

A STUDY OF THE NAPHTHO[1,2]TRIAZOLES

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A THESIS

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by

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Approved:

Handwriting practice lines showing cursive letters 'l', 'n', and 'o' written on a set of three horizontal lines. The letter 'l' is on the top line, 'n' is on the middle line, and 'o' is on the bottom line. There are also some faint, illegible markings on the lines.

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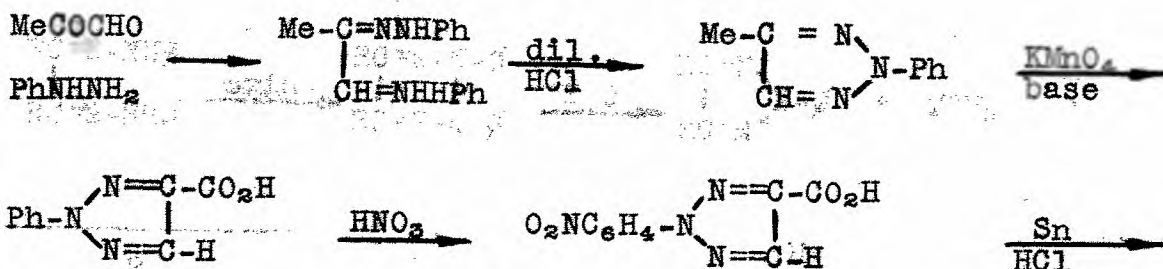
INTRODUCTION

The triazole series embraces a ring structure of three nitrogen atoms and two carbon atoms. Of the various triazoles known, this work deals only with the 1,2,3-triazole type, in which the three nitrogen atoms occur consecutively in the ring instead of being interspersed with carbon atoms.

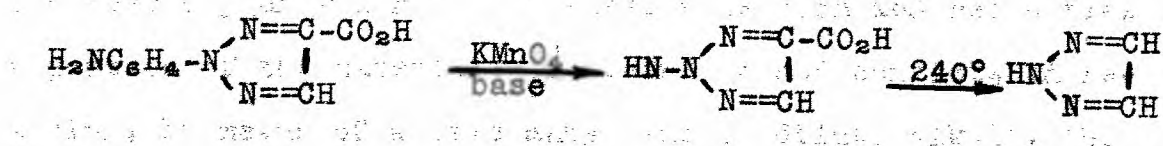
According to Whitmore¹, osotriazole is the simplest 1,2,3-triazole. It boils at 206° and is made from

$$\begin{array}{ccc} \text{HN} = \text{N} \equiv \text{N} & \longrightarrow & \text{HN} \diagup \text{N} \diagdown \\ & & | \quad | \\ \text{HC} \equiv \text{CH} & & \text{HC} = \text{CH} \end{array}$$

which indicated the greater stability of the five-carbon acetylene and hydrazoic acid. The action of pyruvic aldehyde on phenylhydrazine gives a hydrazone, and the hydrazone proceeds to the 1,2,3-triazole upon treatment with dilute hydrochloric acid and ferric chloride.

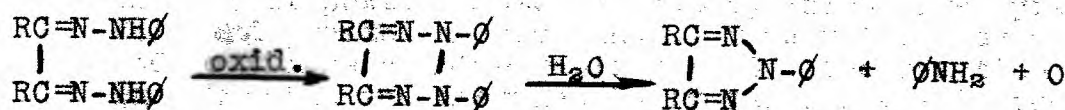


¹F. C. Whitmore, Organic Chemistry, New York: D. van Nostrand, 1937. pp. 898-899.



Once the triazole is formed, it is stable to potassium permanganate in basic solution, to nitric acid, to reduction with tin and hydrochloric acid, and to elevated temperatures.

According to Cohen², the osotriazoles are mostly oils with an alkaloidal smell, and weak basic properties. At the same time they are remarkably stable towards oxidizing agents, the side chains being oxidized to carbonyl groups. Nitro-compounds and sulfonic acids can be obtained also. v. Pechmann³ was the first to prepare them by a reaction which indicates the greater stability of the five-carbon over the six-carbon ring. When an osazone is oxidized it is converted into a tetrazone, which, by the action of dilute mineral acids, loses one nitrogen group as primary amine.



