employed. At 75° the maximum is much lower than at 50°. This is in harmony with the relative yields of lactic acid obtained from this sugar. Furthermore, it is evident that rhamnose and glucose[2e] at 50° will yield pyruvic aldehyde osazone in amounts that are of the same general magnitude. There is no way to differentiate between glyceric and lactic aldehydes as the sources of pyruvic aldehyde osazone in the case of rhamnose. It is clear from Fig. 3 that rhamnose is more like the hexoses than it is arabinose in this respect. Evans and Conaway have shown that arabinose and xylose are likewise much the same. The interest that attaches to the comparison with mannose lies in the fact pointed out above, namely, the substitution of the primary alcohol group in mannose for the methyl group of rhamnose—the asymmetrical portion of each molecule being the same.

Concerning the mechanism suggested by Evans and Hass[2e] for the conversion of glyceric aldehyde to pyruvic aldehyde, it has been pointed out by Mr. Harry Gehman of this Laboratory that the same end could be attained through the hydrogen of the water molecule reducing the primary alcohol group and the oxygen forming an aldehyde group on the other terminal carbon atom of the postulated intermediate oxidic ring.[9]

Acknowledgment.—In conclusion the authors wish to acknowledge their great indebtedness to The Cyrus M. Warren Fund of The American Academy of Arts and Sciences for very valuable assistance rendered during the progress of these experiments.

(9) *Cf.* Bernhauer, "Grundzüge der Chemie und Biochemie der Zuckerarten," Verlag von Julius Springer, Berlin, 1933, p. 118.

COLUMBUS, OHIO

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Reaction of Phthaloylnaphthol with Hydroxylamine and with Diazomethane[1]

BY LOUIS F. FIESER

The exact nature of the two carbonyl groups of phthaloylnaphthol is still an open problem. The Grignard reagent appears to attack only one of the two ketonic groups,[2] and a further peculiarity is to be found in the anomalous, and still unexplained, course of the oxidation.[3] It thus seemed of interest to study the action of some other carbonyl reagent, and hydroxylamine was selected for the purpose. It was found that phthaloylnaphthol may be converted in an alkaline medium into either one or the other of two monoximes, and that a dioxime is not formed under any of the conditions investigated. The most striking observation to be recorded in this

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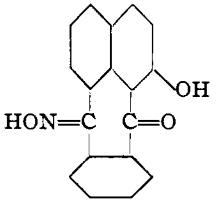
(1) Seventh paper. Sixth paper: THIS JOURNAL, 55, 3342 (1933).

(2) Fieser, *ibid.*, 53, 3546 (1931).

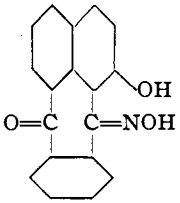
(3) L. F. and M. Fieser, *ibid.*, 55, 3010 (1933).

connection is that phthaloylnaphthol and hydroxylamine combine in cold alkaline solution to form an addition product composed of equivalent quantities of the two reactants. The formation of this remarkable substance will be described and discussed later, and it is mentioned at this point only in order to indicate the importance of considering in some detail the nature of the two oximes.

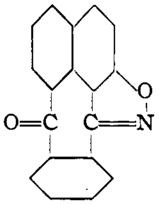
In a hot alcoholic solution, and in the presence of only a small amount of alkali, phthaloylnaphthol is converted exclusively into an oxime to which, for reasons to be indicated presently, we assign the structure of I. Adopting the new nomenclature,[3] according to which the starting material is named 1-hydroxy-7,12-pleiadenedione, this substance may be referred to as the "7-oxime." In the presence of considerably more alkali, some of this oxime is still produced, but the chief product is an isomeric substance which we regard as the 12-oxime, II, the reason being that it is easily converted into an anhydro compound, III. The dehydration is brought about by the action of strong mineral acids, by hot acetic anhydride, and by aqueous, but not alcoholic, alkali. It may be noted that this ready cyclization is in marked contrast to the behavior of the oxime of *o*-hydroxybenzophenone described by Meisenheimer and Meis.[4] The difference in behavior may be due to a difference in the spatial characteristics of the two molecules.



I



II



III

There is no evidence to show that the second oxime is not derived from a tautomeric, quinonoid form of phthaloylnaphthol, for an oxime group at position 1 could still combine with a hydroxyl group at position 12 with the production of an anhydro compound. It is known, however, that a quinonoid carbonyl group is less easily attacked by hydroxylamine than is the corresponding group of a diaryl ketone. This is shown by the behavior of the aroylanthraquinones on oximation. Thus the alternate structure appears to be a remote possibility and formula II, though not definitely proved, is given preference.

The first oxime might be a stereoisomer of the second one, but the evidence does not point in this direction. If this were true the isomers would probably be interconvertible, but this does not appear to be the case. A high alkalinity in an aqueous solution favors both the formation of II and its conversion into the sparingly soluble anhydro compound, but boiling alkali is without effect on the isomeric oxime. The compound is almost

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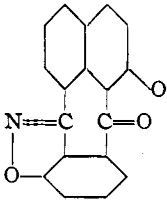
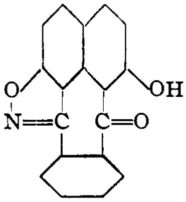
(4) Meisenheimer and Meis. *Ber.*, **57**, 289 (1924).

equally resistant to the action of strong sulfuric acid; it is unchanged at 100° and at 200° it is converted into an isomeric substance (not the 12-oxime) by a reaction which is probably of the Beckmann type. Under these conditions the 12-oxime would yield the stable anhydro compound.

