

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MICHIGAN]
THE SYNTHESIS OF BIARYL COMPOUNDS BY MEANS OF THE DIAZO REACTION

BY M. GOMBERG AND W. E. BACHMANN

RECEIVED JUNE 27, 1924

PUBLISHED OCTOBER 4, 1924

The formation of biaryl compounds through the diazo reaction has been observed at various times by different investigators. These compounds are produced principally under the following conditions.

Reduction of the Diazonium Salts.—When the reduction of the salt, accompanied by liberation of nitrogen, is only partial, then there ensues in addition to the formation of the hydrocarbon also a coupling of two aryl radicals: $RN_2X + H_2 = RH + N_2 + HX$; $2RN_2X + H_2 = R.R + 2N_2 + 2HX$.

Diazonium salts which contain negative substituents in the benzene nucleus are particularly prone, under these conditions, to give rise to biaryl derivatives. As reducing agents, alcohol and sodium alcoholate,¹ stannous chloride alone or in conjunction with formic acid,² finely divided copper,³ cuprous chloride,⁴ have been used. Only symmetrical biaryls are produced in this reaction.

Direct Coupling.—In a few instances it has been observed that a diazonium salt may couple directly with some other component so as to form an unsymmetrical biaryl. A notable example of this is the formation of *p*-hydroxybiphenyl from phenyl-diazonium chloride and phenol.⁵

Employment of Dry Diazonium Salts.—This is in the nature of a Friedel and Crafts' reaction. The dry diazonium chloride is suspended in benzene or other compound of ring structure and to the mixture aluminum chloride is added. Biphenyl, phenyl-thiophene, phenyl-pyridine, phenyl-naphthalene and other unsymmetrical biaryls have been prepared in this manner.⁶

Coupling of Isodiazo Esters, Isodiazo Hydroxides, and of Diazo Oxides with Benzene, Thiophene, etc.—Kühling⁷ found that the isodiazo esters when dry are very reactive and couple, for instance, as follows: $p\text{-NO}_2\text{C}_6\text{H}_4\text{N}_2\text{OCOR} + \text{C}_6\text{H}_6 = p\text{-NO}_2\text{C}_6\text{H}_4\text{C}_6\text{H}_5 + \text{N}_2 + \text{HOCOR}$. It was, however, shown by Bamberger⁸ that the isodiazo hydroxides are

¹ Griess, *Ann.*, **137**, 79 (1866). Oddo, *Gazz. chim. ital.*, **20**, 633 (1890). Beeson, *Am. Chem. J.*, **16**, 235 (1894).

² Culmann and Gasiorowski, *J. prakt. Chem.*, **40**, 97 (1889).

³ Gattermann, *Ber.*, **23**, 1226 (1890). Knoevenagel, *Ber.*, **28**, 2049 (1895). Niementowski, *Ber.*, **34**, 3325 (1901).

⁴ Ullmann and Forgan, *Ber.*, **34**, 3802 (1901).

⁵ Hirsch, *Ber.*, **23**, 3705 (1890); **25**, 1973 (1892).

⁶ Mohlau and Berger, *Ber.*, **26**, 1196, 1994 (1893).

⁷ Kühling, *Ber.*, **28**, 41, 523 (1895); **29**, 165 (1896).

⁸ Bamberger, *Ber.*, **28**, 403 (1895).

equally effective for this reaction. Bamberger also developed a new method for accomplishing the same purpose, employing for the coupling reaction what he designates as "diazonium oxides," or diazo anhydrides:⁹
 $\text{NO}_2\text{C}_6\text{H}_4\text{N}_2\text{O}\cdot\text{N}_2\text{C}_6\text{H}_4\text{NO}_2 + 2\text{C}_6\text{H}_6 = 2\text{NO}_2\text{C}_6\text{H}_4\cdot\text{C}_6\text{H}_5 + \text{N}_2 + \text{H}_2\text{O}$.
These oxides are obtained usually as precipitates by adding acetic acid to a concentrated solution of the alkali aryl diazotate, RN_2OK , or in some instances by the cautious addition of alkali to an acid solution of the diazonium salt. They are very unstable and when dry are powerfully explosive, the violent decomposition occurring at times without apparent provocation. Thus, for instance, *p*-chlorobenzene diazo oxide, which may be considered as one of the more stable of this class of oxides, is more explosive than is diazobenzene nitrate.

Whether these unstable substances really have the constitution assigned to them by Bamberger on the basis of the analysis of one individual only, must be left undecided. Suffice it for our purpose that they represent that tautomeric form of the diazonium base which is most reactive.

The New Procedure

In connection with some work in progress in this Laboratory, the need arose for a considerable amount of *p*-bromobiphenyl. In order to avoid possible contamination of our product with *p,p'*-dibromobiphenyl, we turned, as other have done,¹⁰ to Bamberger's method of preparation in preference to the direct bromination of biphenyl. Because the dry diazo oxides are so very explosive, Bamberger employed for the coupling reaction freshly precipitated and only partially dried oxides. Even under these conditions explosions could not always be avoided. Thus, *p*-toluene diazo oxide on several occasions exploded when still on the filter paper and mixed with ice; in other experiments it gave rise to mild explosions when in solution and at -4° . Benzene diazo oxide is described as being even more explosive than the toluene compound. In one experiment an explosion occurred when the benzene diazo oxide, mixed with ice and water, was in a freezing mixture at -18° .

