STUDIES IN THE PREPARATION
OF META-BIPHENYL COMPOUNDS

by

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STUDIES IN THE PREPARATION OF META-BIPHENYL COMPOUNDS

I. INTRODUCTION

After reviewing the literature related to biphenyl compounds, it is surprising to note the lack of investigations concerning the monosubstituted meta derivatives. The symmetrical derivatives, the multisubstituted derivatives, and the ortho and para monosubstituted derivatives of biphenyl seem to be very well investigated.

In many theoretical investigations, the comparison of the biphenyl radical requires quantities of the ortho, meta, and para derivatives. Because the meta derivative is not easily obtained, many of the theoretical studies cannot be made.

This research was therefore proposed to make a systematic investigation of the meta derivatives of biphenyl, and, if possible, to improve and coordinate the existing methods of synthesis in such a manner as to make this type of compound readily available in good yields for further studies.
Historical.— The preparation of derivatives of biphenyl attracted the attention of many workers as early as 1872, when Schultz (73) prepared the bromo derivative which has since been proven to be para bromo biphenyl.

Throughout this work the term "biphenyl", as applied to two linked benzene nuclei, will be used. The following system of numbering the rings is now generally accepted.

Biphenyl itself may be readily obtained by passing benzene vapors through a hot tube (16, 76) which is the industrial method used today. As a by-product of the process considerable quantities of the ortho, meta, and para diphenyl benzenes are formed, the meta isomer predominating. These compounds have been studied by many of the earlier workers, and the meta diphenyl benzene has been claimed to have been oxidized, using chromic acid, to 3-carboxy biphenyl (23, 64, 71, 72, 74).

However, the principal product obtained is benzoic acid, and the 3-carboxy biphenyl is isolated in only very small quantities. This may be a matter of conditions and should ideal conditions of oxidation be worked out,
the meta diphenyl benzene may serve as a source for the meta biphenyl derivatives.

The symmetrical derivatives of biphenyl are readily prepared by a reaction developed by Ullmann (81,82) and co-workers, whereby a substituted aryl halide is heated with copper powder. This reaction has been used to an advantage (19,20) in preparing the various symmetrical and multisubstituted derivatives which have been widely studied because of their interesting property of restricted rotation and consequent optical activity (2).

The direct substitution reactions with biphenyl, such as nitration, halogenation, and sulfonation, produce unsymmetrical biphenyl derivatives; and all enter the biphenyl nucleus in the 2 or 4 positions, with the largest amount entering the 4 position, and none at all in the 3 position. This is probably the principal reason why the ortho and para biphenyl derivatives have been well investigated (27,32,57,60,65,76,78,85,86,87,88,89,90).

The unsymmetrical derivatives have been prepared by many unique reactions. However, most of them are rather limited in their application and require unusual materials for synthesis. Collet (26) treated bi-
phenyl with chloro acetyl chloride and aluminum chloride and isolated only \( p \)-phenyl phenacyl chloride.

This result does not quite agree with the synthesis of Adam (1), who treated biphenyl with methyl chloride and aluminum chloride, isolating meta methyl biphenyl. Neither does it agree with Epelberg and Lowy (30) who used dimethyl sulfate and aluminum chloride, isolating meta methyl biphenyl as the principal product with a much smaller amount of the para isomer.

Barth and Schreder (9) fused benzoic acid with sodium hydroxide, and obtained small amounts of \( 3 \)- and \( 4 \)-carboxy biphenyl. Weger and Doring (84) fused fluorene with potassium hydroxide and obtained a small amount of \( 2 \)-carboxy biphenyl. Graebe and Rateanu (39) also used fluorene to prepare 2-amino biphenyl in about 50% yields. Sherwood, Short, and Stansfield (79) prepared 3-methyl biphenyl in 70% yields using meta bromo toluene and cyclo-hexanone. This reaction involved a Grignard reaction and a dehydrogenation.

