Summary.

1. A thorough study of various phenylhydrazones of *o*-hydroxyaldehydes and ketones indicates that the introduction of any atom or group of atoms into any part of the molecule causes the solubility in 10% aqueous alkali to decrease.

2. Five different explanations for this alkali insolubility are briefly discussed and shown to be out of the question. A sixth explanation suggested by Torrey, namely, tautomerism between phenol and quinoid form is taken up in detail and from new experimental data the improbability of it is also shown.

3. A simple explanation is offered and it is shown to agree with all the experimental facts. The insolubility is due to the great tendency of the sodium salts of these phenols to hydrolyze, coupled with the fact that the free phenols are extremely insoluble in water.

4. A brief discussion is given of the various nitrophenol derivatives, many of which cause the molecule to increase in solubility in alkali instead of decrease as might be expected. This is probably due to the formation of the aci-nitro compounds which are much stronger acids than the phenols themselves.

[Contribution from the Laboratory of Soil Fertility, Bureau of Plant Industry, U. S. Department of Agriculture.]

THE PREPARATION OF METOL (*N*-METHYL-*p*-AMIDOPHENOL SULFATE).

By Rolla N. Harger.

Received November 21, 1918.

In 1890 Andresen[1] obtained a German patent for the application as photographic developers of *p*-amidophenol, *p*-amidocresol and the "substituted compounds of *p*-amidophenol and *p*-amidocresol." In the following year Hauff[2] secured patents in Germany and England for the use as photographic developers of *N*-alkylated derivatives of amidophenols, amidocresols, amidoxylenols, and aromatic diamines, the German patent stating that it is dependent upon the patent of Andresen "insofar as it is concerned with the derivatives of the *p*-amidophenols." In the specifications for Hauff's patent he gives directions for making up a developing solution using "methyl-*p*-amido-*m*-cresol (Metol)." This appears to be the first use of the word "Metol," which word Hauff later registered as a trade-mark in Germany,[3] England,[4] and the United States.[5] Paul,[6]

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[1] D. R. P. 60174.

[2] D. R. P. 69582, E. P. 15434.

[3] German Waarenzeichen No. 21540 (1897).

[4] English trade-mark No. 170477 (1893), English trade-mark No. 222388 (1899).

[5] U. S. trade-mark No. 57145 (1906).

[6] *Z. angew. Chem.*, 10, 171–4 (1897).

who made some investigations of metol in 1897, decided from his analyses that the "Metol" then sold by the Hauff Company was not a cresol derivative but the sulfate salt of *N*-methyl-*p*-amidophenol. Due, no doubt, to the statements quoted, the various reference books do not agree as to the structure of metol, Richter and Beilstein giving the formula as found by Paul, while Meyer-Jacobson, Merck and various organic text-books use the formula given in the Hauff patents. In view of these conflicting statements it was thought best to repeat the analyses of Paul with german "Metol" purchased just previous to the war. This was done and we were able to confirm his results. It would appear that Hauff later abandoned the cresol derivative in favor of the corresponding phenol compound, but it is not clear when he made this change or whether Hauff or Andresen first synthesized the amidophenol compound now sold as "Metol."

Hauff's patents cover simply the use of the above-mentioned compounds as photographic developers and do not state how he introduced the alkyl radicle into the NH_2 group. Paul[1] attempted to form "Metol" by heating under pressure *p*-amidophenol with methyl alcohol and also with methyl chloride, but was unsuccessful. However he states that he obtained the compound by heating *p*-hydroxyphenylglycine

$$(HO.C_6H_4.NHCH_2COOH)$$

slightly above its melting point, splitting off carbon dioxide. We repeated the experiment with *p*-hydroxyphenylglycine, but for some reason the result was very unsatisfactory. The Gesellschaft für Anilin Fabrikation secured in 1908 patents[2] for the formation of *p*-amidophenol and *N*-alkylated *p*-amidophenols by heating under pressure *p*-chlorophenol and ammonia or alkylamines, using copper sulfate as a catalyst. A somewhat similar process for the formation *p*-alkylamidophenols was patented in 1913 by Merck & Co.,[3] which consists in heating together hydroquinone and a mono-alkylamine, the specifications calling for a temperature of 200–250° for a period of 5 to 20 hours.

