best result. Such a mixture contains nearly twice as many molecules of manganese dioxide as of ferric oxide; and, although a molecule of ferric oxide is about four times as active as a molecule of manganese dioxide, this is balanced by the fact that the latter is more improved by a promoter than is the former.

Part of the experimental work for this paper was performed by Myron A. Snell, to whom acknowledgement is hereby made.

Summary

The fact that commercial manganese dioxide is a more effective catalyst than the C. P. material in the decomposition of potassium chlorate is ascribed to the presence of 8.8% of ferric oxide in the former.

Experiments with mixtures of these two oxides confirm this view and show that each oxide is a promoter for the other.

The action of cupric oxide and manganese dioxide as mutual promoters is also demonstrated.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE LABORATORY OF PROFESSOR EDWARD KREMERS]

A STUDY OF AMINO AND OXIMO DERIVATIVES OF THYMOQUINONE[1]

BY RALPH M. HIXON[2]

RECEIVED NOVEMBER 20, 1922

The study of the reaction of the amines with the quinones dates from the time of Hofmann's report[3] of the isolation of a compound of the composition $C_6H_2O_2.N(C_6H_5)H$ from the reaction mixture of aniline and benzoquinone. Some years later, the reaction was studied thoroughly by Zincke.[4] He concluded that the amines reacted with the quinones in different ways under different conditions, giving the formulas of the following reaction products as proof of his statement.

Phenanthraquinone + methyl amine give $(C_{14}H_{18})(:N—CH_3)=O$ and $(C_{14}H_{18})(:N—CH_3)_2$ (1)

Phenanthraquinone + ammonia give $(C_{14}H_{18})(:N—H)=O$ (2)

Benzoquinone + aniline give $(C_6H_2O_2)_2(NHC_6H_5)_2$ (3)

In 1881, Zincke[5] concluded that the amines reacting with the quinones, replace a hydrogen atom of the quinone nucleus. This conclusion rested

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[1] This communication is a portion of a thesis submitted to the University of Wisconsin in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry.

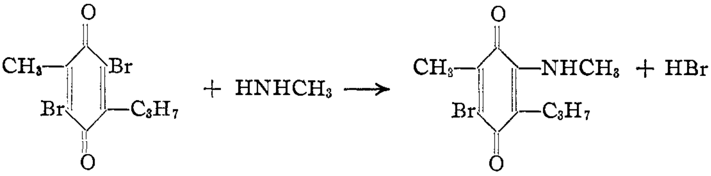
[2] Fritzsche Brothers Fellow.

[3] Hofmann, *Jahresber.*, **1863**, 415.

[4] Zincke, *Ber.*, **12**, 1641 (1879).

[5] Zincke, *Ber.*, **14**, 92 (1881).

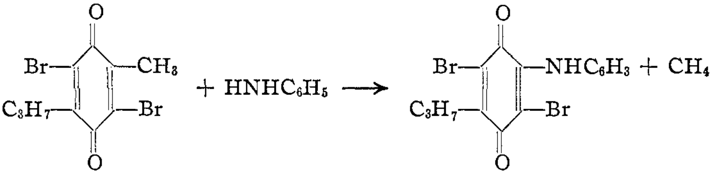
on the synthesis of the amine derivatives by reactions of the following type.



(4)

It should be noted that in drawing this conclusion, Zincke ignored the analyses of the phenanthraquinone derivatives which he had previously reported.

As a result of Zincke's work, the reactions of the amines with the quinones have been written as though direct union took place at the positions of the hydrogen atoms in the quinone nucleus. In 1901, Hofmann[6] reported the following reaction for dibromo-thymoquinone with aniline.



(5)

It will be seen that the reaction differs markedly from Reaction 4.

Considerable light is thrown upon the anomalous behavior of the quinones when their structure is compared to that of similar aliphatic compounds. The carbonyl group adds ammonia (or ammonia derivatives) to give addition compounds of the type $=C(OH)NR_2$; reference may be made to the aldehyde ammonia[7] and to the stable compound described by Nef.[8] Unsaturated aliphatic and aromatic compounds containing a carbonyl group may also add ammonia derivatives at the double bond[9] as in the cases of the action of ammonia on certain unsaturated acids and the action of hydroxylamine on carvone.