²J. B. Cohen, Organic Chemistry for Advanced Students, Part I, London: Edward Arnold, 1928. pp. 303-304. Quoted from O. Dimroth, Ann., 335: 1, 1904.

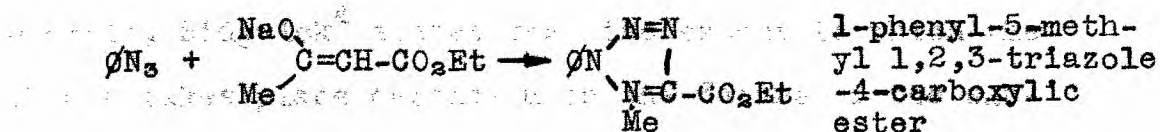
³Baltzer, von Pechmann, Ann. 262: 303, 1891.

The free oxygen which is liberated acts upon and resinifies a portion of the material. A second method consists in removing, by means of acetic anhydride or dilute alkali, the elements of water from the hydrazoxime of a 1,2-diketone:



Sidgwick states⁴,

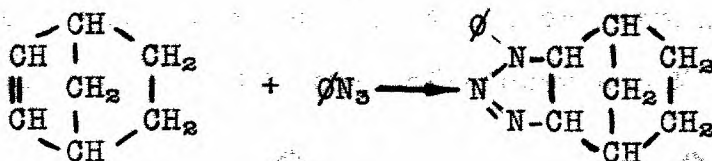
"The addition reactions of the azides, which have been mainly studied with phenyl azide, can be divided into two classes, those in which addition takes place to a compound containing a reactive methylene or methine group, that is, compounds which are capable of tautomerism of the keto-enol type, and those in which it takes place to an ethylene or an acetylene."



"The addition of phenyl azide to unsaturated compounds leads to triazoles or triazolines but take place much less readily than the very similar addition of aliphatic diazo compounds, which give pyrazole and pyrazoline compounds. Thus while diazomethane and acetylene combine rapidly at 0°, the reaction of phenyl azide and acetylene only takes place if the components are heated in acetone in a sealed tube at 100° for 70 hours. Again diazo acetic ester will combine with an aromatic system. The conditions which determine whether addition takes place or not are not

⁴N. V. Sidgwick, The Organic Chemistry of Nitrogen, Oxford: Clarendon Press, 1937. pp. 371, p. 372, p. 351.

fully known, but in general it can be said that if a double bond is conjugated with an aromatic nucleus the addition takes place much less readily, while if the double bond is in a cyclic system in which there is any appreciable ring-strain, the addition product is formed very easily.¹



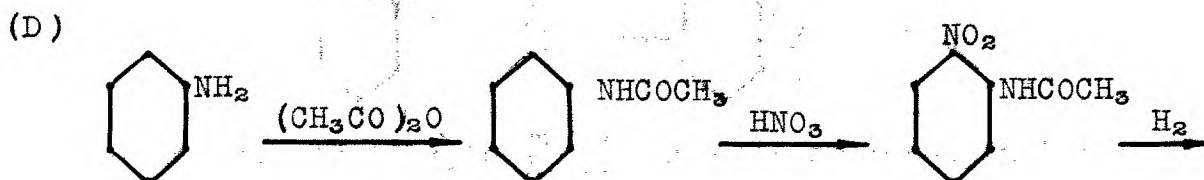
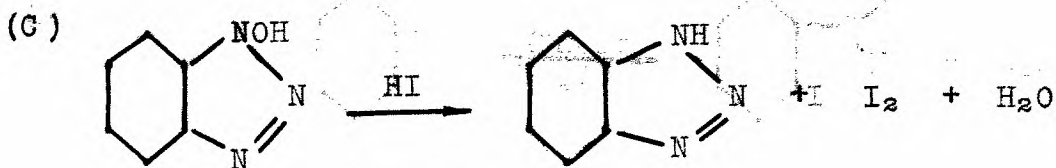
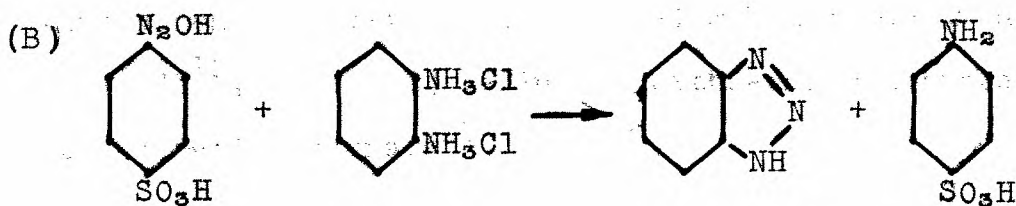
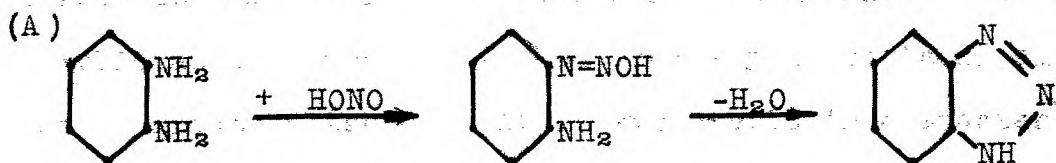
It is also noted⁴ that certain hydroxy triazoles, which are stable as their alkali salts, change spontaneously, either totally or in part, into diazo derivatives of acid amides when set free from those salts. As an example, Sidgwick⁴ states that the extent to which the change takes place depends upon the nature of the substituents R and R'. In some cases a true equilibrium is thought to exist between the compounds.