With the progress of the war and the urgent need for metol, the preparation of this compound was investigated. The last two methods were especially scrutinized, since the other methods failed to give satisfactory returns. The preparation of metol using hydroquinone and methylamine would seem to be impractical on account of the high cost of methylamine.[4] The work of Brochet and Cambrier[5] and the more recent work by Werner[6]

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[1] *Loc. cit.*

[2] D. R. P. 205415, E. P. 4044 (1908), Fr. P. 397524.

[3] D. R. P. 260234; this does not seem to be patented in England, France or the United States.

[4] Quotations for a 33% solution of CH_3NH_2 were \$0.85 in 1913 and \$1.35 in 1917 for 10 g. and for $CH_3NH_2.HCl$ were \$1.00 an 1913 and \$2.60 in 1917 for 10 g.

[5] *Bull. soc. chim.*, [3] **13**, 535 (1895).

[6] *J. Chem. Soc.*, **11**, 844 (1917).

and by Jones and Wheatley[1] upon the methylation of ammonium chloride by means of formaldehyde gives, however, a good yield of methylamine, at a moderate cost.

In view of the comparative cheapness of hydroquinone and also of methylamine when prepared by the above method, it was decided to conduct experiments upon the preparation of *N*-methyl-*p*-amidophenol from hydroquinone varying the conditions of temperature, duration of heat, concentration of methylamine, solvent for methylamine, etc. The course of the reaction was followed by making determinations of the loss in amino nitrogen as shown by the Van Slyke method, the quantity of unchanged hydroquinone which was found by extracting with ether after acidifying with sulfuric acid, the quantity of metol precipitated after evaporating the solution to a given volume, and in a few experiments the decrease in pressure during the heating, the autoclave used being fitted with a pressure gage. The disappearance of methylamine or hydroquinone does not necessarily mean the formation of an equivalent amount of the metol base since there is always the possibility of side reactions, but at least the quantity of these substances remaining after the heating furnishes an easy negative test for the progress of the reaction; and in those experiments where the quantity of methylamine was only slightly decreased it was thought unnecessary to proceed further, thus avoiding the somewhat tedious operation of evaporation and subsequent separation, drying, and weighing of the metol formed. As a matter of fact, the results show that the disappearance of methylamine and hydroquinone corresponds almost exactly with the yield of metol except in those experiments where the heating was prolonged, and there no doubt the prolonged heating caused subsequent decomposition of the base since in those cases a large amount of tarry material was formed.

Had it been possible to spend more time upon the work, results of greater precision and over a wider range could no doubt have been obtained, but in view of the apparent need for a satisfactory method for the preparation of this compound the present results are given, although incomplete. These results show that a lower temperature and consequently a very much lower pressure, and a much shorter period of heating than those given in the Merck specifications are the conditions under which the reaction should be carried out and they indicate conditions whereby a yield of 73% of the theoretical may be obtained.

Experimental Data.

Methylammonium chloride was made by the method of Werner, which gave a good yield. The free base was then liberated with sodium hydroxide and absorbed in water or alcohol.

The first experiments were carried out in a small steel autoclave (100 cc.)

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[1] THIS JOURNAL, 40, 1411 (1918).

heating equimolar quantities of hydroquinone and 10 N aqueous methylamine for 20 hours at 220–250°, but the yield of the metol base was very small and much tarry material resulted. This result was thought to be due to a catalytic action of the iron, so the next heats were carried out in glass. However, later experiments indicate that the iron has no ill effect.