In analogy to these reactions of ammonia derivatives with less complex compounds, the following reactions may be expected with the quinone nucleus under different conditions:[10]

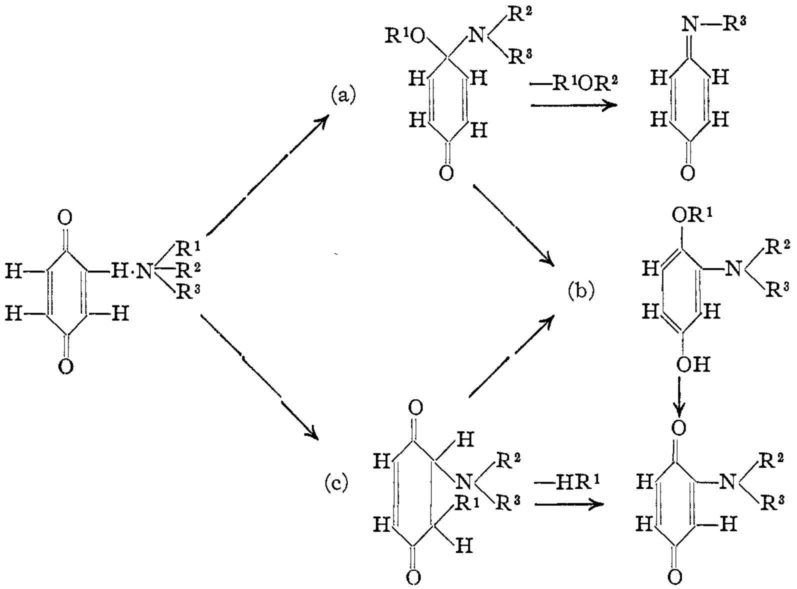
[6] Hofmann, *Ber.*, **34**, 1559 (1901). Böters, *Ber.*, **35**, 1502 (1902).

[7] Richter-Smith, "Organic Chemistry," Blakiston, 8th ed., **1900**, pp. 205–6.

[8] Nef, *Ann.*, **270**, 267 (1922).

[9] Weyl, "Methoden der organischen Chemie," Vol. I, p. 642.

[10] The intermediate compound has been written in this form to show its analogy with the ammonia salts, such as $NH_3.HCl$. The existence of such union follows at once from consideration of the quinone structure in terms of the "Octet Theory." The cubical structure of Lewis and Langmuir has been avoided to prevent undue confusion, although their conclusions have played an important part in this study of thymoquinone.



(6)

The action of hydroxylamine upon the quinones and ammonia upon phenanthraquinone fall under type "a," but for most of the other reactions either "a" or "c" seems equally possible. The final product undoubtedly depends upon the basicity of the nitrogen derivative as well as upon the characteristics induced in the quinone nucleus by modifying its structure.

Thus dibromo-thymoquinone splits off hydrogen bromide in the expected way in the presence of the relatively strong base, monomethyl amine, but unexpectedly splits off methane with the weak base, aniline (see Reactions 4 and 5). McPherson and Dubois[11] have pointed out that the ketonic characteristics of the quinone carbonyl groups decrease with the introduction of negative groups in the quinone nucleus. The reaction of hydroxylamine with monohydroxy-thymoquinone to give monohydroxyamino-thymoquinone[12] instead of an oxime as was to be expected is to be explained by this decreased carbonyl characteristic and by the greater lability of the hydrogen induced by the presence of negative groups. Likewise, the action of hydroxylamine with dihydroxy-benzoquinone and monochloro-dihydroxy-benzoquinone reported by Kehrmann[13] shows only one carbonyl group reacting to give an oxime, while one hydroxy group is replaced by an amino group in analogy to these reactions. Phenanthraquinone reacts with ammonia to give an imide,[4] which would indicate an

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[11] McPherson and Dubois, This Journal, **30**, 816 (1908).

[12] Kowalski, *Ber.*, **25**, 1658 (1892).