Such studies have been helpful in the development of the subject of tautomerism.

In continuing the study, it might be well to outline some of the methods which have been used to synthesize some of the higher triazoles. Benzotriazole has been made in

small yields by (A) the action of nitrous acid on ortho-phenylenediamine⁵, by (B) the action of para-diazobenzene-sulfonic acid in a water solution of ortho-phenylenediamine hydrochloride⁶, and by (C) heating 1-hydroxybenzotriazole with hydriodic acid in a tube⁷. A better method of making 1,2,3-benzotriazole is (D) that of Fieser and Martin⁸.

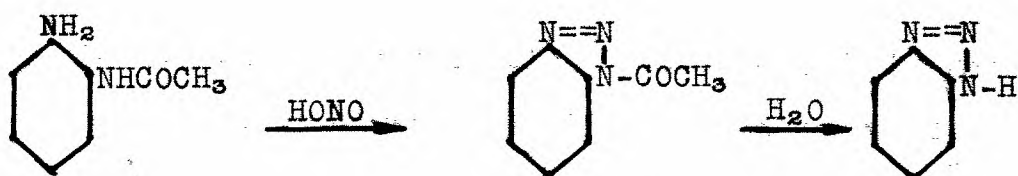


⁵A. Ladenberg, Ber., 9: 222, 1876.

⁶P. Griess, Ber., 15: 2195, 1882.

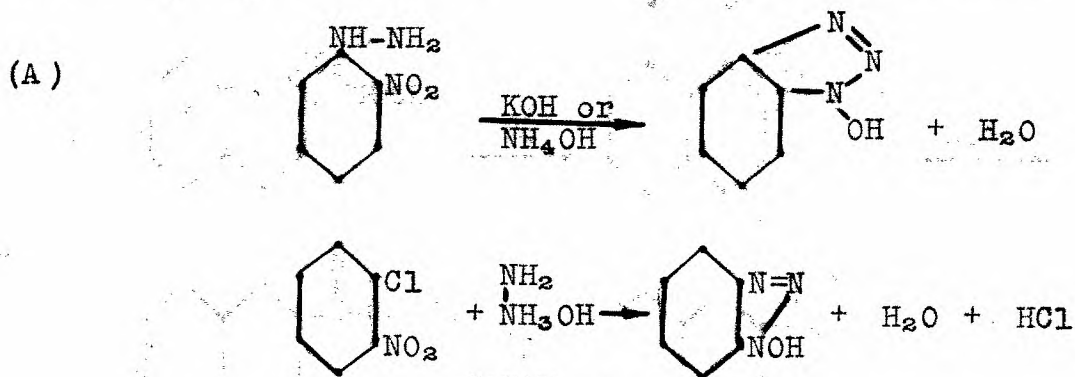
⁷Zincke, Schwarz, Ann., 311: 333, 1900.

⁸L. F. Fieser, and E. L. Martin, J. Am. Chem. Soc., 57: 1835, 1840, 1935.



Benzotriazole melts at about 99° and the triazole ring is stable to oxidation with potassium permanganate while carboxylic acid groups are formed from any aromatic or aliphatic groups attached. It is amphoteric in character⁹.