Twenty g. of hydroquinone and 20 cc. of 10 N aqueous methylamine were introduced into each of 6 bomb tubes, an evolution of heat taking place when the two were mixed, due probably to the formation of the methylammonium salt of hydroquinone,[1] since the solution of hydroquinone alone in water is endothermal. The tubes were then sealed and placed in an oil bomb furnace, fitted with an Ostwald gas regulator which kept the temperature constant to within 5°. The period of heating of the different tubes varied from 1 to 24 hours at a temperature of 200°. Upon cooling, the contents of all the tubes which had been heated for more than one hour separated into two layers, an upper yellowish layer and a lower layer which ranged from reddish brown to black. The relative heights of the two layers varied, the upper layer increasing from 20% of the total in the 2-hour run to 46% in the 24-hour run. This was doubtless a result of the subsequent decomposition of the metol base caused by prolonged heating. The tubes were then opened and the contents poured into sulfuric acid (1–20), containing a quantity of the acid just equivalent to the methylamine used. The mixture was then boiled to insure solution and the solution made up to one liter. A sample was analyzed for amino nitrogen by the Van Slyke[2] method. Van Slyke states that to obtain a complete reaction between methylamine and nitrous acid, shaking for one hour is necessary, but it was found possible by keeping the room at 28° and shaking at a constant speed for 15 minutes to obtain uniform results, giving 94% of the total gas. Since merely approximate and comparative results were desired it appeared unnecessary to shake for the longer period. The solution was then extracted with ether and the ether solution evaporated to dryness and weighed. It consisted principally of such hydroquinone as had remained unchanged. The water solution was concentrated to 100 cc. and cooled in ice, and the resulting crystals collected on a Büchner funnel, washed with alcohol, dried and weighed. Analysis showed that they were practically pure metol. They were of a grayish color and were easily rendered pure white by recrystallizing from boiling water containing one g. of decolorizing charcoal for each 100 cc. of water. The results of the 6 runs are given in the following table. They show that the reaction at 200° is practically complete at the end of the third hour and that longer heating merely lowers the yield of metol and produces tarry products insoluble in dil.

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[1] Gibbs, THIS JOURNAL, 28, 1404 (1906).

[2] *J. Biol. Chem.*, 7, Proc. XXXIV (1910).

sulfuric acid. The yield given does not represent the portion remaining in the 100 cc. of mother liquor and is therefore given too low.

TABLE I.—REACTION OF HYDROQUINONE AND METHYLAMINE AT 200°.

Time. Hrs.	N evolved. Van Slyke method. Cc.	Ether-sol. material. G.	Wt. of metol. G.	Yield. %.	Remarks.
0	22.33 22.40	...	..	..	
1	7.85 7.55	3	11.5	37	
2	4.00 4.80	2			Lower layer clear; no tar.
$3^1/_2$	4.47 4.40	0.8	14	45	
6	3.50	1.8	13	42	A little tarry matter.
15	2.93 3.13	1.6	poor		More tarry matter; offensive odor.
24	3.25 3.60	1.2	7	25	Much tarry matter; ether-sol. material almost black.

An experiment was then carried out as above but using alcoholic methylamine (7.4 *N*) and heating for 3 hours. No separation into layers occurred upon cooling and analysis showed that 21% of the amino nitrogen and 25% of the hydroquinone remained and that the yield of metol was 38%.

Twenty g. of hydroquinone were next heated with two equivalents of aqueous methylamine (10 *N*) for 4 hours at 200°. No layers separated upon cooling and there remained 53% of the methylamine used equal to a disappearance of 94% of one equivalent of the amine. The yield of metol was 19.8 g. and 3 g. more was recovered from the mother liquor, making a total yield of 73%. The crystals were almost white.

A still lower temperature than 200° was now tried, equivalent quantities of hydroquinone and 10 *N* aqueous methylamine being heated for 20 hours at a temperature of 120 to 160°. Two layers separated upon cooling, the upper one being 16% of the total height of the fluids in the tube, the lower being of a much lighter color than the corresponding layers obtained at 200°. The disappearance of amino nitrogen was 82%, and 28% of the hydroquinone was recovered unchanged. The yield of metol was 7 g. from 10 g. of hydroquinone (45%) or a yield of 62% on the basis of hydroquinone actually utilized. This does not include the quantity of metol remaining in the mother liquor.

In a similar experiment, using 7.4 *N* alcoholic methylamine, the loss in amino nitrogen was only 60% and the material was not further investigated.

Equivalent quantities of hydroquinone and 10 *N* aqueous methylamine were heated for 6 days in the steam bath. A decrease of 24% in the amino nitrogen was shown, which would indicate that the reaction begins even at this temperature.

An experiment was carried out at 200° adding an equivalent of sulfuric acid to the hydroquinone and aqueous methylamine, but no reduction in amino nitrogen took place.