The diazo reaction with many modifications has been applied with varied success to the synthesis of unsymmetrical biphenyl derivatives. However, of all the reactions investigated, it seems to have the most general application.
Previous to 1924, Bamberger (4,5,6,7), Fischer (33), Hantzsch (43), Hirsch (50), and many others noted the fact that under certain conditions diazo compounds would couple with benzene to produce derivatives of biphenyl. No general application of the reaction was made until Gomberg and co-workers (37,38) generalized the reaction and applied the method to the synthesis of a large number of unsymmetrical biphenyl derivatives. The principal disadvantage was that the yields seldom exceeded 20%. The Gomberg reaction utilized the procedures of Fischer, Hantzsch, and Hirsch, whereby a substituted arylamine is diazotized and the corresponding diazohydroxide is produced by making the solution basic. The concentrated aqueous diazohydroxide solution is vigorously stirred with a neutral aromatic liquid, keeping the mixture cold. Nitrogen is evolved and the substituted biaryl is formed. The most characteristic feature of the reaction is the fact that irrespective of the nature of the so-called "directing group" the biaryl linkage is ortho or para to the group already present. For example, from diazotized aniline and bromo-benzene, toluene, and nitro-benzene, there was obtained, respectively, 2- and 4-bromo biphenyl, 2- and 4-methyl biphenyl, and 4-nitro biphenyl.
This unusual feature was also earlier noted by Kuhling (58,59), who, from diazotized p-nitro aniline and nitrobenzene, obtained 4,4'-dinitro biphenyl and 4,2'-dinitro biphenyl. This is in exact contradiction to what would be expected, especially when diazotized aniline and nitrobenzene are reacted together. The expected product would be 3-nitro biphenyl because of the meta orientation of the nitro group.

Fischer (33) and Bamberger (4,5,6,7) studied the N-nitrosoacylarylamines, which are considered as an isomeric form of the diazo compounds. They are probably tautomeric with benzene iso-diazo acetate (4,43,66)

\[
\begin{align*}
\text{C}_6\text{H}_5\text{N}(\text{NO})\text{COCH}_3 & \quad \leftrightarrow \quad \text{C}_6\text{H}_5\text{N}=\text{NOCOCH}_3 \\
\text{N-nitroso acetanilide} & \quad \leftrightarrow \quad \text{benzene iso-diazo acetate}
\end{align*}
\]

because of the fact that they act as diazo compounds in coupling with aromatic hydrocarbons with loss of nitrogen.

A close correlation would therefore be expected between the reactions of the diazo hydroxides studied by Gomberg and the reactions of nitrosoacylarylamines. Such a correlation has been found by Grieve and Hey (40), who have shown that when nitrosoacetanilide reacts in turn with toluene, chlorobenzene, nitrobenzene, and benzalde-
hydro, 4-methyl biphenyl, 4-chlorobiphenyl, 4-nitrobiphenyl and 4-phenyl benzaldehyde, respectively, are formed. The phenyl group enters the aromatic nucleus at the para position in each case.

The N-nitrosoacylarylamines are formed by the action of nitrous fumes on an acetic acid solution of an anilide. From acetaldehyde, Fischer (33) obtained nitroso-acetanilide, which was later used by Bamberger (7), who showed that in benzene solution, nitrogen was evolved and biphenyl was formed:

\[ \text{C}_6\text{H}_5\text{N(NO)}\text{COCH}_3 + \text{C}_6\text{H}_6 \rightarrow \text{C}_6\text{H}_5\text{C}_6\text{H}_5 + \text{N}_2 + \text{CH}_3\text{COOH} \]

Similar reactions were carried out with nitroso-\(p\)-bromoacetanilide by Hantzsch and Weschsler (43) in 1902. Aside from these instances, the reaction received scant attention until 1934, when Grieve and Hey (40) carried out the series of reactions between nitrosoacetanilide and various aromatic liquids, showing the close relationship between these reactions and those of the aryl diazoates studied by Gomberg and his co-workers (37, 38). Since 1934, the reactions of nitrosoacetanilide and its derivatives have been extensively studied by Grieve and Hey and their co-workers (18, 34, 41, 42, 45) until 1940,
when the reaction was so developed that they could obtain unsymmetrical biphenyl compounds in yields of approximately 60% (35,36). The same year, Elks, Haworth, and Hey (29) announced a modification of the Gomberg reaction, giving yields of unsymmetrical biphenyls as high as 60%.