The 1-hydroxybenzotriazole is made by (A) treating 2-nitrophenylhydrazine with potassium hydroxide or ammonium hydroxide¹⁰, or by (B) refluxing ortho-chloronitrobenzene with hydrazine hydrate¹¹.



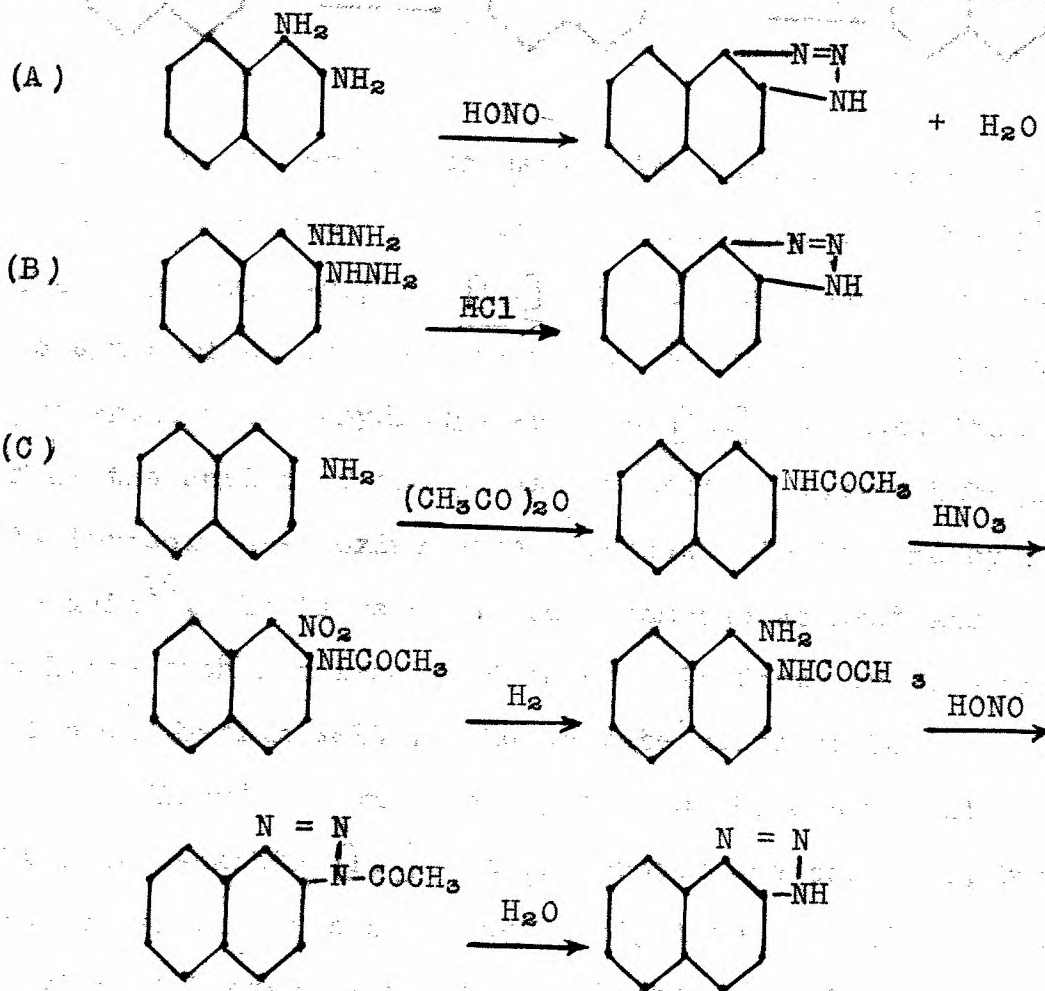
The simplest naphtho[1,2]triazoles are made in low yields from (A) the 1,2-diamine derivatives of naphthalene

⁹J. D. Clary, A Study of the Naphtho[1,2]Triazoles, Unpublished doctoral dissertation, Ohio State University, 1938.

¹⁰R. Nietzki, and E. Braunschweig, Ber., 27: 2281, 1894.

¹¹E. Muller, and others, J. prakt. Chem., 111: 273-312, 1925.

by the action of nitrous acid¹² and from (B) the hydrazo derivative by treatment with 15 per cent hydrochloric acid¹³. A better method of synthesis is (C) that of Clary⁹ which is a modification of Fieser's⁸ method of making benzotriazole.

