THE PRODUCTION OF METOL

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THE PRODUCTION OF METOL

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OBJECT

The object of this thesis is twofold. The first part consists of a survey of the different series of chemical reactions that might be employed in the preparation of metol. The different series that are theoretically possible are discussed in the light of commercial practicability and the characteristics of the individual reactions involved. The second part consists in the selection of that particular series which seems most favorable and the study of that series more with respect to its industrial application than to a critical study of the separate reactions themselves.
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INTRODUCTION

Two primarily different formulas have been ascribed to metol. Bodies corresponding to each of these have been prepared and put on the market. Their properties as a photographic developer, in conjunction with hydroquinone, seem to be very similar. The earlier type of metol was para methylaminometacresol sulphate, having the structural formula -

\[ \text{CH}_3 \quad (\text{SC}_4)_1 \text{CH}_3 \]

The later type produced is para methylaminophenol sulphate or hydrochloride, having the structural formula -

\[ \text{H} \quad \text{O} \quad \text{N} \quad \text{Cl} \quad \text{CH}_3 \quad \text{H} \quad \text{H} \]

The latter structure and formula are the ones considered throughout this thesis.
PART ONE

This part deals with a survey of the different series of chemical reactions that might be employed in the preparation of metol. It also includes a discussion of the theoretically possible series from the viewpoint of the manufacturing chemist.
The present world-wide war has created an unprecedented situation in the chemical industry in the United States. This country suddenly finds itself completely shut off from the source of practically all of its synthetic organic chemicals. And likewise the supply of intermediates, from which most of these chemicals could be made, is also cut off.

Metol is one of the best of all photographic developers, especially when used in conjunction with hydroquinone or para dihydricphenol. This developing solution gives a very black and contrasting negative and consequently is the developer most desired for motion picture films, both negative and positive. This use alone creates a large demand for the body.

Metol is an organic chemical preparation whose synthesis is rather difficult. We obtained what we wished from Germany and were content to let the matter rest with that.
Now that the source of our supply has been cut off, we find that we are both without the necessary chemicals and the ever-needed technical information with which we could produce the metol required.

The production of metol involves a series of reactions by which an hydroxyl and an amino group are attached to the benzene ring and a methyl radical is attached to the amino group. Furthermore, the amino group is in para position to the hydroxyl radical. However, we will not here consider benzol to be the source of metol, but instead some simple derivative such as phenol or aniline which is at present a commercial body.

There are two general methods that are theoretically possible and practicable for the production of metol. The first is the production of para aminophenol and the methylation of this. The second general method is to first
introduce the methyl radical into the amino group and then introduce the hydroxyl radical into the proper position.

There are a number of methods for the preparation of para aminophenol, namely:

1. The nitration of phenol with the subsequent separation of the para nitrophenol and the reduction of this with nascent hydrogen to para aminophenol.

2. The nitration of acetanilide with the subsequent separation of the para nitroacetanilide and the hydrolysis of this to para nitraniline by conversion with mineral acids. The para nitraniline is then diazotized and heated and the NH$_2$ group thereby replaced with an OH group. The resulting para nitrophenol is then reduced with nascent hydrogen to para aminophenol.

3. The electrolytic reduction of nitrobenzene
to give para aminophenol directly.

4. The neutral reduction of nitrobenzene to phenylhydroxylamine and the conversion of this through an intramolecular change, brought about by boiling with mineral acid, to para aminophenol.

The second general method for the production of metol is the methylation of the amino group before the introduction in the proper place of the phenol radical. This involves either the manufacture of monomethylaniline or its recovery as a by-product from the manufacture of dimethylaniline. Whether the latter can or cannot be done at a cost less than the former, we are not in a position to state. However, it seems highly probable that a manufacturer of dimethylaniline could increase his yield of monomethylaniline (which is, we believe, about 5% of that of the dimethylaniline under present conditions of manufacture) such that it could be profitably separated and re-
covered without materially interfering with the recovery of the dimethylaniline.

The manufacture of monomethylaniline involves either the foregoing procedure, giving a small yield, or the use of the more expensive reaction of Fittig-Wurtz, in which no dimethylaniline is formed. The details of this reaction will be explained later.