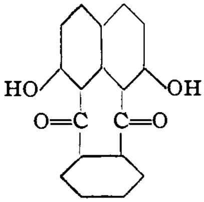
These facts point to the formula of a structural, rather than a spatial, isomer as indicated in I. One further observation may be cited which is at least consistent with this formulation. On being heated to 300°, the oxime in question is converted in part, possibly through a disproportionation, into a dehydro compound having the composition and the properties consistent with either formula IV or V. The compound corresponding to V was synthesized for comparison by the action of hydroxylamine in aqueous alkaline solution on the known[5] dihydroxy compound VI, and the two substances were found to be different. They are both of similar physical properties and both dissolve in alcoholic, but not in aqueous, alkali. Thus the product obtained from the 7-oxime may be assigned the structure of IV with a reasonable degree of confidence.



IV



V



VI

While the addition of hydroxylamine to the deep orange-yellow solution of phthaloylnaphthol in alkali or alcoholic alkali produces in the hot solution no noticeable change but results in the gradual production of an oxime, a striking and immediate color change occurs when the solution is at or below a temperature of 20–25° at the time when the reagent is added. The deep color at once disappears and the solution becomes very faintly yellow and acquires a purple fluorescence. Using an aqueous solution, and adding an excess of the amine in the form of the hydrochloride until the alkali present is neutralized, a micro-crystalline solid separates in quantitative yield. This is colorless when moist, but becomes pale yellow on drying. The composition is that of the sum of the two components, and the compound is easily re-converted into these substances. This breakdown occurs almost immediately on bringing the addition product into contact with acetic or hydrochloric acid. The substance dissolves very readily in cold alkali or in cold alcohol and the solutions are at first nearly colorless. On warming, the yellow phthaloylnaphthol is at once formed.

So unstable is the addition product that it can be dehydrated only under carefully controlled conditions. Treated with pyridine and acetic anhydride at a low temperature, it was converted in small part into the acetate of

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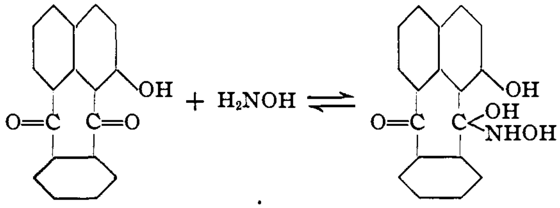
(5) Rieche, Sauthoff and Müller, *Ber.*, **65**, 1371 (1932).

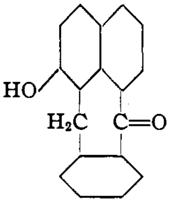
phthaloylnaphthol, but the chief product was an oxime diacetate, m. p. 163°. This on hydrolysis yielded the 12-oxime (II) in a pure condition. The diacetate of the isomeric oxime was not present in the acetylation mixture. That the reaction follows the simple course of dehydration followed by acetylation, without a preliminary breakdown and recombination of the components, is clearly shown by an experiment in which the addition product was heated with pyridine, and as a result of which both oximes were formed. Here there evidently is a preliminary breakdown of the molecule.

The addition product being thus related to the 12-oxime, it might at first be regarded as a simple hydrate of this oxime, formed by the addition of a molecule of hydroxylamine to the 12-carbonyl group of phthaloylnaphthol as indicated in the equation.

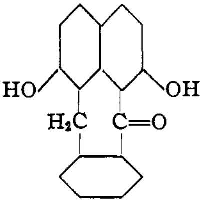


To this formulation, however, there are certain objections. In the first place it is improbable. The only compounds which are known to form such addition products (or hydrates) are substances of the type represented by chloral, which possesses an unusually reactive carbonyl group. It is difficult to imagine that the carbonyl group of the diaryl ketone in question possesses any such inherent additive capacity.

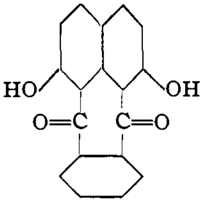
Further grounds for questioning the interpretation under discussion were furnished by a study of the two mono ketones VII and VIII. These are



VII



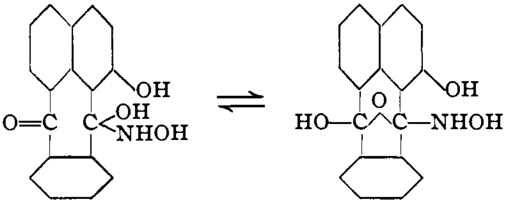
VIII



IX

both soluble in cold alkali and the solutions are highly colored, so that it would be easy to observe the formation of an addition product with hydroxylamine if such a reaction were to take place. In each case the test was negative. The carbonyl group of VII occupies a position in the molecule similar to that of the apparently reactive group of phthaloylnaphthol, and hence the failure of the compound to react might be attributed to the absence of an adjacent hydroxyl group, which might in some way induce reaction, possibly through a tautomerization. Such a group is present, however, in the dihydroxy compound VIII, and still no addition product is formed. These two mono ketones, indeed, do not even form oximes in a strongly alkaline, hot solution. A single carbonyl group flanked in this way by a naphthalene and a benzene nucleus, is if anything unusually unreactive.