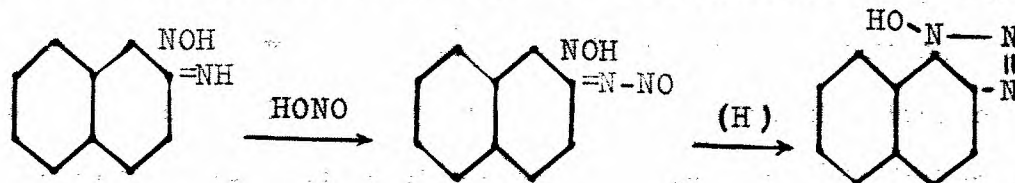


The present work deals primarily with the hydroxy naphtho [1,2] triazoles. The 1-hydroxy-1-naphtho [1,2] triazole has been made from the action of the potassium salt

¹²P. Friedlander, and von Zakrzewski, Ber., 27: 3381, 1894.

¹³Franzen, J. prakt. Chem., (2) 76: 217, 1907.

of 1,2-naphthoquinone-2-nitrosoimine-1-oxime on stannous chloride and hydrochloric acid¹⁴. It melts at 244° and



decomposes at 245°. Its nature is acidic. The above synthesis was successfully repeated and studied by Clary⁹.

The 3-hydroxy-3-naphtho[1,2]triazole has been reported as synthesized by the same method as given above for the preparation of 1-hydroxy-1-naphtho[1,2]triazole, that is, from the action of the potassium salt of 1,2-naphthoquinone-1-nitrosoimine-2-oxime with stannous chloride and hydrochloric acid¹⁵. It is reported to decompose at 222° and to crystallize with a molecule of water. It forms the sodium, potassium and barium salts. The acetate melts at 109°.

Clary's attempt to repeat the above synthesis of 3-hydroxy-3-naphtho[1,2]triazole proved unsuccessful, but he suggested that its preparation might be accomplished by the action of hydrazine hydrate on 1-chloro-2-nitronaphthalene.

¹⁴A. Harden, and J. Okell, Proc. Chem. Soc., (London), 16: 229, 1900.

A. Harden, Ann., 255: 159, 1889.

¹⁵M. Ilinski, Ber., 19: 346, 1886.

It is the above suggestion which led to the present work.

The present problem is primarily to follow up the suggestion that hydroxy [1,2] triazoles may possibly be formed by the action of hydrazine hydrate on the corresponding 1-halogeno-2-nitro- or 2-halogeno-1-nitronaphthalene. In attacking the problem the chief difficulty lay in obtaining sufficient quantities of the halogenated nitronaphthalenes, which are not so common and well known as the simplicity of their structure would seem to indicate. The casual investigator is often misled as to the amount of available information concerning the naphthlene compounds. in general.

The intermediate compounds chosen for the preparation were the 1-chloro-2-nitronaphthalene and the 1-nitro-2-bromonaphthalene. The first has been reported by only one group of investigators¹⁶. It was supposedly prepared by the Sandmeyer-type reaction to yield yellow needles melting at 76°. The 1-nitro-2-bromonaphthalene has been reported by two different groups of workers^{17,18}. One investigation indicated the melting point to be 102-103° and the other 80°.

¹⁶H. H. Hodgson, and E. Kilner, J. Chem. Soc., 1926: 8-10.

¹⁷V. Vesely, and L. Chulozilov, Chem. Listy, 19: 260-4, 1925.

¹⁸Contardi, Mor, Rend. ist. lombardo, 57: 646-54, 1924.

The reported synthesis was by the Sandmeyer-type reaction on the corresponding amino compound, and again by the dehydrogenation of a nitrobromotetralin with bromine at high temperatures. There is some doubt as to which, if either, of the investigators has synthesized the pure compound.

There should be other and simpler methods of preparing 1-chloro-2-nitronaphthalene. The first purpose of this work is necessarily to search out those methods and to try them. Two procedures showed some promise. One is Ullmann's synthesis¹⁹ of 1-chloro-2,4-dinitronaphthalene by refluxing 2,4-dinitro-1-naphthol with a mixture of diethyl aniline and para-toluenesulfonylchloride, the other is the action of phosphorus pentachloride on naphthols. Picryl chloride²⁰, 4-chloro-1,3-dinitrobenzene²¹, and ortho-chloronitrobenzene²² have been prepared from the corresponding phenolic compounds by treatment with phosphorus pentachloride, but often in small yields.