After the production of monomethylaniline, it is converted to methylacetanilide by a similar procedure to the manufacture of acetanilide from aniline.

The methylacetanilide is then nitrated by the same method and procedure as is used in the nitration of acetanilide. This gives a large yield of para nitromethylacetanilide. This is subsequently reduced to para aminomethylacetanilide. This body is also termed para phenyleneemethylacyldiamine and has the following structural formula:
This is then diazotized and boiled in dilute acid solution by which the amino group is replaced by the hydroxyl radical.

The para methylacylaminophenol is then hydrolyzed to para methylaminophenol by boiling in strong caustic alkali solution. The hydrochloride or sulphate of this is then metol.

Now considering these foregoing reactions in more detail, we have the following facts to bring out:

The nitration of phenol for the production of para aminophenol is at best a poor method unless the ortho nitrophenol produced can be disposed of at a good price. The yield of the para body in the nitration is only 10 to 12%, and even when the operation is conducted at a temperature of -40°C., the yield seldom exceeds 25%. The separation of the
ortho from the para body is rather a tedious task, involving a steam distillation of all of the ortho nitrophenol and the recovery from the residue of the para body by water extraction and subsequent crystallization.

The production of para aminophenol through para nitraniline seems to be much more feasible. This is accomplished as follows: acetanilide is nitrated, the yield being about 80% of the para body. The para nitroacetanilide is hydrolyzed by boiling in strong alkali solution. This resulting para nitraniline is then diazotized and boiled in acid solution whereby the NN₂₂ is replaced by an OH. This gives para nitrophenol, which is then easily reduced to para aminophenol. It is true that the procedure is a long one, and also true that phenol cannot be as cheaply produced by the diazo reaction as it can by the fusion of benzene sulphonate. Nevertheless, because of the high yield of the para body in the nitration, the proposi-
tion as a whole seems much more feasible than the direct nitration of phenol.

The electrolytic reduction of nitrobenzene for the production of para aminophenol does not seem at all practicable because of the small yield and the difficulty of separation and purification. F. M. Fredericksen gave a discussion of the "Electrochemical Synthesis of Phenylhydroxylamine" before the American Electrochemical Society, in which he brings out the following facts:

The best yield is about 25%. It is produced by electrolyzing nitrobenzene mixed with fifty times its weight of 60% alcohol, using zinc electrodes and cooling the cell to 19°C.

Perkin describes a method of reduction in acid solution at 80°C. by which the phenylhydroxylamine is converted to para aminophenol as fast as it is formed. We made two runs using this method and the yields were 14% and 16%.
<table>
<thead>
<tr>
<th></th>
<th>#1</th>
<th>#2</th>
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<tbody>
<tr>
<td>Nitrobenzene</td>
<td>25 grams</td>
<td>25 grams</td>
</tr>
<tr>
<td>Conc. $\text{H}_2\text{SO}_4$</td>
<td>200 cc.</td>
<td>200 cc.</td>
</tr>
<tr>
<td>Water</td>
<td>5 cc.</td>
<td>5 cc.</td>
</tr>
<tr>
<td>Platinum electrodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cur. Den.</td>
<td>5 to 6 amps./ sq. dm.</td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>75° to 80°C.</td>
<td></td>
</tr>
<tr>
<td>E. M. F.</td>
<td>7.4 volts.</td>
<td>7.6 volts.</td>
</tr>
<tr>
<td>Porous pot diaphragm used.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yield</td>
<td>14%</td>
<td>16%</td>
</tr>
</tbody>
</table>

We made two runs on the chemical reduction of nitrobenzene in neutral solution using powdered zinc as a reductor. In both cases the yield was below 12%. A good discussion of the possibilities of reduction in neutral solutions is given in the article by F. M. Fredericksen previously mentioned.

The methylolation of para aminophenol is accomplished by heating the hydrochloride of para aminophenol with methyl alcohol to 180 to 200° C. for a period of 6 to 8 hours.
It may better be accomplished by heating in a similar way with methyl chloride. In either case the tendency is for the formation of the dimethyl body and if the theoretical quantities are used, a large amount of the dimethyl body is formed and much of the para aminophenol remains unattacked. This reaction was not studied but the general trend of information from different sources seems to corroborate these statements.