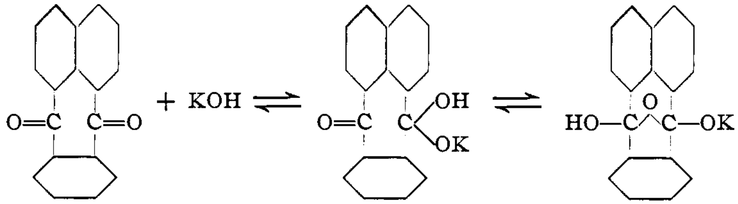
Why, then, does one carbonyl group of phthaloylnaphthol possess, or appear to possess, a reactivity of just the opposite degree? The answer in our opinion is to be found in a comparison of VIII with phthaloylnaphthol or, better, with the diketone IX which forms a similar hydroxylamine addition product. The only essential difference is that the latter compounds possess a second carbonyl group, and it may be inferred that this is a factor essential for the reaction. The influence can hardly be an indirect one, for the second carbonyl group is too far removed in the carbon chain from the first one. The second carbonyl group may, however, promote the reaction in a direct manner by accepting from the first group a part of the addenda. The reaction may be pictured as follows



The hypothesis of the formation of the oxygen bridge becomes particularly appealing on an examination of the space models. The carbon atoms concerned are so situated that the bridge can form without strain. According to this interpretation, the primary addition product probably forms as pictured in the first equilibrium shown above, but only to a very slight extent; the equilibrium is then displaced by the intramolecular addition of the hydroxyl group to the second carbonyl group.

It is of course equally possible that it is the amino hydrogen atom which enters into the second addition, with the production of a nitrogen rather than an oxygen bridge, but it is a difficult matter to make such a fine distinction. Various alkyl, aryl and acyl derivatives of hydroxylamine and also of hydrazine were tested in the hope of deciding the point, but the only other compound found to form an addition product was hydrazine. On the other hand, the following derivatives of 7,12-pleiadenedione were tested and in each case found to form hydroxylamine addition products: 1,2-dihydroxy-, 1,6-dihydroxy-,[5] 2,6-dimethyl-1-hydroxy- and 1-hydroxy-4,5-benz-7,12-pleiadenedione. The preparation of the new compounds mentioned here, and also of VIII, above, will be described in the eighth paper of the series. It may be said that all of the known alkali-soluble pleiadenediones exhibit the reaction. It is perhaps only a fortuitous circumstance that in all of these compounds there is a hydroxyl group adjacent to one of the carbonyl groups.

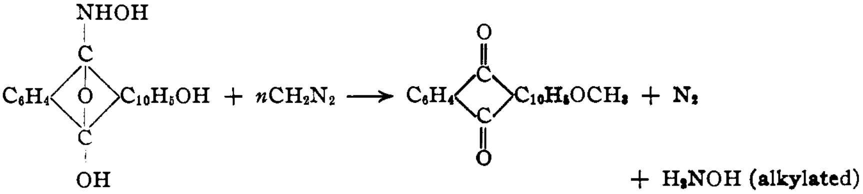
The present observations furnish a clue to the solution of another problem. It was noticed in an earlier investigation[2] that a compound now known to be pleiadenedione (phthaloylnaphthalene) is distinctly more soluble in alcoholic alkali than in alcohol alone. The observation was confirmed by Rieche and his collaborators,[5] who further showed by titration experiments that no true salt is formed and who suggested that the increased solubility was due to the addition of the alkali to a carbonyl group. At a later date various substitution products of the parent diketone were found to show a similar solubility in alcoholic alkali.[3] In the light of the present results, the formation of a definite, if unstable, addition product may be represented as follows



It was stated above that the formation of an oxygen bridge is particularly favored by the spatial configuration of the seven-membered ring which is held in a fixed position between the two aromatic nuclei. In *o*-dibenzoylbenzene a similar configuration can be attained but it represents only one of several possible arrangements, and it is significant that the solubility of this compound in alcohol is not increased by the addition of alkali. This is taken to mean that the formation of the oxygen bridge compounds takes place not only because it is possible, but because the close and fixed proximity of the hydroxyl to the carbonyl group forces an addition to occur.

It is worth noting that the intramolecular addition reaction here pictured is not without analogy, a somewhat similar reaction has been well established in the case of *o*-benzoyl-triphenylcarbinol.[6]

One further reaction of the hydroxylamine addition product is of particular significance on account of the unexpected results encountered in the course of the study. The substance reacts very vigorously with an ethereal solution of diazomethane, and the chief reaction product is the methyl ether of phthaloylnaphthol (X, below). The reaction evidently proceeds thus



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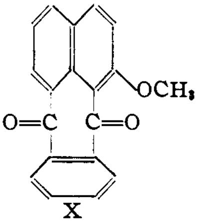
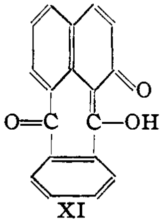
[6] Seidel and Bezner. *Ber.*, **65**, 1566 (1932).