It is apparent that the preparation of biaryl compounds in appreciable amounts through the agency of the diazo oxides in the manner hitherto practiced is a task which entails serious difficulties. We have sought to obviate these difficulties by avoiding altogether the isolation of the diazo oxides as such. Indeed, Bamberger himself remarks that *p*-nitrobenzene diazo oxide couples readily with benzene when, in the presence of the hydrocarbon, the oxide is being precipitated from a solution of the corresponding diazonium chloride by means of alkali. The yield of the biaryl compound was, however, found by him to be small, and we found no mention

⁹ Bamberger, *Ber.*, 29, 446 (1896).

¹⁰ Schlenk, *Ber.*, 46, 1478 (1913).

that Bamberger used this procedure with the less stable or with any other diazo oxides. Borsche¹¹ later coupled phenyl-diazonium chloride in water with a cold alkaline aqueous solution of *p*-nitrosophenol and obtained, instead of the anticipated azo compound, phenyl-nitrosophenol in a yield of 7-8%. Though unable to explain the peculiar course of the reaction, he attributed it to something more than merely the presence of a nitroso group in the phenol molecule.

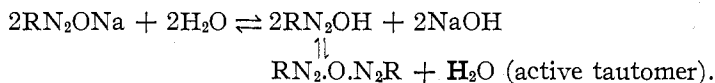
Our own experiments indicate without doubt that diazonium salts in aqueous solution, under certain conditions, can couple with hydrocarbons and many diverse derivatives therefrom, free nitrogen being evolved and a biaryl formed. The reaction is quite general, but the yields vary with the individual components. However, even when the yield is small, this reaction still constitutes the readiest means for establishing the constitution of unsymmetrical biaryls. The method is rapid, easy to carry out, and is free from danger. We have carried out in this Laboratory over three hundred such coupling reactions, often with 100 g. of diazotized amine, and have not had a single explosion or any violent decomposition in the course of the experiments.

Our procedure has been as follows. The amine, Component A, is diazotized in the usual manner, the bulk of the water being kept as small as possible. Benzene, Component B, or whatever the desired second component for the reaction may be, is added, the cooled mixture is well stirred and to it is added, drop by drop, a 15 to 25% solution of sodium hydroxide. As soon as the excess of acid has been neutralized the reaction begins to be apparent. As the alkali comes now in contact with the diazonium salt solution a yellow to an orange precipitate or a mere coloration is produced, due to the formation of the so-called diazo oxide. This is taken up by the second component, reaction ensues and nitrogen is evolved. The addition of alkali is continued until the mixture contains about 1 to 2% of free alkali. After the mixture has reached room temperature and the evolution of nitrogen has ceased, the immiscible layer is separated from the water, the excess of component B is distilled, and the biaryl is separated from the mixture by steam distillation. The residue in the distilling flask is a mixture of many high-melting compounds, for the coupling reaction is far from simple. With benzene, for instance, it was possible to prove that there is produced in addition to biphenyl, also *p*-diphenylbenzene; thus, $C_6H_5N_2Cl + NaOH + C_6H_6 = C_6H_5.C_6H_5 + N_2 + NaCl + H_2O$; $C_6H_5N_2Cl + NaOH + C_6H_5.C_6H_5 = C_6H_5.C_6H_4.C_6H_5 + N_2 + NaCl + H_2O$. Moreover, the indications are that the coupling with benzene proceeds even further than indicated above in the second equation, and that there are produced long chains with 4, or 5, and perhaps more, benzene nuclei condensed

¹¹ Borsche, *Ber.*, **32**, 2935 (1899); *Ann.*, **312**, 211 (1900).

into one molecule.¹² In other words, the diazo compound enters into combination not only with Component B but also with the biaryl derivative thus produced.

It has been mentioned above that the coupling reaction ensues usually as soon as the excess of acid in the diazonium solution has been neutralized and the diazo oxide commences to be produced. The coupling may occur, however, even when the solution is distinctly alkaline. Thus, we obtained equally good results in the preparation of biphenyl when phenyl-diazonium chloride was slowly added to a well-stirred mixture of benzene and alkali in water, so that the solution was maintained continuously alkaline, and at the end of the operation contained 2% of free alkali. There is no doubt, it seems, that under these conditions the normal sodium diazotate is first produced, and this being a salt of a weak acid, is partially hydrolyzed:¹³