Recently, Hodgson and Marsden (51,52) offered two entirely different approaches to the synthesis of biphenyl compounds. The two approaches are based on their ability to stabilize the diazo compound in such a manner as to enable it to be isolated and dried. The dry stabilized diazonium salt may be decomposed with substituted aryl hydrocarbons such as benzene, producing the biaryl compound in yields as high as 70%. If the dry stabilized salt is stirred with ethyl alcohol and gradually decomposed with zinc or copper powder, it is possible to replace the amine group with hydrogen in yields as high as 90%.

In this research, an attempt was made to apply these various methods of synthesis to the preparation of meta nitrobiphenyl which would serve as a suitable starting material for studies involving the meta biphenyl radical.
Methods of synthesis.-- For a method of synthesis to be of practical value, it is necessary that the starting material be reasonably easy to obtain at low cost, and that good yields be obtained in as few steps as possible.

Of the many different methods of synthesis given in the literature applicable to the preparation of meta biphenyl derivatives, there are several that might be suitable for the preparation of the meta biphenyl derivatives in large quantities. The methods fall into two distinct classes, direct and indirect.

Under the direct method of synthesis may be classified the reactions of the nitrosoacylarylamines studied by Grieve and Hey and their co-workers (36,40,45). Applying this synthesis to the preparation of m-nitro biphenyl, the following step-wise reactions should be possible;

\[
m-\text{NO}_2\text{C}_6\text{H}_4\text{NHCOCCH}_3 + \text{N}_2\text{O}_3 \rightarrow m-\text{NO}_2\text{C}_6\text{H}_4\text{N(NO)COCCH}_3 \]

\[
m-\text{NO}_2\text{C}_6\text{H}_4\text{N(NO)COCCH}_3 + \text{C}_6\text{H}_6 \rightarrow m-\text{NO}_2\text{C}_6\text{H}_4\text{C}_6\text{H}_5 + \text{N}_2 + \text{CH}_3\text{COOH}
\]

In reaction III, the nitroacetanilide is treated with nitrous fumes, and the nitroso compound formed was separated by pouring into ice water. The nitroso compound is dissolved in benzene and allowed to decompose
slowly, producing the desired 3-nitro biphenyl. The reaction is thought to be non-ionic as it is not affected by the normal polar directing influences. By studying the rate of evolution of nitrogen, which is a good criterion of the speed of the reaction, conditions have been varied in order to determine the optimum conditions for synthesis. In general it was found that for reaction IV, a low concentration of the nitrosoacylarylamine in benzene and room temperature, gave the best results.

Another direct method of synthesis is that of Elks, Haworth, and Hey (29) who, in 1940, modified the Gomberg coupling reaction by substituting aqueous sodium acetate for the sodium hydroxide normally used. The Gomberg reaction has been previously modified by many workers using various buffered solutions, but in no case have the yields greatly exceeded 20%. In the modification of Elks, Haworth, and Hey, using sodium acetate alone, the increased yields were claimed to be as high as 60%. The Gomberg reaction (37) has been definitely established to be inherently poor due to the heterogeneous nature of the reaction, and due to the tendency of the product, as formed, to couple again, and in this way, build up higher molecular weight compounds. By the use of efficient stirring and a buf-
fered alkaline solution, such as given by sodium acetate, these difficulties are thought to be minimized. The reaction may be represented by the following equations:

\[
\begin{align*}
m-\text{NO}_2\text{C}_6\text{H}_4\text{NH}_2\text{HCl} + \text{HNO}_2 & \rightarrow m-\text{NO}_2\text{C}_6\text{H}_4\text{N}_2\text{Cl} \\
\text{CH}_3\text{COONa} & \\
m-\text{NO}_2\text{C}_6\text{H}_4\text{N}_2\text{Cl} + \text{C}_6\text{H}_6 & \rightarrow m-\text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{NO}_2
\end{align*}
\]

The amine diazotized in the normal manner is vigorously stirred with benzene, while an aqueous solution of sodium acetate is gradually added. The mixture is stirred for 48 hours, after which the benzene layer is separated and the biphenyl compound isolated.