It seems very inadvisable to attempt the manufacture of metol by the method just described because of the unsatisfactory means of making para aminophenol and of the great difficulty of the proper methylation of this body.

The second general method for the preparation of metol, namely, that of first introducing the methyl radical, was considered by us to be the most feasible method and consequently is taken up in detail in part two.
References:


PART TWO

This part deals with the selection, in the light of the foregoing discussion, of a particular series of reactions for the production of metol and the investigation of this series with respect to its industrial application.
The second or proposed method involves the following series of reactions:

\[
\begin{align*}
2\text{C}_6\text{H}_5\text{NHC}_2\text{H}_3\text{O} + 2\text{Na} & \rightarrow 2\text{C}_6\text{H}_5\text{NNaC}_2\text{H}_3\text{O} + \text{H}_2 \\
\text{C}_6\text{H}_5\text{NNaC}_2\text{H}_3\text{O} + \text{CH}_3\text{Cl} & \rightarrow \text{C}_6\text{H}_5\text{NCH}_3\text{C}_2\text{H}_3\text{O} + \text{NaCl } (1:4) \\
\text{C}_6\text{H}_5\text{NCH}_3\text{C}_2\text{H}_3\text{O} + \text{NO}_2(\text{HNO}_3) & \rightarrow \text{NO}_2\text{C}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} \\
\text{NO}_2\text{C}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + 6\text{H} & \rightarrow \text{NH}_2\text{C}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + 2\text{H}_2\text{O} \\
\text{NH}_2\text{C}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + 2\text{HCl} + \text{NaNO}_2 & \rightarrow \text{ClNNC}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + \text{NaCl} + 2\text{H}_2\text{O} \\
\text{ClNNC}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + \text{H}_2\text{O} & \rightarrow \text{HOC}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + \text{N}_2 + \text{HCl} \\
\text{HOC}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + \text{H}_2\text{O} & \rightarrow \text{HOC}_6\text{H}_4\text{NCH}_3\text{H} + \text{CH}_3\text{CCOH}
\end{align*}
\]

These reactions will now be taken up in order and discussed in detail.
THE PRODUCTION OF SODIUM ACETANILIDE.

\[
\begin{array}{c}
\text{Na} \\
\text{N} \\
\text{C}_2\text{H}_3\text{O}
\end{array}
\]

Reaction:

\[2\text{C}_6\text{H}_5\text{NH}_2\text{C}_2\text{H}_3\text{O} + 2\text{Na} \rightarrow 2\text{C}_6\text{H}_5\text{NNaC}_2\text{H}_3\text{O} + \text{H}_2
\]

Qualitatively considered, the reaction consists in dissolving the acetanilide in toluene and adding metallic sodium to the hot solution. The sodium gradually dissolves with the liberation of hydrogen. The sodium acetanilide, being much less soluble in the toluene than acetanilide, soon begins to precipitate out as a white curdy mass and when the reaction is complete, the clear solution has changed to a thin white mushy mass.

The reaction was performed a number of times in the laboratory using about a 10% solution of acetanilide in the toluene. This quantity is readily soluble in hot toluene. A slight excess over the required amount of metallic so-
dium was added in the form of thin slices and the temperature gradually raised to about 95° C., at which point it was maintained until nearly all of the sodium was in solution. If the temperature is immediately raised to over 100° C., the sodium melts and diffuses through the liquid under which conditions the reaction proceeds with violence enough to cause great foaming and frothing. For this reason, the temperature was held below the melting point of sodium until most of it had dissolved.

The yield of product in this reaction should be practically theoretical. In the trials made in the laboratory, the yields varied from 73% to 88%. We attributed the small yields to the fact that the reaction was carried out:

1. In stills without agitation.
2. In open kettles with hand agitation.

Neither method was proper for the reaction. In the first case, we had no agitation; and in the second case, we could attain a satisfactory tem-
perature without a high loss of toluene and consequently considerable danger. In all runs we had more sodium left than the excess over the theoretical that was used. This showed incomplete agitation and too thick solutions.