Calcium oxide and alcoholic methylamine were used in another experiment (200° for 3 hours), but the reduction in amino nitrogen was only 30%, due probably to the formation of the calcium salt of the hydroquinone.[1]

The steel autoclave was now fitted with a manometer and 50 g. of hydroquinone and 50 cc. of 10 *N* aqueous methylamine introduced and the autoclave heated in an oil bath kept at 200°, the temperature varying less than 1° and the heating continued for 5 hours. The results were as follows:

Time (min.).	Pressure (atm.).	Time (min.).	Pressure (atm.).
3	23	60	21
8	25	80	19.3
10	25.6	110	17.8
23	25	125	17.2
30	24.3	200	17.1
42	23.5	300	17.2

A similar experiment was carried out at 150°.

Time (min.).	Pressure (atm.).	Time (min.).	Pressure (atm.).
5	5	200	5.3
30	8.2	260	5
40	8	500	5
55	7.0	700	5
120	6	1000	5

These results would suggest that a pressure gauge could be used to follow the reaction.

Analyses.

	Calc. for $(HO—C_6H_4—NHCH_3)_2H_2SO_4$.	German "Metol."		"Metol" from hydroquinone and methylamine.
		Found by author.	Found by Paul.	
C...........	48.84	48.72	48.41; 48.52	48.85
H...........	5.81	5.85	6.03; 6.09	5.96
N...........	8.14	8.16; 8.15	....	8.14; 7.85

That the product made from hydroquinone and methylamine is identical with German "Metol" was further shown by making the benzoyl derivatives[2] of the two (Schotten-Baumann reaction), both of which melted at 174°, and a mixture of the two melted at the same temperature. The method of synthesis is, however, sufficient proof of the structure.

The following characteristics of *N*-methyl-*p*-amidophenol sulfate, hitherto unpublished, may be of interest:

The compound begins to char at 245° and melts with decomposition at 250–260°. One part dissolves in 6 parts of boiling water and in 20

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[1] Forcrand, *Ann. chim.*, [6] **30**, 69 (1893); Wöhler, *Ann. Chem.*, **69**, 299 (1849).

[2] Clark, *J. Ind. Eng. Chem.*, **10**, 892 (1918).

parts of water at 25°. It crystallizes from water in colorless needles which under the microscope appear as six-sided prisms having roof-like ends. When a solution of mercuric acetate is added to a solution of the salt the resulting solution assumes an intense purple coloration. This color comes gradually, about three minutes elapsing before the full color is developed. In solutions of "Metol" stronger than 1–1000 the production of the color is accompanied by the precipitation of beautiful scales which were found to be mercurous acetate, and the color in this concentration is best described as being very similar to that of ordinary grape juice. The formation of mercurous acetate would indicate that the color is an oxidation product. The color observed by Clark[1] upon treating "Metol" with a solution of ferric chloride, is no doubt also produced by oxidation of the amine, but the color caused by mercuric acetate is many times more intense.

Hydroquinone and the salts of *p*-amidophenol give no color at all when treated with mercuric acetate, and since the color is developed by a very small quantity of "Metol" (a solution 1–100000 giving a very good intensity) this reaction might be used to estimate the compound colorimetrically, and some experiments with the Schreiner colorimeter gave promising results.[2]

[CONTRIBUTION FROM THE ORGANIC CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS.]

ORGANIC CHEMICAL REAGENTS.[3] III. β-PHENYLHYDROXYLAMINE AND CUPFERRON.

BY C. S. MARVEL AND OLIVER KAMM.

Received December 3, 1918.

The use of organic reagents as precipitants for metals and acids in inorganic analysis is coming more and more to the fore. Among the special reagents of this class that have been introduced recently into analytical chemistry and which have found an ever-increasing application are dimethylglyoxime, cupferron, nitroso-β-naphthol, and nitron. During the past two years the shortage in the supply of the most important reagent of the above group, dimethylglyoxime, has been met by the preparation of several hundred pounds of this product by the Department of Organic Manufacturers of the University of Illinois. Improved directions for this preparation have recently been published[4] for the aid of anyone wishing to undertake the manufacture of this reagent.

[1] *Loc. cit.*

[2] Amidol ($C_6H_3{\cdot}OH{-}(NH_2)_2$ 1, 2, 4) gives a somewhat similar color but this is changed to pink on the addition of acetic acid while the purple color produced with "Metol" remains unchanged under similar treatment.

[3] For previous papers in this field see: THIS JOURNAL, 40, 1281, 1950 (1918).

[4] THIS JOURNAL, 40, 1281 (1918).