In view of the ease with which hydroxylamine splits off from the molecule in other reactions, it is not surprising that it does so here. What is surprising is that some phthaloylnaphthol was always found in the reaction product, even when a large excess of diazomethane was employed. Indeed the pure hydroxy compound remains unchanged after several hours of contact with an ethereal solution of diazomethane. It might be supposed that the alkylation proceeds in the case noted because the hydroxy compound, normally sparingly soluble in ether, is first brought into solution in the form of the addition product. This, however, cannot be the true explanation, for, although phthaloylnaphthol can be caused to react with diazomethane by using a solution of the diketone in tetrachloroethane, the product formed under these conditions is not identical with the methyl ether (X) formed in the other reaction. It thus appears likely that the breakdown of the hydroxylamine addition compound yields as the immediate product an unstable, tautomeric form of phthaloylnaphthol. Since diazomethane is a reliable reagent for the capture of such an unstable product, and in view of the fact that the structure of the ether formed has been established by synthesis,[3] we are led to the conclusion that the unstable modification has the structure assigned up to the present time to the ordinary, stable form of phthaloylnaphthol. This may be referred to as the naphthol structure.

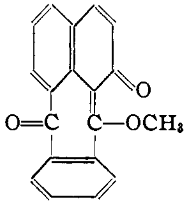
If this reasoning is correct, then ordinary phthaloylnaphthol must have some structure other than that here pictured. The only possibility appears to be the quinonoid structure, XI. It was of considerable interest to study the product of reaction with diazomethane in tetrachloroethane solution, for the structure of this substance might serve to establish the point at issue. The normal reaction product of XI would be the enol ether XII, but this was not the product actually obtained. Instead there was produced a substance having the composition of the starting material plus two methylene groups. Tests and analyses revealed the presence of one methoxyl group, one carbonyl group, and one active hydrogen atom which appears to be enolic. Such a substance might conceivably come from the further reaction of either of the two ethers, X and XII, with a second molecule of diazomethane. The ether of the naphthol form (X), however, was found not to react with diazomethane to the slightest extent in tetrachloroethane solution. The reaction product thus probably results from the addition



X

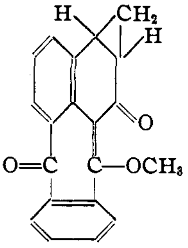


XI

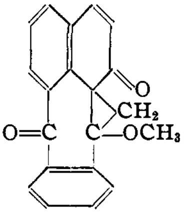


XII

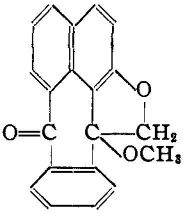
of a methylene group to the ether of the quinoid form, XII. The addition might occur: at the double bond of the quinonoid nucleus to give XIII;



XIII



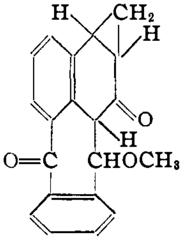
XIV



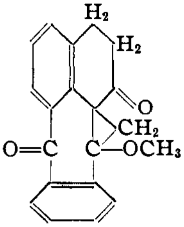
XV

at the double linkage extending to the bridge carbon, forming XIV; or to the ends of the conjugated system, giving XV. Formula XV may be ruled out because it does not indicate a hydrogen atom which can become enolic; the other two formulas are capable of accounting for the properties noted, but it is difficult to distinguish between them.

Several methods of degradation were applied without success, and the only reaction product isolated was that obtained by reduction. The substance was reduced in quantitative yield and in a very few minutes by the action of zinc and acetic acid, forming a nicely crystalline, colorless substance. This is a dihydro derivative of the first compound and contains one methoxyl group. It is not soluble in alkali, but dissolves in alcoholic alkali and is stable toward this reagent, and the Grignard test indicates the presence of one active hydrogen and one carbonyl group. Either XIII or XIV should be capable of easy reduction, and it would be expected that the conjugated system, rather than the cyclopropane ring, would form the point of attack. The reduction product thus might have the structure of either XVI or XVII, and both of these formulas are probably consistent with the properties of the compound.



XVI



XVII

While a distinction between the alternate formulas for the diazomethane reaction product is not yet possible, the facts here presented do make it appear highly probable that phthaloylnaphthol under ordinary conditions possesses the structure of the quinonoid formula XI. There is no reason beyond the argument of probability in support of the hypothesis that the first step in the diazomethane reaction involves the formation of the ether XII, but this point is not essential to the above conclusion. Neither is the problem of the exact structure of the final reaction product; the fact remains that this substance does not come from the naphthol ether X and hence can hardly originate from the naphthol form of phthaloylnaphthol.

