride.**—Ten g. of acetic anhydride, 10 g. of glacial acetic acid (solvent) and 10 g. of *p,p'*-dinitro-diphenic acid were heated at 130–140° for 15 hours. It was possible to recover the dinitro acid unchanged by distilling most of the liquid. Apparently *p,p'*-dinitro-diphenic acid does not form an anhydride under the conditions of this experiment.

In order to facilitate the identification of the ketone acid derivatives obtained by the transformation of the compounds in the diphenic acid series, the methyl and ethyl esters of the ketone acid were prepared.

**Ethyl Ester of Diphenyleneketone-4-carboxylic Acid.**—To 6 g. of diphenyleneketone-4-carboxylic acid 35 cc. of absolute ethyl alcohol and 1 cc. of 95% sulfuric acid were added, and the mixture was refluxed on a water-bath for five hours. The solid that deposited as the liquid cooled was collected on a filter, washed with a 15% solution of sodium carbonate and with water, and dried in a vacuum desiccator; yield, 4.5 g. (quantitative); m. p., 102°. Two g. of ketone acid was secured from the sodium carbonate extract by acidification.

**Methyl Ester of Diphenyleneketone-4-carboxylic Acid.**—The procedure for the preparation of this compound was the same as that described in the case of the corresponding ethyl derivative. From 5 g. of ketone acid and 40 cc. of absolute methyl alcohol, 3.6 g. of the methyl ester (yield, 91.6%) was obtained, m. p., 139° and 1.3 g. of the ketone acid was recovered.

## Transformation of Members of the Diphenic Acid Series into Diphenylene Ketone-4-Carboxylic Acid Derivatives

In our preliminary experiments the dichloride, monomethyl ester, monoethyl ester, the mono-amide and the imide of diphenic acid were each heated with 95% sulfuric acid (2.5 cc. for 1 g. of reactant). The cooled reaction mixtures obtained in the cases of the first three compounds were poured into 175 g. of a cold, 15% solution of sodium hydroxide while it was stirred. Then the mixture was immediately filtered and acidified. By treating the various solid reaction products with a 15% solution of sodium carbonate we were able to separate the compounds involved. Thorough washing with water in all cases served to remove inorganic salts. Reaction mix-

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[4] Schmidt and Kämpf [*Ber.*, **36**, 3738 (1903)] prepared *p,p'*-dinitro-diphenic acid and attempted to make its anhydride. They did not treat the compound with sulfuric acid, and their explanation of its behavior appears to be in error.

tures obtained from the mono-amide and the imide were poured into 200 g. of water rather than sodium hydroxide solution.

If we consider the case of the mono-amide, it is apparent that after one of the rings has turned, the compound may lose water to form diphenyleneketone-4-carboxylic acid amide or ammonia to yield the ketone acid; the latter might also be produced through hydrolysis of its amide. Analogous possibilities are involved in the other compounds dealt with in our work.

Subsequently, we employed 100% sulfuric acid (2.5 cc. for 1 g. of reactant) to effect the desired transformations, with the hope of avoiding hydrolysis. In this work each of the reaction mixtures was poured with stirring into a beaker containing 100 g. of water and 100 g. of ice. The temperature of the mixture did not rise above 5° at any time. Solid materials were immediately collected on filters, washed with water, and treated as usual with a 15% solution of sodium carbonate. The acid filtrates were made almost neutral with a 10% solution of sodium hydroxide, and allowed to stand for several days. When solids were thereby deposited, these were added to the other products.

Practically all of the ketone acid derivatives secured in our experiments were identified by mixed melting points. Results obtained are shown in Table I.