As a result of the experiments made, we would suggest the following apparatus and mode of procedure:

The reaction to be carried out in an enamel-lined still, mechanically agitated, and equipped with both ordinary and reflux condensers. The still should be jacketed for live steam under pressures ranging up to 100 pounds. About a 5% solution of acetanilide in toluene is made and charged into the still. About 80% to 85° of the theoretical amount of sodium is then added in small lumps and the temperature raised to about 95° C., at which point it is maintained until most of the sodium is in solution. The temperature is now run up to the boiling point of the toluene, 110° C., and the
mixture boiled and agitated until the sodium is entirely consumed. This should take place quite rapidly; the sodium being above its melting point and about the same specific gravity as the mixture, spreads itself in minute globules throughout the mass and hastens the reaction. The whole reaction should be complete in about two hours. The contents of the still should be cooled to about 30° C. and then filter-pressed in a small deep-frame press. The precipitate will be nearly pure sodium acetanilide, enclosing small quantities of acetanilide. It should be washed with a little toluene and the filtrate and wash toluene should go back to the original still. Approximately the quantity used for washing should be distilled off and saved for the next washing. The reflux condenser should then be turned on, the acetanilide and sodium added and the process repeated. The press cake should be dried in a vacuum pan and further toluene recovered.

Unless the sodium is all consumed in the
reaction, the resulting mass is a hazardous one to handle, since a little water coming in contact with the sodium will react with a flash and ignite the toluene present. The fire could only be put out by smothering as more water would spread the fire and float the burning toluene in all directions. Samples of such a nature in the laboratory, even after standing under water for hours, have burst into flame when shaken up. Until all of the sodium is removed, the hazard is indeed great.

If the sodium is not all consumed in the reaction, the resulting mass blackens when dried at 100°C., and turns brown at lower temperatures. Just what the nature of the decomposition is, was not investigated.

For the two preceding reasons, we suggest that only 80% to 85% of the theoretical amount of sodium be added at the start of the reaction, thus insuring greater freedom from hazard and a much easier product to purify.

The sodium acetanilide produced is of
sufficient purity to proceed with in commercial work and needs no further treatment.

THE PRODUCTION OF METHYLACETANILIDE.

\[
\text{C}_6\text{H}_5\text{NNaC}_2\text{H}_3\text{O} + \text{CH}_3\text{Cl} \rightarrow \text{C}_6\text{H}_5\text{NCH}_2\text{C}_2\text{H}_3\text{O} + \text{NaCl}
\]

Owing to the inability to obtain methyl chloride under present conditions, we could not make a study of this reaction. However it is a typical Fittig-Wurtz reaction and is carried out in a similar manner to the others. The sodium acetanilide will dissolve to the extent of about 15% in ether. We would suggest that the solution be placed in an autoclave and the methyl chloride introduced under pressure until the reaction is complete. The methyl acetanilide produced crystallizes from hot water in splendid long needles melting at 99°C. The methylacetanilide used by us was made by the acetylation of monomethyl-
aniline in a manner similar to the production of acetanilide from aniline. In case mono-methylaniline can be obtained from a more economical source, the latter method would be used in preference to the Fittig-Surtz reaction.

The methylacetanilide appears to exist in two isomorphous forms. If the mixture of acetic acid and methylacetanilide resulting from the acetylation reaction be poured into water while still hot, the methylacetanilide appears on the surface as an oil with a specific gravity very close to unity. When allowed to cool below 48°C, this oil would solidify as an amorphous mass. On allowing it to stand in contact with water for a few days, this amorphous mass would change over to the white crystals described.

THE PRODUCTION OF PARA NITROMETHYLCETANILIDE.

\[
\begin{array}{c}
\text{NO}_2 \\ \text{C}_6\text{H}_5 \\
\text{N} \\ \\
\text{CH}_3 \\ \\
\text{C}_2\text{H}_5\text{C}
\end{array}
\]

In our work on the nitration of methylacetanilide we found that the characteristics
of the reaction to be very nearly identical with those of the nitration of acetanilide. The nitration mixture, temperature, and method of treating the product were exactly the same.

Nölting A. Collin, (B. 17, pg. 262) discusses fully the details of the nitration of acetanilide.