There remains for consideration the question as to how well this new conception of structure agrees with the other known reactions of phthaloylnaphthol. One such reaction is that with dimethyl sulfate, which leads to the formation of the naphthol ether, X. The methylation is conducted in an alkaline solution, however, and the composition of the tautomeric equilibrium mixture may be quite different in this medium from the composition in tetrachloroethane solution. Even if it is the quinonoid form which predominates, the formation of the ether isolated would still be possible through a 1,4-addition to the conjugated system. The same may be said of the formation of the primary addition product with hydroxylamine, for this also occurs in an alkaline medium. With these, and with the other known reactions, the new formulation is thus not inconsistent. Whether or not this idea, together with the conception of the formation of the bridge compounds, will aid in the solution of all of the problems connected with the peculiar properties of phthaloylnaphthol is still an open question. We still fail to see any adequate explanation of the course of the oxidation, but in the Grignard reaction it appears probable that the new ideas can be applied to advantage, and this problem will be investigated further.

Experimental Part[7]

1. Oximes of Phthaloylnaphthol

1-Hydroxy-7,12-pleiadenedione-7-oxime (I).—Ten grams of phthaloylnaphthol was dissolved in a mixture of 200 cc. of alcohol and 20 cc. of 6 *N* sodium hydroxide solution and an aqueous solution of 15 g. of hydroxylamine hydrochloride was added to the cold, deep orange-yellow solution. The color changed at once, and the solution became practically colorless and showed only a slight purple fluorescence. On heating under a reflux condenser on the steam-bath the solution soon acquired a yellow color and in about fifteen minutes yellow crystals of the oxime began to separate. After the heating had been continued for two hours, the mixture was cooled and the crystalline product was collected and washed with alcohol; yield, 9 g.; m. p. 242°. The material precipitated from the mother liquor melted at 235°.

The oxime is not appreciably soluble in benzene; it is sparingly soluble in alcohol and moderately soluble in glacial acetic acid. From the latter solvent it crystallizes slowly in the form of small yellow needles melting at 243°.

Anal. Calcd. for $C_{18}H_{11}O_3N$: C, 74.72; H, 3.84. Found: C, 74.35; H, 3.98.

The oxime dissolves in cold alkali and may be recovered unchanged after boiling the yellow solution for several hours. It does not react further with hydroxylamine, even in a strongly alkaline solution. The oxime dissolves in cold concentrated sulfuric acid

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(7) The carbon-hydrogen analyses (semi-micro) were carried out by Dr. C. Harold Fisher; Miss Gertrude M. Ware performed the Zeisel determinations (micro).

and the yellow solution becomes deep red when heated, but this apparently does not represent a far-reaching change. Thus the substance was recovered unchanged after being heated for one hour on the steam-bath with 82% sulfuric acid. On heating the red solution at a temperature of 200° for five to ten minutes, however, and pouring the solution onto ice, there was obtained a yellow, alkali-soluble substance melting at 251° which has the composition of the starting material (found: C, 74.60; H, 4.10), and which may be the product of a Beckmann rearrangement.

The diacetate of the oxime crystallizes from glacial acetic acid as pale yellow prisms melting at 237°.

Anal. Calcd. for $C_{22}H_{15}O_5N$: C, 70.76; H, 4.05. Found: C, 70.77; H, 4.25.

The oxime was converted into a **dehydro product, probably IV,** by the action of heat. When the oxime is melted in a capillary tube, the formation of gas bubbles is observed at a temperature only a few degrees above the melting point. A quantity of the material was heated in a metal bath under vacuum at 300–320° until the reaction was complete and the residue was then distilled and crystallized from glacial acetic acid. There was thus obtained a substance melting sharply at 260° and forming long, slender, orange-yellow needles. It is insoluble in aqueous sodium hydroxide solution, but dissolves in hot alcoholic alkali solution. The solution shows no change on heating, and the compound may also be recovered after short heating with concentrated sulfuric acid.

Anal. Calcd. for $C_{18}H_9O_3N$: C, 75.25; H, 3.16. Found: C, 75.19; H, 3.25.

The presence of a single hydroxyl group is indicated by the formation of a **monoacetate.** This forms small, pale yellow needles melting at 208° from benzene–ligroin.

Anal. Calcd. for $C_{20}H_{11}O_4N$: C, 72.93; H, 3.37. Found: C, 73.05; H, 3.39.

The isomeric **anhydro compounds of 1,6-dihydroxypleiadenedione oxime, V,** was prepared by heating a solution of this diketone[5] in aqueous alkali with hydroxylamine for several hours. The reaction product is but sparingly soluble in alkali and thus separates from the hot solution as it is formed. It crystallizes well from glacial acetic acid, forming long, yellow needles melting at 292°. The compound is not identical with the above substance of melting point 260°, but resembles it in the stability to the action of acids and alkalies and in being soluble in alcoholic alkali.

Anal. Calcd. for $C_{18}H_9O_3N$: C, 75.25; H, 3.16. Found: C, 75.04; H, 3.42.