¹⁹ F. Ullmann, and W. Bruck, Ber., 41: 3932, 1908.

²⁰ Clemm, J. prakt. Chem., (2) 1: 150.

F. Ullmann, and Nadai, Ber., 41: 1875, 1908.

C. L. Jackson, and F. H. Gazzolo, Am. Chem. J., 23: 384, 1900.

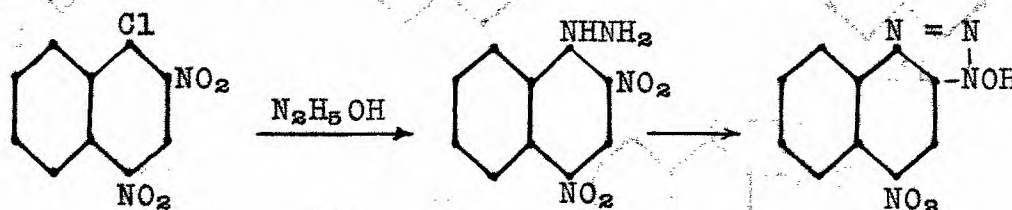
²¹ Clemm, J. prakt. Chem., (2) 1: 167.

F. Ullmann, and G. Madai, Ber., 41: 873, 1908.

²² Engelhardt and Latschinow, Z. Chem., 1870: 231.

It was thought that the larger ring structure of the 2-nitro-1-naphthol might aid in the production of 2-nitro-1-chloronaphthalene.

If and when the above halogenated nitronaphthalenes were synthesized, it was proposed to study their reactions with hydrazine hydrate and possibly to perfect a simple, general method of preparing the hydroxynaphthotriazoles. E. Muller and his co-workers⁹ have previously explored this field. They claim to have prepared the corresponding hydroxynaphtho [1,2] triazole in low yields from 2,4-dinitro-1-chloronaphthalene, by heating with hydrazine hydrate.



As an alternate method of preparation of the triazole, the action of hydrazine hydrate on 2-nitro-1-naphthol would eliminate the difficult step of proposed halogenation.

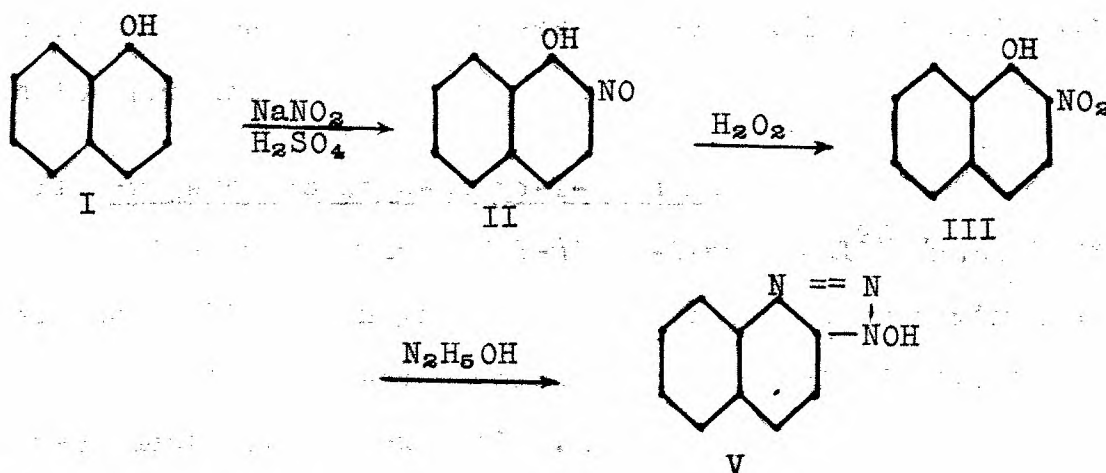
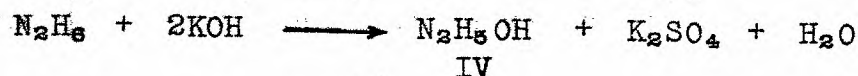
To summarize, the primary purpose of this work is to ascertain whether the naphtho [1,2] triazoles, especially the 3-hydroxy-3-naphtho [1,2] triazole, can be synthesized in any appreciable percentage yields through the use of simple beginning materials and simple type reactions, and to study their properties if synthesized.