TABLE I

DIPHENYLENE-KETONE-4-CARBOXYLIC ACID AND DERIVATIVES

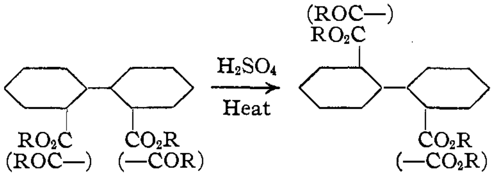
| Reactants | | Products | | | | |
|---|---|---|---|---|---|---|
| Diphenic acid | G. | Ketone acid G. | Amide G. | M. ester G. | E. ester G. | Unchanged material G. |
| Dichloride | 8 * | 4.8 | ... | ... | .. | .. |
| Diamide | 5 | 0.1 | 1.5 | ... | .. | .. |
| Diethyl ester | 5 | ... | ... | ... | 0.17 | .. |
| Dimethyl ester | 5 | 2.35 | ... | 1.2 | .. | .. |
| Mono-ethyl ester | 8 * | 5.3 | ... | ... | .. | 0.6 |
| Mono-ethyl ester | 5 | .. | ... | ... | Trace | 0.1 |
| Monomethyl ester | 8 * | 5.4 | ... | 1.2 | .. | .. |
| Monomethyl ester | 5 | 1.45 | ... | 0.4 | .. | .. |
| Mono-amide (diphenamic acid) | 10 * | 5.3 | 2.7 | ... | .. | .. |
| Mono-amide | 5 | .. | 0.8 | ... | .. | 2.9 |
| Imide | 5 | 2.2 | 2.0 | ... | .. | .. |
| Phenanthridone | 5 | See note | | | | |
| *p,p'*-Dinitro-diphenic acid | 2 * | .. | ... | ... | .. | 1.88 |

Reactants marked * were treated with 95% sulfuric acid; in all other cases 100% acid was employed. The terms amide, M. ester and E. ester used refer to the amide, methyl ester and ethyl ester of diphenyleneketone-4-carboxylic acid. The reaction product obtained from the diamide yielded 1.5 g. of diphenamic acid in addition to the compounds given in the table.

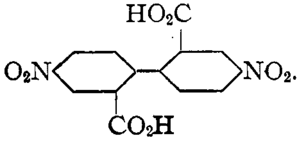
In the experiments in which 95% sulfuric acid was employed the mixtures were heated at 125–130° for two hours; when 100% sulfuric acid was used the materials were kept at 100–105° for 0.5 hour and then at 125–130° for 1.5 hours longer. Many of the products were crystallized from alcohol or from an alcohol-water mixture. The washed and dried material obtained by the treatment of phenanthridone with sulfuric acid weighed 2.1 g. and melted at 254°; a mixture of this substance and purified phenanthridone melted at 265°. The reaction product appears to be impure phenanthridone. In the attempt to transform *p,p'*-dinitro-diphenic acid 25 cc. of sulfuric acid was used. More or less sulfonation took place in each of our experiments; this is particularly noticeable in the case of the mono- and the diethyl esters.

A consideration of our results does not justify rigid conclusions regarding the lability of the groups in the side chains of the diphenic acid derivatives. The presence of diphenyleneketone-4-carboxylic acid in the products obtained from the dimethyl ester and the imide of diphenic acid shows clearly that hydrolysis occurred even when special precautions were taken. Since diphenamic acid was found among the substances resulting from the transformation of the diamide, it is certain that one of the amino groups in a portion of the compound was replaced by hydroxyl; perhaps the ketone acid amide was formed from the diphenamic acid by the loss of water. The preparation of the ketone acid amide from diphenimide is much more convenient than synthesis directly from the ketone acid.

Our work shows clearly that the transformation of those members of the diphenic acid series which contain modified carboxyl groups and no substituents in the rings into the corresponding diphenyleneketone-4-carboxylic acid derivatives is general. We may write



Since *p,p'*-dinitro-diphenic acid does not form an anhydride it might be said that the presence of the nitro groups had caused the carboxyl groups to be removed as far from one another as possible. On this basis the formula for the compound[5] might be written



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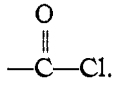
[5] We recognize the validity of the evidence which has been presented recently by a number of investigators in support of the Kaufler formula for biphenyl derivatives, but since the older formula is more easily visualized we have used it here and elsewhere in the paper.

We should expect that a substance having this structure would produce a dinitro-diphenyleneketone-4-carboxylic acid upon treatment with sulfuric acid; such a transformation does not take place. A plausible explanation of all our results may be found by utilizing Flürscheim's ideas regarding the alternation of weak and strong bonds. In these Laboratories it has been shown that *m*-nitrobenzoyl chloride reacts much more rapidly with ethyl alcohol than does benzoyl chloride; evidently the *meta* orienting nitro group has loosened the chlorine atom in the side chain  $—\overset{\overset{\displaystyle O}{\|}}{C}—Cl$. If each of the nitro groups in *p,p'*-dinitro-diphenic acid loosens the hydroxyl group and strengthens the bond holding the hydrogen atom in the carboxyl attached to the same nucleus as well as the ring hydrogen which is *meta* to the nitro group, then we should expect that the compound would not form an anhydride or a ketone acid. We plan to carry out other experiments to test the validity of this hypothesis.