1-Hydroxy-7,12-pleiadenedione-12-oxime (II).—The 12-oxime is formed along with the 7-oxime in the reaction of phthaloylnaphthol with hydroxylamine in alcoholic alkaline solution if the amount of alkali present is much greater than that specified above. Following the procedure given, but using twice the quantity of alkali, the yield of the 7-oxime was about 10% lower and a small quantity of the 12-isomer was isolated from the mother liquor. With a four-fold quantity of alkali (80 cc. of 6 *N* sodium hydroxide solution for a 10-g. sample), no crystals of the 7-oxime separated even on cooling the reaction mixture, but the solution was found to contain some of this substance along with a larger quantity of the 12-oxime. The latter compound was isolated in a fairly good condition by carefully adding water and acid until about one-third of the material present had been precipitated. The 7-oxime was carried into the precipitate, and the isomer then could be precipitated from the mother liquor.

A somewhat surer method of preparing a sample of the 12-oxime which is free from traces of the isomer was found in the hydrolysis of the acetate prepared, as described below, from the hydroxylamine addition product.

The oxime in question does not crystallize well from any of the usual solvents. The best samples were obtained by precipitating the material from a solution in pyridine by means of alcohol, and then by acidifying and gradually diluting a solution of the material in cold alcoholic alkali. The product separated slowly as a yellow, microcrystalline powder. It melts fairly sharply at 262° with loss of water and conversion into the anhydro compound (see below).

Anal. Calcd. for $C_{18}H_{11}O_3N$: C, 74.72; H, 3.84. Found: C, 74.07; H, 3.96.

The oxime appears to be fairly stable in an alcoholic solution containing alkali, even at the boiling point, but in an aqueous solution of alkali it is converted rapidly into the anhydro compound, which precipitates as it is formed. The same substance is the chief product obtained by the action of acetic anhydride on the oxime, even in the presence of sodium acetate. The oxime is also dehydrated by the action of hot, 82% sulfuric acid.

The best method found for the preparation of the **12-oxime diacetate** consists in the use of pyridine as catalyst. A solution of the oxime in pyridine was cooled in an ice-bath and treated with acetic anhydride. After one-half hour in the ice-bath, the solution was allowed to stand at room temperature for several hours (heating the solution causes the anhydro compound to form) and it was then poured into water. The crude product melted at 155–160°, and it was only after several crystallizations from alcohol that a homogeneous substance was obtained. This formed small, pale yellow crystals melting at 174°. It is converted into the oxime on hydrolysis with alcoholic alkali and yields the anhydro compound when heated with sulfuric acid.

Anal. Calcd. for $C_{22}H_{15}O_5N$: C, 70.76; H, 4.05. Found: C, 71.15; H, 4.15.

The anhydro compound, III, of the 12-oxime was obtained in a variety of ways which for the most part have been indicated already. The loss of a molecule of water from the oxime takes place easily in an aqueous solution of sodium hydroxide, while the reaction is arrested by the presence of a considerable quantity of alcohol. Thus the substance may be prepared directly from phthaloylnaphthol by heating 1 g. of this substance with 50 cc. of water, 4 cc. of 6 *N* sodium hydroxide solution and 1.5 g. of hydroxylamine hydrochloride; a small quantity of the 7-oxime was isolated from the mother liquor. The anhydro compound was also obtained in nearly quantitative yield by boiling for two hours a mixture of 1 g. of phthaloylnaphthol methyl ether, 30 cc. of alcohol, 8 cc. of 6 *N* alkali and 1.5 g. of hydroxylamine hydrochloride. The product separated in a crystalline condition from the boiling solution. The compound is moderately soluble in glacial acetic acid and crystallizes in the form of very long, colorless needles melting at 227°. It is not soluble in alkali or in alcoholic alkali, and it was recovered unchanged after boiling a solution of the material in 82% sulfuric acid.

Anal. Calcd. for $C_{18}H_9O_2N$: C, 79.69; H, 3.35. Found: C, 79.41; H, 3.43.

2. Phthaloylnaphthol–Hydroxylamine Addition Product

One gram of pure phthaloylnaphthol was dissolved by heating in a mixture of 30 cc. of water and 2 cc. of 6 *N* sodium hydroxide solution and the orange yellow solution was cooled and filtered. A cold solution of 1 g. of hydroxylamine in water was then added in small portions. The first few drops caused the precipitation of the yellow starting material, which redissolved on shaking, and then the color of the solution changed from deep orange-yellow to a very pale yellow with a faint purple fluorescence. This point was reached when approximately one equivalent of the reagent had been added. With the addition of the remainder of the amine salt the solution became weakly acidic and a white precipitate having a definite microcrystalline structure soon separated. This was collected, washed thoroughly with water, and dried in a vacuum desiccator over potassium hydroxide. The material on drying retained the crystalline character but acquired a pale yellow color. A sample which had been dried for two days gave the following analytical figures.

Anal. Calcd. for $C_{18}H_{13}O_4N$: C, 70.34; H, 4.26. Found: C, 70.11; H, 4.39.