[13] Kehrmann and Tiesler, *J. prakt. Chem.*, **41**, 87 (1890).

intermediate addition compound similar to the aldehyde ammonia; in this connection it should be pointed out that the structure of phenanthraquinone is quite different from that of the true quinones, since the double bonds in the former are a part of neighboring phenyl rings and so are not capable of the rearrangements characteristic of the other quinones.

An intermediate addition compound similar to the ammonium salts in structure is indicated in Reaction 6; the possible existence of such compounds follows when the structure of the quinone is expressed according to the octet theories of Lewis and of Langmuir.[10] Colorless crystalline addition compounds between amines and quinones have been frequently observed and various structures assigned to them; a summary of this work is given by Meyer and by Suide.[14] The original work of Hebebrand[15] on these compounds indicates that they have an ammonium structure.

It seemed possible that similar addition compounds would be formed by tertiary amines with the quinones which would be less apt to rearrange and, therefore, be more satisfactory for study. Examination of the literature gave but one confirmation of the existence of such compounds. Jackson and Clark[16] state that dimethyl-aniline yielded colored addition products with all the quinones at their disposal. Most of these compounds were unstable but analyses were obtained for several which indicated union in equimolecular proportions.

Action of Dimethyl-aniline on Thymoquinone.—A few qualitative tests confirmed the statement of Jackson and Clark. It was found that thymoquinone dissolved in dimethyl-aniline with considerable absorption of heat; 8.2 g. of thymoquinone dissolved in two equivalents of dimethylaniline (12.1 g.) produced a drop in temperature from 23° to 10°, no precautions being taken to prevent the absorption of heat from external sources.

Although considerable time has been devoted to the study of this reaction, the conclusions are not definite. In the absence of solvents and oxidizing agents, including air, the mixture remains unchanged for months but in the presence of a solvent or of an oxidizing agent a purple tar is produced which is soluble in acids but decomposed by aqueous alkaline solutions. Saponification of the purple tar with 50% sulfuric acid yielded some dihydroxy-thymoquinone and the merest trace of monohydroxythymoquinone, which would seem to indicate that actual condensation had taken place just as between the primary and secondary amines and the quinones. The conclusion is not fully justified, however, until such a condensation product has been actually isolated. After the hydrolysis, small quantities of an intermediate crystalline compound (m. p. about

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[14] Suide, *Ann.*, **416**, 113 (1918).

[15] Hebebrand, *Ber.*, **15**, 1973 (1882).

[16] Jackson and Clark, *Am. Chem. J.*, **34**, 441 (1905).

140° with decomposition) were isolated but could not be obtained pure enough for analysis.[17]

From the structural standpoint of the octet theory, these addition reactions are analogous to the addition of tertiary amines with carboxyl chlorides[18] and also to the addition reaction between the carbonyl group and phosphorus trichloride recently studied by Conant.[19]

Preparation of Nitroso-thymol and Nitroso-carvacrol.—The nitroso-thymol and nitroso-carvacrol were prepared in amounts of 200 g. each.[20] Directions for purifying these large quantities of crude materials follow.

1. Draw off as much as possible of the mother liquor with the aid of a suction pump, and wash the compound well with water. If the compound is dried without further purification, either in air or in a vacuum, it will become discolored in the course of a few days, oxides of nitrogen being slowly evolved in the decomposition. Preparations containing only a small amount of impurities show this decomposition.
2. Transfer the wet nitroso compound from the funnel to a large beaker and wash it twice with sufficient alcohol to form a thick paste; then remove as much of the alcohol as possible by means of a filter pump. An excess of alcohol should be avoided as the compound is quite soluble.
3. Remove the alcohol by washing the solid with a small amount of ether and dry the compound in a vacuum desiccator as rapidly as possible.
4. Beautiful crystals of nitroso-carvacrol can be obtained by crystallizing the dry compound from hot benzene. Benzene is also the best solvent for recrystallizing the nitroso-thymol, but the crystals of the latter are not so well formed nor as stable as the nitroso-carvacrol.
5. In case it is desired to separate the nitroso compounds from quantities of red, oily decomposition products which are frequently encountered in working with these compounds, benzene or a benzene-ether mixture will be found more efficient than either ether or alcohol as recommended in the literature.