Another recent development that may be applied to the direct synthesis of meta biphenyl compounds is the method of Hodgson and Marsden (52), using the stabilized diazo salt. The stable salt is prepared by adding to the diazotized solution either zinc chloride, naphthalene sulfonic acid, or naphthalene disulfonic acid. The precipitated double salt may be filtered and dried. It is stable enough that it may be kept for several weeks. The dry salt is suspended in dry benzene and decomposed by a mixture of acetic anhydride and sodium acetate. As the diazo compound decomposes, it couples with benzene to form a bi-
phenyl compound. The principal advantage of the isolation and drying of the diazo salt is that it eliminates the usual aqueous medium. The reactions may be illustrated as follows:

\[ \text{m-NO}_2\text{C}_6\text{H}_4\text{NH}_2\text{HCl} + \text{HNO}_2 \rightarrow \text{m-NO}_2\text{C}_6\text{H}_4\text{N}_2\text{Cl} \]  
VII

\[ \text{m-NO}_2\text{C}_6\text{H}_4\text{N}_2\text{Cl} + \text{C}_{10}\text{H}_7\text{SO}_3\text{H} \rightarrow \text{m-NO}_2\text{C}_6\text{H}_4\text{N}_2\text{Cl} \cdot \text{C}_{10}\text{H}_7\text{SO}_3\text{H} \]  
VIII
(Stable salt)

\[ \text{m-NO}_2\text{C}_6\text{H}_4\text{N}_2\text{Cl} \cdot \text{C}_{10}\text{H}_7\text{SO}_3\text{H} + \text{C}_6\text{H}_6 \rightarrow \text{m-C}_6\text{H}_5\text{C}_6\text{H}_4\text{NO}_2 + \text{N}_2 \]  
IX

+ \text{HCl} + \text{C}_{10}\text{H}_7\text{SO}_3\text{H}

The method of Hodgson and Marsden may also be applied to the indirect synthesis of meta biphenyl compounds, principally based on the improvement of the method of removal of the amine group and replacement by hydrogen (51). When the stable diazo salt is suspended in alcohol and decomposed with zinc dust, the diazo group is replaced with hydrogen in almost quantitative yields. This, therefore, makes it possible to use as a starting material such a compound as 4-amino biphenyl, commonly called xenylamine (63). For, when xenylamine is acetylated, then nitrated, the entering nitro group enters the 3 position of the biphenyl nucleus, or ortho to the acetamido group, which is already present (10,12). Fichter and Sulzberger (32),
Bell and Kenyon (11) and Banus and Tomas (8) prepared 3-nitro 4-amino biphenyl in better than 80% yields by the following series of reactions:

\[
\begin{align*}
\text{p-} & \text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{NH}_2 + (\text{CH}_3\text{CO})_2\text{O} \rightarrow \text{p-} \text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{NHCOCH}_3 \\
p- & \text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{NHCOCH}_3 + \text{HNO}_2 \rightarrow \text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{NHCCOCH}_3
\end{align*}
\]

Bell and Kenyon (11, 56), and Scarborough and Waters (69) also prepared 3-chloro 4-acetamido biphenyl in better than 80% yield by direct chlorination of 4-acetamido biphenyl. Since these compounds seem to be easily obtained, the application of Hodgson and Marsden's method of replacement of the amine group by hydrogen to these compounds, should result in the preparation of the corresponding meta biphenyl derivatives as indicated in the following equations:

\[
\begin{align*}
\text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{NHCOCH}_3 + \text{NaOH} & \rightarrow \text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{NH}_2 \\
\text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{NH}_2 + \text{HCl} + \text{HNO}_2 & \rightarrow \text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{N}_2\text{Cl}_2 \\
\text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{N}_2\text{Cl}_2 + \text{C}_{10}\text{H}_7\text{SO}_3\text{H} & \rightarrow \text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{N}_2\text{Cl}_2 \cdot \text{C}_{10}\text{H}_7\text{SO}_3\text{H} \\
& \text{(Stable salt)}
\end{align*}
\]
Another indirect method of synthesis that may be applied to the synthesis of meta biphenyl compounds is that resulting from the rearrangements of the diacylanilines to acylamino ketones, studied by Chapman (22), Chattaway (24, 25), and others (70, 80).

Applying these studies to xenylamine, a parallel series of reactions should be noted. However, since the para position to the diacylaniline group is already filled, the rearrangement should produce only the ortho ketone.