The freshly-precipitated, colorless material may be a hydrate; except for the fact that it contains external moisture, it behaves exactly like the dried material. The yellow, dried material decomposes at about 135° and yields a mixture containing phthaloylnaphthol and its oximes or their further reaction products. It undergoes slow decomposition even at room temperature and cannot be preserved for more than a few days. The addition product dissolves much more readily than phthaloylnaphthol in organic solvents and in alkali. It dissolves easily in cold alcohol to give a nearly colorless solution. This becomes yellow on standing, or on being heated, and phthaloylnaphthol soon precipitates. The reversion to the starting material is catalyzed by acids, the change taking place at once when the addition product is dissolved in glacial acetic acid, or when a small quantity of this acid is added to a cold solution of the material in alcohol or ether.

The addition product is not soluble in sodium carbonate solution but it dissolves readily in cold alkali. The solution is at first nearly colorless, but on warming it acquires at once the orange-yellow color characteristic of the salt of phthaloylnaphthol. This substance can be isolated from the solution if the heating is interrupted as soon as the color change is complete. When the heating is continued for several hours there is produced a mixture of the 7-oxime and the anhydro derivative of the 12-oxime. These products obviously are not formed directly from the addition product, but are formed from the interaction of its component parts. The same result is obtained on starting with phthaloylnaphthol, hydroxylamine and aqueous alkali.

While the addition product could not be converted directly into an oxime without a preliminary breakdown of the molecule, it was found possible to convert the substance into an oxime diacetate under suitable conditions. With acetic anhydride alone, or in combination with either sodium acetate or sulfuric acid, the addition compound is converted chiefly into phthaloylnaphthol acetate. This acetate was also produced to a certain extent in pyridine solution, but there was also formed a considerable quantity of a **diacetate of the 12-oxime**. One gram of the dry addition product was dissolved in 10 cc. of cold pyridine and 4 cc. of acetic anhydride was added to the pale yellow solution. The mixture became warm and after standing for one hour it was poured into water and the precipitate was crystallized repeatedly from alcohol. The small amount of phthaloylnaphthol acetate usually present is less soluble than the main reaction product and is thus removed only with difficulty. The oxime diacetate, however, was obtained in an apparently pure condition from the more soluble fractions. It forms faintly yellow needles melting at 163°.

Anal. Calcd. for $C_{22}H_{15}O_5N$: C, 70.76; H, 4.05. Found: C, 70.61; H, 4.23.

The diacetate is hydrolyzed easily by alcoholic alkali and too drastic treatment leads to the formation of the anhydro derivative of the oxime. Suspended in cold alcoholic alkali, it soon passed into solution and no precipitate formed on dilution with water. On acidification there slowly separated in quantitative yield a yellow substance melting at 262° and found to be identical with the 12-oxime. No trace of the 7-oxime was found on hydrolysis of either the pure or the crude diacetate. This is in contrast to the result obtained on heating for several hours a solution of the addition product in pyridine: both the 7- and the 12-oxime were isolated from the reaction mixture.

The oxime diacetate, m. p. 163°, here described appears to be different from the diacetate, m. p. 174°, obtained directly from the 12-oxime, though they both yield the same substance on hydrolysis. Mixtures of the two diacetates melted at about 154–157°. It is possible that they are stereoisomers, and it is also possible that the lower melting compound is present in the reaction mixture obtained on acetylation of the 12-oxime, for the higher melting diacetate was isolated in a pure condition only after several crystallizations.

The hydroxylamine addition product was treated with an ethereal solution of diazomethane (containing some methyl alcohol) both in the dry condition (yellow) and when freshly precipitated (white). In each case there was a vigorous evolution of nitrogen and the odor of alkylated hydroxylamine was apparent. The ether was evaporated and the oily residue was converted to a solid by digestion with alcohol. A rather considerable quantity of phthaloylnaphthol was eliminated by digestion with alkali, and the product was then crystallized from glacial acetic acid. Well-formed, yellow crystals melting at 205° were obtained, and the substance was found identical, by mixed melting point determinations, with the methyl ether of phthaloylnaphthol.

The Action of Other Amines.—Since the formation of the hydroxylamine addition product is accompanied by a marked color change, it was a simple matter to determine if derivatives of this amine and other similar compounds are capable of forming addition products with phthaloylnaphthol. The tests were negative with the following compounds: N-methylhydroxylamine, phenylhydrazine, diphenylhydrazine, semicarbazide and nitroxyl (from benzenesulfohydroxamic acid). The solution remained yellow and the starting material was recovered unchanged.

Hydrazine itself was the only other compound found to enter into reaction.

A solution of 1 g. of phthaloylnaphthol in 30 cc. of hot water and 4 cc. of 6 *N* alkali was cooled, and to the suspension of the sodium salt thus formed there was added in portions a solution of 2 g. of hydrazine hydrochloride. The sodium salt dissolved, a pale yellow solution with a purple fluorescence was produced, and then a faintly yellow addition product was precipitated. It did not have as good a crystalline character as the other addition product and it could not be obtained in a form suitable for analysis. Like the other product, the substance dissolves in alkali or in alcohol to give faintly yellow solutions which became deep yellow on heating. It also dissolves in dilute hydrochloric acid, but phthaloylnaphthol begins to separate even before the dissolution is complete. The addition product was converted by acetylation in a cold pyridine solution into a substance having the composition of the **hydrazone diacetate.** The compound crystallizes from alcohol in the form of small, faintly yellow crystals melting at 199–200°.