Preparation of the Benzoyl Derivatives of Nitroso-thymol and Nitroso-carvacrol.—These compounds have been previously prepared and studied in connection with the structure of the nitroso compounds.

In this study, they were prepared in amounts of 90 g. each, according to the Schotten-Baumann method as outlined by Sherk.[21] Sherk reports that alcoholysis takes place upon recrystallizing these compounds from alcohol. This can be avoided to a large extent by pulverizing the crude reaction product and thoroughly washing it with a dilute solution of sodium hydroxide and then with water. The compound can be recrystallized from hot alcohol as Sherk describes but a better product can be obtained by recrystallizing the dry compound from hot heptane after removing the water by washing it with alcohol and ether and then drying it in a vacuum. A yield of 92% is easily attainable by this method.

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[17] A similar compound has been obtained by Nellie Wakeman in this Laboratory from the hydrolysis of the reaction mixture of piperidine with thymoquinone (unpublished results).

[18] Freudenberg and Peters, *Ber.*, **52**, 1463 (1919).

[19] Conant, THIS JOURNAL, **43**, 1705 (1921).

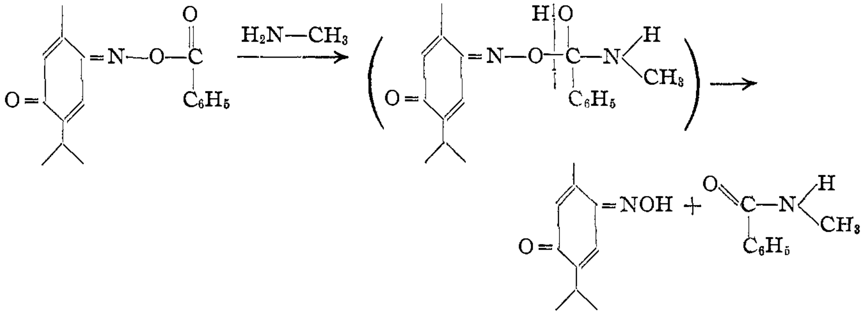
[20] Hixon, "Production of Thymoquinone on a Semi-commercial Scale," *J. Am. Pharm. Assoc.*, **11**, 696 (1922).

[21] Sherk, *Am. J. Pharm.*, **93**, 207 (1920).

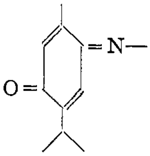
Action of Methylamine upon the Benzoyl-nitroso-phenols.—The study of this reaction was begun at this Laboratory by Miss Julia Whelan.[22] It was hoped that amino derivatives might be obtained analogous to the amino-quinones. She reported that a white crystalline compound (m. p., 128–130° with decomposition) was produced by the action of a 33% aqueous solution of methylamine upon a heptane solution of benzoyl-nitroso-thymol. The reaction was also repeated using methylamine hydrochloride with an equivalent of powdered sodium carbonate in dry heptane. Only small quantities of the feathery white crystals could be isolated. The crystals were contaminated with small quantities of darkly colored tar which was believed to be an amino derivative.

In order to push the reaction to completion and also to avoid the presence of water, dry methylamine gas was passed into a solution of benzoyl-nitroso-thymol in dry heptane at 100°. White feathery crystals identical with those obtained by Miss Whelan separated almost immediately. It was almost impossible to free these crystals by fractional crystallization from the tar which was also formed in the reaction. By pressing them on a porous plate and then recrystallizing them from a mixture of ether and heptane, chloroform, and benzene, in the order named, the compound was purified and identified as nitrosothymol. The reaction has also been carried out with benzoyl-nitroso-carvacrol and found to yield the nitroso-carvacrol. Yields of 75% of the calculated nitroso-phenol content have been recovered and, since the tar still contained considerable quantities of the compound, there is no doubt that "hydrolysis" is the principal reaction taking place. It has not been possible to identify the other constituents of the tar.

It is to be noted that the reaction takes place in a water-free medium and cannot be considered as "hydrolysis of an ester" as the term is ordinarily used. If the methylamine is considered to add to the carbonyl oxygen of the benzoyl group in analogy with the previous reactions, a simple explanation of the reaction is possible.