Another indirect method of synthesis is suggested, using the industrially available compound*, 3-bromo 4-hydroxy biphenyl, which may be readily obtained by bromination of 4-hydroxy biphenyl (12, 13, 14, 48), a by-product of the preparation of phenol. Replacement of the hydroxy group with hydrogen would give the much desired 3-bromo biphenyl.

* The Dow Chemical Company
II. EXPERIMENTAL

1. Grieve and Hey Isodiazol Reactions

\textit{m-Nitroacetanilide}.-- The acetylation of meta-nitro aniline was accomplished by refluxing for twenty minutes one-half mole of meta-nitro aniline with one-half mole of acetic anhydride. The meta-nitro acetanilide was precipitated by pouring into cold water. After drying, 89 g. (98\%) of material, which melted at 152-4^\circ, was obtained.

\textit{Nitrosation of \textit{m}-nitroacetanilide}.-- Nitrous fumes, generated by heating a mixture of \textit{As}_2\text{O}_3 and nitric acid, were passed for 2\frac{1}{2} hours into a stirred solution of \textit{m}-nitroacetanilide (10 g.) in a mixture of glacial acetic acid (150 ml.) and acetic anhydride (50 ml.) cooled to 8^\circ. The nitroso compound separated as a yellow oil when the resulting deep green solution was diluted with ice water. This was immediately extracted with benzene (600 ml.), the extract being washed twice with ice water to remove any acetic acid. The benzene extract was kept at room temperature over anhydrous sodium sulfate as nitrogen was slowly evolved. After 24 hours, the decanted solution was concentrated to a thick viscous, black mass. The viscous mass was purified by vacuum distillation (20
mm.) and recrystallized from methyl alcohol. The yield was 1.5 g. (14%) of 3-nitro biphenyl with a m.p. of 59-60°, previously reported as 58.5° (32) and 61° (37).

This was no improvement over the Gomberg reaction, although Grieve and Hey claimed yields as high as 60%. The reaction was repeated and an attempt made to control the evolution of the nitrous fumes in such a manner as to give a steady rate. It was believed that the greatest loss occurred during the purification process. The boiling point of 3-nitro biphenyl was 195° at 20 mm. pressure, which made fractionation difficult. After repeating the nitrosation twice, the yield rose to 20%, and the control of the nitrosation still was unsatisfactory.

In a more recent publication, Haworth and Hey (45) found it more advantageous to prepare the nitrous fumes by the action of dilute sulfuric acid on solid sodium nitrite, rather than from arsenious oxide and concentrated nitric acid. The reaction was repeated using this modification. Only three grams (27%) of 3-nitro biphenyl were isolated, and some of the original m-nitro acetonilide was recovered, indicating incomplete nitrosation. Because of the difficulty of obtaining the nitrous fumes, the method
was discarded. However, a further study of this reaction should be made.

2. Hodgson and Marsden's Biaryl Synthesis

4-acetamido biphenyl. — One mole of p-amino biphenyl (xenylamine) was acetylated by refluxing for 30 minutes with one mole of acetic anhydride. The reaction mixture was poured into a large volume of cold dilute hydrochloric acid; the precipitated mass broken up and filtered, washed several times and dried. The dry product (201 g., 95%) melted at 169-170°, previously reported as 170° (8).

**Analysis.** Calculated for \( \text{C}_{14}\text{H}_{13}\text{ON} \):  
N, 6.63%  

**Found:** N, %

3-chloro 4-acetamido biphenyl. — Chlorine (7.5 g.) was slowly bubbled through a solution of 4-acetamido biphenyl (0.1 mole) in glacial acetic acid (300 ml.) in a tall vessel. A large precipitate began to form at once, and after the completion of the experiment, the mixture was diluted with 250 ml. of cold water. The light cream precipitate was filtered off and dried. 19 g. of product, melting at 143-146°, was obtained. Recrystallization from alcohol gave colorless needles with a melting point
of 145°, previously reported as 146° (10).