PRODUCTION OF PARA AMINOMETHYLACETANILIDE.

\[
\begin{align*}
\text{H} & \quad \text{N} & \quad \text{CH}_3 \\
\text{H} & \quad \text{N} & \quad \text{C}_2\text{H}_5\text{O}
\end{align*}
\]

\[
\text{N}_2\text{C}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_5\text{O} + 6\text{H} \rightarrow \text{NH}_2\text{C}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_5\text{O} + 2\text{H}_2\text{C}
\]

This reduction is the ordinary reduction of the aromatic nitro body to the amino body. This is carried out by the use of either zinc or iron and acetic acid. Acetic acid is practically the only acid that can be used because of the hydrolytic action of boiling mineral acids upon the acetyl radical with the production of the amino group and acetic acid. The
product of the reaction is a dilute acetic acid solution of para aminomethylacetanilide and either ferrous or zinc acetate. This solution was considered ready for the next reaction without any purification.

THE PRODUCTION OF PARA METHYLACETYLAMINOPHENOL.

\[ \text{NH}_2\text{C}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + 2\text{HCl} + \text{NaNO}_2 \rightarrow \text{CINNC}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} \]

\[ \text{N}^+\text{H}_2\text{O} \]

\[ \text{NaCl} + 2\text{H}_2\text{O} \]

\[ \text{CINNC}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + \text{H}_2\text{O} \rightarrow \text{COC}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_3\text{O} + \text{N}_2 + \text{HCl} \]

This is a typical diazo reaction and is carried out at ordinary temperatures by the addition of either dilute sulphuric or hydrochloric acid together with a concentrated water solution of sodium nitrite. When all of the
sodium nitrite has been added, the solution is heated on a waterbath until the evolution of nitrogen ceases. Some cooling is necessary while the nitrite is being added and provision should be made for agitation. The products of this reaction are; para methylacylamaminophenol and the sodium and iron salts of the mineral acid used.

THE PREPARATION OF PARA METHYLAMINOPHENOL.

\[
\begin{array}{c}
\text{HO} \\
N \\
\text{CH}_3 \\
\text{H}
\end{array}
\]

\[
\text{HOC}_6\text{H}_4\text{NCH}_3\text{C}_2\text{H}_5\text{O} + \text{H}_2\text{O} \rightarrow \text{HOC}_6\text{H}_4\text{NCH}_3\text{H} + \text{CH}_3\text{COOH}
\]

303 18 261 60

The solution resulting from the diazo reaction was made strongly alkaline with caustic soda and boiled to hydrolize the acyl radical. At the same time, the iron or zinc sulphate which was present precipitated as the hydroxide and after boiling settled readily and was separated by decantation.

By this hydrolysis, para methylaminophenol
is secured in solution. This is the metal base and there remains the problem of extracting it.

ATTEMPTS AT RECOVERY.

Portions of the decanted liquor were acidified and efforts made to crystallize out the metal without success. There was so much tarry and resinous matter present that they may have obscured any metal that came out with them.

Both precipitate and filtrate were divided into a number of portions which were then extracted with different organic solvents. These extractions were accomplished both by agitation and by boiling up with a reflux condenser. The following solvents were tried:

1. Benzol- no residue on evaporation.
2. Toluol- " " " " .
3. Chloroform-" " " " .
4. Ether- resins " " .
5. Alcohol- a large quantity of sodium acetate crystals on evaporation.
6. Carbon tetrachloride- no extraction.
As the experiments just mentioned exhausted the supply of solution containing metol base which we had been able to prepare with the chemicals which were available, we were forced to leave this problem unsolved. However this is a detail which should not present very great difficulty once the bodies to be investigated are available.
SUMMARY

We believe that metol base is produced in solution by the reaction just discussed for it is a simple diazotation of an amino body, and there was every indication that the reaction proceeded exactly according to theory. Also, the solution which was at first a deep orange color changed on standing exposed to the air to the dark brown color characteristic of developing solutions which have oxidized.

We believe this to be a fruitful field for further investigation especially as regards a method for recovering the product.

We would suggest as the next step, the synthesis and purification of the para aminomethylacetanilide and the diazotization of this with ethyl nitrite. In this way, metol base would be the only solid material produced, provided the reaction would proceed as we believe it would. This would simplify
investigation and might yield profitable results.

We understand that metol is, at present, made from oxy-glycine. However, we believe that metol could be economically produced by the method suggested and in a manner similar to the one described, provided the problem of extracting the metol base from solution is solved.