It should be indicated that the imide group I



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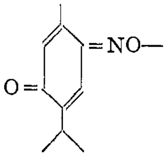

II

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[22] Whelan, unpublished results from this Laboratory, 1921.

is an extremely strong base, so that rupture at this bond is not to be expected, while the nitroso-phenol group II is only weakly acid and together with the phenyl group might be expected to impose conditions on the carbonyl group analogous to those of the aliphatic aldehydes or ketones having negative groups (such as double bonds) adjacent to the carbonyl group.

Nitric Acid Addition Products of Benzoyl-nitroso-thymol and Benzoyl-nitroso-carvacrol.—Benzoyl-nitroso-thymol and benzoyl-nitroso-carvacrol form unstable salt-like addition products with nitric acid. When the benzoyl derivatives are dropped into concd. nitric acid, these compounds separate; they are then collected on a filter and dried with filter paper.

The addition product of benzoyl-nitroso-thymol and nitric acid melts at 53° and contains at least 3 molecules of nitric acid. In view of the numerous possibilities the formula can be written only as $C_{17}H_{17}NO_2.3HNO_3$.

The analogous addition product of benzoyl-nitroso-carvacrol melts at 65° and contains 2 molecules of nitric acid per molecule of benzoyl-nitroso-carvacrol, and the formula may therefore be written as $(C_{17}H_{17}NO_2).2HNO_3$.

Both of these nitric acid addition products decompose slowly in air, and instantaneously when thrown into water. They are apparently analogous to the unstable nitric acid addition product of fluorenone, $(C_6H_4)_2C=O.HNO_3$, described by Schmidt and Bauer[23] and also to the addition compound of phenanthraquinone $(C_6H_4)_2(C=O)_2.HNO_3$ described by Kehrmann and Mattison.[24] Such products are of interest in connection with the study of the action of nitric acid on thymoquinone[25] and also the action of acids in general on the quinones.

Preparation of Thymoquinone-dioxime.—Goldschmidt and Schmid[26] were unable to prepare a dioxime of thymoquinone. In 1890, Kehrmann and Messinger[27] found that an excess of hydroxylamine hydrochloride acting upon a saturated alcoholic solution of nitroso-thymol under a reflux condenser gave small yields of thymoquinone-dioxime. The yield could be increased slightly by adding sodium carbonate at frequent intervals but never in sufficient quantities to neutralize all of the hydrogen chloride formed in the reaction. This reaction has been repeated several times in this Laboratory but the yield of the dioxime was never greater than 6–10%.

There appears to be no statement in the literature regarding the action of hydroxylamine upon nitroso-carvacrol. Following the directions of Kehrmann and Messinger for the reaction with nitroso-thymol, yields of the dioxime were obtained varying between 60 and 70%. It is very

[23] Schmidt and Bauer, *Ber.*, **38**, 3758 (1905).

[24] Kehrmann and Mattison, *Ber.*, **35**, 343 (1902).

[25] Hixon, "Action of Nitric Acid on Thymoquinone," unpublished results.

[26] Goldschmidt and Schmid, *Ber.*, **17**, 2060 (1884).

[27] Kehrmann and Messinger, *Ber.*, **23**, 3557 (1890).

interesting to note that the characteristics of the reaction of thymoquinone with hydroxylamine generally ascribed to "steric hindrance," hold also for the reaction of the monoximes with hydroxylamine.

Thymoquinone-dioxime Dibenzoate.—The dibenzoic ester of thymoquinone-dioxime was prepared by the Schotten-Baumann reaction.

The compound is insoluble in alcohol and ether but crystallizes from hot benzene (5 g. requires about 75 cc. of benzene) as colorless needles. The ester is rapidly saponified by alcoholic sodium hydroxide in the cold. The compound discolors when heated to 170° and melts at 199–200°.

The analysis agrees with the values calculated for the thymoquinone-dioxime dibenzoate.

Analyses. Subs., 0.2000: CO_2, 0.5247; H_2O, 0.0910. Calc. for $C_{24}H_{22}O_4N_2$: C, 71.6; H, 5.4. Found: C, 71.55; H, 5.15.