**Analysis.** Calculated for C\textsubscript{14}H\textsubscript{12}O\textsubscript{11}Cl: Cl, 14.5%

Found: Cl, 14.5%

3-chloro 4-amino biphenyl.-- The hydrolysis of 3-chloro 4-acetamido biphenyl was attempted using 65% sulfuric acid and warming on a steam bath. After making the solution basic, a material with an indefinite melting point (130-140°) was isolated. This was obviously unsatisfactory since the melting point of 3-chloro 4-amino biphenyl is 69° (10). The product was essentially 3-chloro 4-acetamido biphenyl. Hydrolysis was next attempted with 10% alcoholic hydrochloric acid heating on a steam bath. On cooling, the hydrochloride separated in fine colorless needles; m.p. 210°. The free base was obtained by neutralizing the hydrochloric acid with 30% sodium hydroxide; m.p. 69-70°, yield, 23 g. from 27 g. of 3-chloro 4-acetamido biphenyl.

**Analysis.** Calculated for C\textsubscript{12}H\textsubscript{17}NCl: N, 6.89%

Found: N, 6.9%

3-nitro 4-acetamido biphenyl.-- To 4-acetamido biphenyl, (27 g.) dissolved in glacial acetic acid (23 ml.) were added 26 ml. of concentrated nitric acid. The mixture
was warmed for 9 hours, and finally poured into a large volume of water. A reddish brown tarry mass was obtained, from which no alcohol soluble material could be extracted. The nitration was repeated using a mixture of fuming nitric acid (d. 1.52) and glacial acetic acid, refluxing the reaction mixture for one-half hour. The reaction mixture was then allowed to cool, and the mixture poured into twice its volume of water. The resulting deep yellow precipitate was filtered off and dried. Yield, 40 g. (92%) m.p. 128°. After recrystallizing from alcohol, long yellow needles with a melting point of 132° were obtained. The melting point previously given was 132° (8).

3-nitro 4-amino biphenyl.— The hydrolysis of the acetamido compound was accomplished by treating a warm alcoholic solution with 50% potassium hydroxide. The solution immediately turned deep red and a large amount of red needles separated out. From 39 g. of 3-nitro 4-acetamido biphenyl, there was obtained 30 g. (94%) of 3-nitro 4-amino biphenyl, m.p. 169-170°.

Analysis. Calculated for C_{12}H_{10}O_{2}N_{2}: N, 13.1%  
Found: N,  

3-nitro biphenyl.— The method of Hodgson and Mars-
den for the replacement of the amine group with hydrogen was applied to 3-nitro 4-amino biphenyl. Thirty grams of the amine was made into a paste and diazonized in the normal manner. To the diazo solution was added an equivalent quantity of naphthalene 1,5 disulfonic acid* (40 g.). After a few minutes, a precipitate of the stable double salt separated out. The stable salt was filtered off, and the dried salt suspended in ethyl alcohol. To the suspension 40 g. of powdered zinc was gradually added. After the evolution of nitrogen, the reaction mixture was extracted with ether** and the ether extracts concentrated. Yield, 10 g. (35%) of 3-nitro biphenyl, m.p. 60°.

The method of Hodgson and Marsden for the union of two aryl nuclei was next applied to the synthesis of 3-nitro biphenyl. Meta nitro aniline (0.5 mole) was diazonized in the normal manner. To the filtered solution was added a paste of naphthalene 1,5 disulfonic acid (0.5 mole). A light cream precipitate of the stable salt was almost immediately precipitated. After filtering and

* Furnished by National Aniline Chemical Company

** It has subsequently been shown that benzene or chloroform is the better extractant and should give a better yield.
drying, the dry salt was suspended in benzene (600 ml.) and gradually decomposed with a mixture of fused sodium acetate (60 g.) and acetic anhydride (20 ml.). After 48 hours the mixture was warmed until nitrogen ceased to be evolved, and the benzene solution separated and concentrated.

It was found best to purify the concentrated benzene solution of 3-nitro biphenyl by the use of superheated steam at 210°, maintaining the temperature of the material to be steam distilled at 210° by means of a wax bath. At temperatures lower than this, the distillation is too long and tedious because of the low volatility of the 3-nitro biphenyl with steam. At temperatures exceeding 230° the yield is decreased by the tendency to char and polymerize to a tarry mass. From the steam distillation, the 3-nitro biphenyl separates out as light yellow crystalline material which on recrystallization from alcohol had a melting point of 60-61°. Yield, 38 g. (40%).