Anal. Calcd. for $C_{22}H_{16}O_4N_2$: C, 70.95; H, 4.33. Found: C, 70.77; H, 4.60.

3. The Action of Diazomethane on Phthaloylnaphthol

Even in a finely divided condition, phthaloylnaphthol is not appreciably affected by prolonged contact with an ethereal solution of diazomethane. When, however, the material is brought into solution in a suitable solvent a fairly rapid reaction occurs. No difference was noticed in the action of diazomethane in an absolute ethereal solution and in a solution containing some methyl alcohol and water. The yield was never quantitative and there was always an intractable, resinous residue. On using only a small fraction of the diazomethane specified below, the only change was that a considerable quantity of starting material was recovered unaltered.

To a cold solution of 7 g. of phthaloylnaphthol in 180 cc. of tetrachloroethane there was added an ethereal solution of diazomethane prepared either from 10.4 cc. of nitrosomethylurethan or from 10 g. of nitrosomethylurea. A steady, if not vigorous, reaction became apparent and continued for about two hours. After standing for two to three hours longer, the ether was evaporated and the remaining solvent removed by steam distillation. An oily residue adhered to the flask and the water could be removed from this by decantation. Sufficient alcohol was added to dissolve the oil and the solution on cooling deposited good crystals of the nearly pure reaction product; yield, 2.8–3.1 g. On evaporation of the mother liquor, trituration of the glassy residue with glacial acetic acid or with alcohol, and repeated crystallization of the product, there was obtained about 0.1 g. of a second substance, melting at 205° and identified as phthaloylnaphthol methyl ether. In separate experiments it was established that this ether does not react with diazomethane in tetrachloroethane solution.

The diazomethane reaction product (XIII or XIV) dissolves readily in glacial acetic acid or in benzene and is moderately soluble in alcohol. It crystallizes from alcohol or from benzene–ligroin as small, faintly yellow needles melting at 208°. It is not soluble in alkali and forms in concentrated sulfuric acid a deep red-purple solution which turns brown on heating. A suspension of the finely divided material in cold alcohol dissolves slowly on adding a few drops of alkali solution and shaking the mixture. It is easily oxidized and it reacts with hydrogen bromide in glacial acetic acid solution, but a clean reaction product was not isolated in either case. In a quantitative test with the Grignard reagent, using as solvent a mixture of diphenyl ether and xylene,[8] 1 mole of substance was found to yield 1.2 moles of gas and to consume (total) 2.14 moles of reagent. The solution of the reactants had a brilliant red color.

Anal. Calcd. for $C_{20}H_{14}O_3$: C, 79.45; H, 4.67; OCH_3, 10.26. Found: C, 79.25, 79.07; H, 4.70, 4.67; OCH_3, 10.24, 10.40.

A reduction product (XVI or XVII) was obtained as follows. Two grams of the above material was dissolved in 50 cc. of glacial acetic acid and the solution was boiled under reflux for ten minutes with 5 g. of zinc dust. The yellow color of the original solution disappeared in about five minutes. The combined filtrate and washings from the zinc were treated with water, which precipitated a nearly colorless solid melting at 243°; yield, 1.9 g. The compound is only moderately soluble in alcohol and crystallizes slowly from this solvent as well-formed, colorless prisms melting at 245°.

Anal. Calcd. for $C_{20}H_{16}O_3$: C, 78.92; H, 5.30; OCH_3, 10.20. Found: C, 78.79; H, 5.31; OCH_3, 10.49, 10.17.

The compound is not soluble in alkali but dissolves in alcoholic alkali, precipitating from the solution on dilution with water. The material was recovered unchanged after boiling for three hours a solution in alcoholic alkali. In diphenyl ether–xylene solution 1 mole of the substance liberated 1.16 mole of gas and consumed (total 2.02 moles of Grignard reagent. The reduction product forms in concentrated sulfuric acid an intensely colored solution with a blue-purple fluorescence.

The acetate of the reduction product crystallizes from alcohol in the form of clusters of colorless plates, m. p. 184°.

Anal. Calcd. for $C_{22}H_{18}O_4$: C, 76.28; H, 5.24. Found: C, 75.99, 75.78; H, 4.68, 5.13.

A further substance obtained only in small quantity and not identified was prepared by boiling a suspension of the reduction product in benzene with aluminum chloride. The mixture became intensely green and an oily green substance separated. In five minutes this had all dissolved to give a deep red solution. On working up the mixture there was obtained a substance forming yellow needles, m. p. 257°, and soluble in hot alkali.

Summary

Phthaloylnaphthol forms with hydroxylamine an unstable addition product which can be converted into an oxime derivative by loss of water. This remarkable reaction is attributed not to an unusual reactivity of the carbonyl group but to a secondary stabilization involving an addition to the second carbonyl group.

The reaction of phthaloylnaphthol with diazomethane furnishes certain indications that the compound in question exists largely in a tautomeric, quinonoid form.

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(8) Schmitz-Dumont and Hamann, *Ber.*, **66**, 71 (1933).