EXPERIMENTAL

ATTEMPTED PREPARATION OF 3-HYDROXY-3-NAPHTHO [1,2] TRIAZOLE

A. From 2-nitro-1-naphthol

The preparation of hydroxynaphtho [1,2] triazoles was attempted by the action of hydrazine derivatives on 2-nitro-1-naphthol or on its derivatives.

I Alpha-naphthol

The Baker Chemical Company's commercial technical alpha-naphthol was used as the beginning material in the following work.

II Preparation of 2-nitroso-1-naphthol

A mixture of the isomeric nitrosonaphthols were prepared in yields of over 90 per cent by the method of Hodgson and Kilner¹⁶.

'Pure a-naphthol was prepared by dissolving the commercial product in dilute caustic soda solution

containing alkali equivalent to the α -naphthol present (about 20 per cent) and distilling with steam.

"Nitrosation was effected as follows: To a well-stirred mixture of 2500 cc of water, 500 g of sodium nitrite were added, followed by a cold solution of 20 g of α -naphthol and 10 g of caustic soda in 200 cc of water. The greenish-yellow precipitate was collected after twelve hours, redissolved in the theoretical quantity of very dilute aqueous caustic soda (not more than 1 part of the nitroso compound in 200 cc of solution), and reprecipitated from the filtered solution by dilute hydrochloric acid. These precautions were necessary to prevent resinification. A bright, canary yellow mixture of 2- and 4-nitroso-1-naphthols was obtained in almost quantitative yield."

The mixture of isomers obtained was not separated at this stage because of the ease of separation of their oxidation products.

III Preparation of 2-nitro-1-naphthol

The preparation of 2-nitro-1-naphthol²³ (m.p. 128°C.) was accomplished in yields of 45 per cent from a mixture of 2- and 4-nitroso-1-naphthols. Phthalic acid derivatives are by-products of the oxidation.

"A paste of 10 g of the mixture (of nitrosation products of α -naphthol), 35 cc of 100 vol. (30 per cent) hydrogen peroxide, and a drop of 10 per cent ferrous sulfate solution was treated with 8 cc of 20 per cent caustic soda solution; heat was developed, but very little gas disengaged. When the vigor of the reaction abated, more caustic soda solution was added, until 20 cc in all had been utilized. After twelve hours the mixture was diluted to 300 cc, dissolution completed by boiling, and the filtered, cooled, acidified solution distilled with steam; 6 g of the pure 2-nitro-1-naphthol being obtained. The balance of initial material was represented by a less accessible substance than the 2,4-dinitro-1-naphthol, scarcely any of which was obtained by heating the liquid in the distilling flask with warm nitric acid."

²³H. H. Hodgson, and E. Kilner, J. Chem. Soc., 125:809, 1924.

Much gas was evolved in the first step of the reaction and a 1500-cc beaker was used as the reaction flask.

IV Preparation of hydrazine hydrate

Hydrazine hydrate was made in good yields from a modification of the method reported by Lobry de Bruyn²⁴. Direct distillation was applied to a mixture of 100 g of hydrazine sulfate, 100 g of potassium hydroxide, and 250 g of water in a 1000-cc distilling flask. Care must be taken in the beginning of the reaction to have an extra lighted burner to heat the neck of the distilling flask to prevent foam from being carried over into the condenser. That fraction boiling between 116-118°C. was used in most of the accompanying work.

V a. Action of the 2-nitro-1-naphthol on hydrazine sulfate in the presence of potassium hydroxide

Four grams of 2-nitro-1-naphthol were added to a mixture of 7 g of hydrazine sulfate and 3 g of potassium hydroxide in concentrated aqueous solution. The solution turned a red color characteristic of nitro-hydroxy compounds in presence of base²⁵. The undissolved solid material took on the same color. Upon refluxing the mixture for about four hours,

²⁴C. A. Lobry de Bruyn, Compt. rend., 126: 1042, 1896.

²⁵E. Wertheim, Textbook of Organic Chemistry, Philadelphia: P. Blakiston's Son, 1939. p. 429.

the color returned to yellow, whence another 1.5 g of potassium hydroxide was added to restore the red color. At no time did all of the solid material dissolve.