The reaction was repeated, but the yield remained the same (40%).
3. Elks, Haworth, and Hey Diazoc Coupling

3-nitro biphenyl.-- One half mole of m-nitro aniline was diazotized in the normal manner, and to the filtered solution was added 1000 ml. benzene. To the mixture maintained at 5-8° and well stirred, was added 80 g. of a solution of sodium acetate in 200 ml. of water. Stirring was continued for 48 hours, the reaction being allowed to proceed at room temperature after the first three hours. The benzene layer was separated and distilled with superheated steam (210°) after removal of the excess benzene. Yield, 26 g. (30%).

The method was repeated using two stirrers, which made the reaction mixture more homogeneous. On two successive runs, the yields rose to 44% and 57%, which was quite satisfactory.

4. Miscellaneous

4-diacetylamino biphenyl.-- This was prepared after the method of Scarborough and Waters (70), whereby 4-acetamido biphenyl (7 g.), as previously prepared, is refluxed with acetic anhydride (35 ml.) and sodium acetate (3.5 g.) for six hours. The crystalline material produced
was filtered off and recrystallized from petroleum ether (b.p. 60-80°). Seven grams (83%) of a fine white crystalline material, m.p. 121°, was isolated. The m.p. was previously given as 121° (70).

3-bromo 4-hydroxy biphenyl.--- A crude sample of this material was obtained from the Dow Chemical Company, and after three recrystallizations from hot alcohol, obtained a white crystalline material, m.p. 94.5°.

Analysis: Calculated for C₁₂H₈Br(OH): OH, 6.83%
              Found: OH, 6.9%

An attempt was made to produce 3-bromo biphenyl by removal of the hydroxyl group from this compound using zinc dust. One-fifth of a mole of 3-bromo 4-hydroxy biphenyl was mixed with one-fifth of a mole of zinc dust, the mixture placed in a small distilling flask and heated. The boiling point rapidly rose to greater than 360°, and on cooling, the material solidified to an insoluble black resinous mass. From this mass no product could be extracted with alcohol or ether.

3-bromo 4-methoxy biphenyl.--- Twenty grams of recrystallized 3-bromo 4-hydroxy biphenyl (m.p. 94.5°) was dissolved in 10% sodium hydroxide (40 ml.), shaken with 12.6 g. of dimethyl sulfate, diluted with 40 ml. of water.
After half an hour the mixture was warmed on a water bath. The granular solid, which separated on cooling, gave on recrystallizing from alcohol, 3-bromo 4-methoxy biphenyl, m.p. 76-77°. Yield, 20 g. or 95%.

Analysis: Calculated for C₁₂H₈Br(OCH₃): OCH₃, 11.8%  
Found: OCH₃, %
The preparation of m-nitro biphenyl.-- The results obtained from the different syntheses tried indicate that the application of the method of Elks, Haworth, and Hey is the most promising. The method of Grieve and Hey, involving the use of nitrous fumes, was, in general, unsatisfactory, because of the difficulty of handling the nitrous fumes, and the control of their production. The method of Hodgson and Marsden was quite promising, but because of the large amount of naphthalene 1,5 disulfonic acid required, this was abandoned in favor of the Elks, Haworth, and Hey modification. It was also found superior to use superheated steam (210°) for the purification of the 3-nitro biphenyl in preference to solvent extraction or vacuum distillation. The following modified procedure was found to give the best yields (57%).

The diazotization of m-nitro aniline (0.5 mole) is followed in the usual manner, keeping the volume at a minimum. To the resulting filtered diazonium solution benzene was added and the mixture vigorously stirred. A solution of sodium acetate (30 g. of trihydrate) in
water (200 ml.) was gradually added. Stirring was continued for 48 hours, the reaction being allowed to take place at room temperature after the first three hours. The benzene layer was separated, the benzene distilled off, transferring the residue while still warm to a flask for steam distillation. The flask containing the material to be steam distilled was heated in a wax bath to 210°. After the removal of the residual benzene, the flask was connected to a source of superheated steam maintained at 210°. The 3-nitro biphenyl separated in light yellow crystals, and may be filtered off and dried. The fairly pure product may be recrystallized from ethyl alcohol, giving a product with a melting point of 60-61°.

In connection with the literature survey, it was thought advisable to tabulate the various physical constants of the m-biphenyl compounds. The results are shown in table I.