In fact, we are inclined to believe that a certain definite concentration of hydroxyl ion is essential before the reactive "diazo oxide" is actually produced. We find, for instance, that a solution of phenyl-diazonium hydroxide which has been prepared by shaking phenyl-diazonium chloride in water with silver oxide, does not react appreciably with benzene unless a drop of sodium hydroxide solution is added to the mixture. We stated in the description of the general procedure that the coupling reaction commences soon after the excess of acid in the diazotized solution has been neutralized, and the liberation of the diazonium base has begun. We interpret the formation at this initial stage of the active tautomer of the diazo compound on the basis that there is a temporary local preponderance of hydroxyl ions as each drop of concd. alkali solution comes in contact with the solution of the diazonium salt. The question naturally arises: since the diazonium hydroxides are quite strong bases, why is not the process of activation in this case autogenic? Further work is now being carried on in this Laboratory in connection with this subtle, apparently catalytic, influence of alkali on the cause of the coupling reaction.¹⁴

In the following table is given a summary of the results we have obtained on various amines. The yields indicated have been obtained when the general procedure has been followed. There can be no doubt, however, that in many instances the yields will be improved when the most favorable conditions of temperature and hydroxyl-ion concentration have been determined for each specific instance.

¹² See Gerngross and Dunkel, *Ber.*, 57, 739 (1924). Our work had been completed before the publication of that interesting paper.

¹³ Hantzsch and Davidson, *Ber.*, 31, 1643 (1898). Bamberger and Müller, *Ann.*, 313, 124 (1900).

¹⁴ Hantzsch, *Ber.*, 28, 1735, 1748 (1895); 29, 1067 (1896).

TABLE I
RESULTS OBTAINED ON COUPLING DIAZOTIZED AMINES WITH VARIOUS COMPOUNDS

Component A	Component B	Product	M. p. °C.	B. p. °C.	Yield %
Aniline	Benzene	Biphenyl	70.5	22
Aniline	Thiophene	Phenylthiophene	42-43	11
Aniline	Cyanobenzene	<i>p</i> -Cyanobiphenyl	88	10
Aniline	Bromobenzene	<i>o</i> - and <i>p</i> -Bromobiphenyl
Aniline	Methyl benzoate	Methyl <i>p</i> -phenyl-benzoate	118.5
Aniline	Nitrobenzene	<i>p</i> -Nitrobiphenyl	113
Aniline	Pyridine	Phenylpyridine	54-55
<i>p</i> -Bromo-aniline	Benzene	<i>p</i> -Bromobiphenyl	91.2	40-46
<i>p</i> -Bromo-aniline	Thiophene	* <i>p</i> -Bromophenyl-thiophene	100	20
<i>m</i> -Bromo-aniline	Benzene	* <i>m</i> -Bromobiphenyl	299-301	28
<i>p</i> -Chloro-aniline	Benzene	<i>p</i> -Chlorobiphenyl	77.7	41
<i>p</i> -Chloro-aniline	Thiophene	* <i>p</i> -Chlorophenyl-thiophene	83	24
<i>m</i> -Chloro-aniline	Benzene	* <i>m</i> -Chlorobiphenyl	284-285	27
<i>p</i> -Nitro-aniline	Benzene	<i>p</i> -Nitrobiphenyl	114	30
<i>p</i> -Nitro-aniline	Thiophene	* <i>p</i> -Nitrophenyl-thiophene	137-138	23
<i>m</i> -Nitro-aniline	Benzene	<i>m</i> -Nitrobiphenyl	61	18
<i>o</i> -Nitro-aniline	Benzene	<i>o</i> -Nitrobiphenyl	36.7
<i>p</i> -Cyano-aniline	Benzene	<i>p</i> -Cyanobiphenyl	88	15
<i>m</i> -Cyano-aniline	Benzene	* <i>m</i> -Cyanobiphenyl	49	19
<i>m</i> -Cyano-aniline	Thiophene	* <i>m</i> -Cyanophenyl-thiophene	53-54	15
<i>p</i> -Aminobiphenyl	Benzene	<i>p</i> -Diphenylbenzene	209-210
Ethyl- <i>p</i> -amino benzoate	Benzene	<i>p</i> -Phenyl-ethyl benzoate	50	12

Compounds marked with an asterisk are those prepared for the first time.

Summary

When diazonium salts in aqueous solution are neutralized, a slight excess of the alkali activates the diazo hydroxides in such a manner that now they can couple with aromatic hydrocarbons and various derivatives therefrom. A large number of unsymmetrical biaryls have thus been prepared, many for the first time. The yields vary with the individual components that partake in the coupling process.

ANN ARBOR, MICHIGAN

[CONTRIBUTION FROM THE COLOR LABORATORY, BUREAU OF CHEMISTRY, UNITED STATES
DEPARTMENT OF AGRICULTURE, No. 96]

THE HYDROLYSIS OF AURAMINE

BY WALTER C. HOLMES¹ AND J. FERRIS DARLING²

RECEIVED JULY 14, 1924

PUBLISHED OCTOBER 4, 1924

Under favorable conditions auramine is readily hydrolyzed in aqueous solution, with the formation of tetramethyl-*p*-diamino-benzophenone (Michler's ketone) and ammonium chloride. The factors which influence the hydrolysis are of obvious practical interest to those concerned in the manufacture or application of the dye.

The volumetric method for the estimation of the dye by means of titration with a standard solution of indigotin, in the manner proposed by

¹ Associate Chemist, Color Laboratory, Bureau of Chemistry.

² E. I. du Pont de Nemours and Company.