**Action of Stannic Chloride and of Heat on Phenoldiphenein.**—After 2 g. of phenoldiphenein and 7 g. of fuming stannic chloride had been heated at 120–130° for five hours, the reaction mixture was cooled; solid materials were collected on a filter and subsequently taken up in a 10% solution of sodium hydroxide. Acidification of the latter yielded a white precipitate which weighed 1.9 g. and melted at 250°, after washing and drying; this was identified as phenoldiphenein.

A 2g. sample of phenoldiphenein was placed in a test-tube connected to another tube containing barium hydroxide solution, and then heated at 260–270° for 1.5 hours while dry air free from carbon dioxide was drawn through the system. The phenoldiphenein melted, and there was evidence of carbon dioxide evolution. When the cold reaction product was powdered it was very light brown in color. It dissolved in sodium hydroxide solution with the development of a yellow color. It softened at 136–147°, became liquid at 154° and effervesced slightly at 175–180°. After crystallization from acetic acid it melted at 290°. A molecular-weight determination by the freezing-point method (glacial acetic acid as a solvent) gave a value of 350; the molecular weight of phenoldiphenein is 394. Subsequently 2 g. of phenoldiphenein was heated at 260–270° for three hours, and the carbon dioxide evolved was collected in a Geissler bulb; the increase in the weight of the latter was about 10% less than that calculated for the evolution of one molecular equivalent of carbon dioxide. In this case the powdered reaction product was deep red-brown, and the solution of its sodium salt was yellow. The material softened at 243°, and became liquid at 275–283°. A mixture of the substance and pure phenoldiphenein softened at 220–223°, and melted almost completely at 243°; at 250° a slight effervescence took place. A quantitative analysis showed that our reaction product contained 80.9% of carbon. The amount of carbon in phenoldiphenein is 79.16%, and the compound which would be formed by the loss of one molecule of carbon dioxide should contain 85.68% of carbon.

These results show that heat does not transform phenoldiphenein into an isomeric ketone acid derivative, but rather produces a partial decomposition which involves the loss of some carbon dioxide. It seems unlikely that a compound with the structure indicated in Formula II would behave in this way.

## Summary

When the dichloride, diamide, diethyl ester, dimethyl ester, mono-ethyl ester, monomethyl ester, mono-amide and imide of diphenic acid are heated with concd. sulfuric acid, each compound is transformed into a member of the diphenyleneketone-4-carboxylic acid series; these changes involve rotation of the rings in the biphenyl nucleus. The mechanism of the reactions has not been precisely determined since hydrolysis occurs in every case, even when special precautions are taken. No isomerization of phenanthridone was brought about by treatment with sulfuric acid. *p,p'*-Dinitrodiphenic acid is unique in that it does not form an anhydride or a ketone acid; a plausible explanation of the behavior of this compound may be found by postulating that the *meta* orienting nitro group in each ring loosens the hydroxyl group in the carboxyl and strengthens the bond which holds the hydrogen atom in the latter as well as the force holding the ring hydrogen which is *meta* to the nitro group.

The action of heat or of fuming stannic chloride does not isomerize phenoldiphenein. If the latter be maintained for some time at a temperature slightly above its melting point, carbon dioxide is evolved. In case this fact is used in an interpretation of the structure of phenoldiphenein, it might be employed as an argument against the diketone formula (II) which we have proposed for consideration.

Cambridge A, Massachusetts

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[Contribution from the Evans Memorial]

# ETHER STUDIES

## II. THE QUANTITATIVE DETERMINATION OF PEROXIDE AS A CONTAMINANT[1]

By Allan Winter Rowe and Edward Parkhurst Phelps

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Some three years ago, as the result of a too frequent incidence of respiratory difficulties subsequent to surgical operation (several bronchites and at least one broncho-pneumonia), a chemical examination was made of the ether used for anesthesia. This was found to be contaminated seriously, and as a result of this initial observation a simple analytical procedure was outlined and all ethers for anesthesia were subjected to examination.[2]

It was soon apparent that a very considerable percentage of ether samples (one-third of all the ethers examined) contained deleterious impurities and that aldehyde and more especially "peroxide" were the chief contaminants. As both of these substances are indicated as causes for exclusion by practically all of the Pharmacopeias of

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[1] Presented before the American Chemical Society, New Haven, April 5, 1923.

[2] The results of these analyses have been reported recently by the senior author [Rowe, in press, *Ind. Eng. Chem.*].