In dealing with the problem of purification of the 3-nitro biphenyl, the solubilities of 3-nitro biphenyl were determined and the results tabulated in table II.
<table>
<thead>
<tr>
<th>NAME</th>
<th>FORMULA</th>
<th>N. W.</th>
<th>M. P.</th>
<th>B. P.</th>
<th>mm. press.</th>
<th>Solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-nitro</td>
<td>m-C₆H₅C₆H₄NO₂</td>
<td>199</td>
<td>61</td>
<td>200-3°</td>
<td>20</td>
<td>s. alc., ether</td>
</tr>
<tr>
<td>3-amino</td>
<td>m-C₆H₅C₆H₄NH</td>
<td>169</td>
<td>30</td>
<td>254°</td>
<td>135</td>
<td>sl. s. w., s. alc.</td>
</tr>
<tr>
<td>3-acetamido</td>
<td>m-C₆H₅C₆H₄NHCOCH₃</td>
<td>211</td>
<td>148</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-cyano</td>
<td>m-C₆H₅C₆H₄CN</td>
<td>179</td>
<td>49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-carboxy</td>
<td>m-C₆H₅C₆H₄COOH</td>
<td>198</td>
<td>160-1</td>
<td></td>
<td></td>
<td>s. ether, benzene</td>
</tr>
<tr>
<td>3-chloro</td>
<td>m-C₆H₅C₆H₄Cl</td>
<td>188</td>
<td>89</td>
<td>284°</td>
<td></td>
<td>s. alc., ether</td>
</tr>
<tr>
<td>3-bromo</td>
<td>m-C₆H₅C₆H₄Br</td>
<td>233</td>
<td></td>
<td>170-3°</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>3-iodo</td>
<td>m-C₆H₅C₆H₄I</td>
<td>280</td>
<td></td>
<td>195-7°</td>
<td>20</td>
<td>sl. s. w., v. s. alc.</td>
</tr>
<tr>
<td>3-hydroxy</td>
<td>m-C₆H₅C₆H₄OH</td>
<td>170</td>
<td>75-8</td>
<td>360°</td>
<td></td>
<td>s. alc., ether</td>
</tr>
<tr>
<td>3-ethoxy</td>
<td>m-C₆H₅C₆H₄OC₂H₅</td>
<td>197</td>
<td>34</td>
<td>305°</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-methyl</td>
<td>m-C₆H₅C₆H₄CH₃</td>
<td>168</td>
<td></td>
<td>148-9°</td>
<td>20</td>
<td>s. h. alc., s. ether</td>
</tr>
<tr>
<td>3-phenyl</td>
<td>m-C₆H₅C₆H₄C₆H₅</td>
<td>230</td>
<td>66-7</td>
<td>363</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 - d. l.-410 n. l. 6411
2 - d. l.-031 n. l. 595
TABLE II

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Solubility in g./100 ml. at 25°</th>
<th>Solubility in g./100 ml. at the B.P. of the solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ether</td>
<td>50</td>
<td>170</td>
</tr>
<tr>
<td>Ethanol</td>
<td>2.5</td>
<td>36</td>
</tr>
<tr>
<td>Isopropyl</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>Chloroform</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Methanol</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

Because many compounds have characteristic spectral transmission curves, these were determined for some of the unsymmetrical biphenyl compounds, by means of a Cenco-Sheard Spectrophotometer. These characteristic curves are shown in figure I.
FIGURE I

SPECTRAL TRANSMISSION CURVES
FOR UNSYMMETRICAL BIPHENYL COMPOUNDS

O.l.g. in 10 ml. Abs. Alc.
IV SUMMARY

1. The various methods of synthesis that could be applied to the synthesis of the m-biphenyl derivatives have been tried.

2. Conditions which gave satisfactory results were not found for the method of Grieve and Hey.

3. The method of Hodgson and Marsden may be applicable, but requires the use of large quantities of naphthalene sulfonic acid. Yields obtained by this method were as high as 40%.

4. The method of Elks, Haworth, and Hey was found to be the most satisfactory, obtaining yields as high as 57%.

5. An improved method of synthesis for 3-nitro biphenyl is given.

6. The solubilities of meta nitro biphenyl in some of the common organic solvents was determined and tabulated.
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