In view of the fact that the production of the ester from the dioxime takes place practically quantitatively, this compound is of value for purposes of identification.

Summary

1. It is pointed out that the quinones, being unsaturated cyclic ketones, should be expected to add ammonia (or ammonia derivatives): (*a*) at the carbonyl group, in analogy with the aldehyde ammonia compounds; (*b*) at the double bond, in analogy with some of the unsaturated aliphatic acids. Evidence is presented which indicates that both types of reactions take place with the quinones.

2. Evidence is presented that the intermediate addition compounds between amines and quinones have structures analogous to that of ammonia salts. Tertiary amines would be expected to form similar addition compounds with the quinones which would not rearrange. Jackson and Clark have reported that dimethyl-aniline yielded colored addition products with all the quinones at their disposal.

3. The reaction between dimethyl-aniline and thymoquinone has been studied. An addition compound appears to be formed which rearranges to a purplish tar. This latter reaction product is difficultly hydrolyzed by 50% sulfuric acid, both mono- and dihydroxy-thymoquinone being obtained. This evidence is indicative (but not conclusive) that tertiary amines may react with quinones just as do primary and secondary amines.

4. Details are given for the preparation of nitroso-thymol and nitroso-carvacrol in the crystalline state in quantity from the crude amorphous compounds. The crystalline compounds discolor very slowly in direct sunlight, whereas the crude products are quite unstable.

5. Benzoyl "nitroso-thymol" and benzoyl "nitroso-carvacrol" are decomposed by dry methylamine in dry heptane. This reaction cannot be considered as "hydrolysis of an ester" as the term is ordinarily applied.

The reaction is easily explained by the assumption of an intermediate addition compound similar to the aldehyde ammonias.

6. Unstable nitric acid addition products of benzoyl "nitroso-thymol" and benzoyl "nitroso-carvacrol" are described for the first time.

7. Thymoquinone-dioxime can be prepared more conveniently from nitroso-carvacrol than from nitroso-thymol; the former yielding 70% of the calculated quantity of dioxime whereas the latter yields only 10%.

8. The dibenzoic ester of thymoquinone-dioxime is described for the first time. The compound is of value for the identification of the dioxime.

AMES, IOWA

THE SALTS OF MALEIC, FUMARIC AND INACTIVE MALIC ACIDS

BY JOHN MORRIS WEISS AND CHARLES RAYMOND DOWNS

RECEIVED MARCH 27, 1923

In various investigations which had for their purpose the development of analytical methods for mixtures of maleic, fumaric and malic acids, a number of salts of these three acids were prepared and studied. The results are admittedly incomplete and in certain instances the compounds deserve further study. We are presenting here the results obtained, regretting that we did not have the time to study all the compounds thoroughly but hoping that others will do so. We wish to express our thanks to Dr. G. C. Bailey, Dr. H. E. Williams and Dr. Wolesensky for the careful work which they carried on under our direction in preparing and determining the formulas and solubilities of a number of the compounds described, and to Mr. E. C. Buck for the very careful preliminary search of the literature which he made in this connection.

Ammonium Salts

Analysis.—These salts were analyzed by distilling the material with an excess of standard sodium hydroxide solution and collecting the distillate in an excess of standard sulfuric acid. The distillate, titrated back with methyl orange as indicator, gave the ammonia content; and the flask residue, titrated back with phenolphthalein as indicator, gave the acid radical content.

Ammonium Fumarate.[1]—The product was best prepared by treating fumaric acid suspended in water with concd. ammonium hydroxide in slight excess of the calculated amount, concentrating in a vacuum at not over 60°, adding a little ammonium hydroxide to make up for losses in concentration and allowing the substance to crystallize. The crystals were filtered and washed with alcohol.

Analyses. Calc. for $(NH_4)_2C_4H_2O_4$: NH_3, 22.67; $C_4H_4O_4$, 77.33. Found: NH_3, 22.55; $C_4H_4O_4$, 77.40.

The aqueous solution of the salt is stable at 60° but when boiled it loses ammonia; 4.5506 g. of salt was dissolved in 200 cc. of water and the solution distilled, the distillate

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[1] Keiser and McMaster, *Am. Chem. J.*, **49**, 84 (1913).