After four and one-half hours the reflux mixture was cooled, filtered, and acidified with concentrated hydrochloric acid. At this point a small amount of white precipitate was noted which dissolved on dilution and therefore could not have been the desired triazole, since it dissolved in acid medium. A small amount of the white material was isolated and found to be hydrazine hydrochloride (some potassium chloride probably precipitated in the concentrated solution to redissolve on dilution).

The whole reaction mass was acidified and distilled with steam. Two and one-half grams of the original 2-nitro-1-naphthol was recovered (m.p. 128.5°C.)

b. Action of the 2-nitro-1-naphthol on hydrazine hydrate, without solvent

A mixture of 3.6 g of 2-nitro-1-naphthol and 3 g of hydrazine hydrate (b.p. 116-118°C.) was refluxed on an air bath for three hours. A tarry mass was obtained which was insoluble in water and cold 5 per cent hydrochloric acid but partially soluble in hot potassium hydroxide solution. Upon filtration and acidification, a gelatinous or finely divided crystalline material was obtained which was practically insoluble in ether and alcohol. Hot alcohol dissolved enough

of it to take on a red brown color. After evaporating off most of the alcohol, a red-black solid was left which did not melt below 250°C . but melted to a red tarry oil over the open flame. From the physical properties known¹⁴, this was not the desired triazole compound. Sodium fusion gave positive tests for both halogen and nitrogen.

The high-melting material was probably the hydrazine hydrochloride of 2-nitro-1-naphthol. Effervescence was noted in the presence of nitric acid. Muller¹¹ obtained a somewhat similar material by treatment of a dichlorodinitro derivative of benzene with hydrazine hydrate. Brown crystals of a compound which they supposed to be the dihydrochloride of dinitro-dihydrazobenzene were obtained but not characterized; attempts to make a triazole from it were unsuccessful¹¹.

c. Action of 2-nitro-1-naphthol on hydrazine hydrate,
with alcohol as solvent

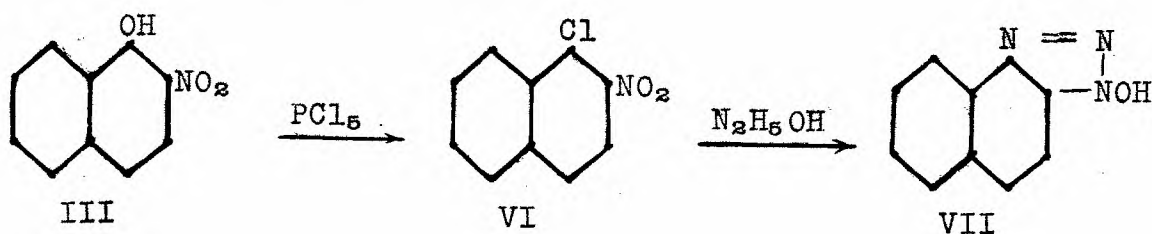
Five grams of 2-nitro-1-naphthol (m.p. 128°C .) and 9 g of hydrazine hydrate were placed in 50 to 75 cc of alcohol, in which it did not dissolve, but turned a red color. The mixture was refluxed in an air bath for seven hours and filtered hot. The cold filtrate yielded a yellow precipitate which melted at $128-130^{\circ}\text{C}$. and was shown to be the beginning material. The part of the reaction mass less soluble in alcohol and remaining as red crystals on the filter paper

was recrystallized from more hot alcohol. It melted at about 176° but showed some evidence of partially melting from 165° . It gave light yellow needles of a picrate melting at $183-185^{\circ}$.

The above red material may have been the hydrazo derivative (some of its properties corresponded to those of 2,4-dinitrophenylhydrazine); but if so, it was unstable in the presence of hydrochloric acid. The hydrochloric acid derivative, when recrystallized from alcohol, gave yellow needles melting at $128-129^{\circ}$ and dissolved in potassium hydroxide to produce the characteristic color of hydroxy-naphthols. It gave a mixed melting point of 128° with 2-nitro-1-naphthol. A triazole was not formed.

B. From 1-chloro-2-nitronaphthalene

The preparation of 1-chloro-2-nitronaphthalene was attempted by several methods. The preparation of hydroxy-naphtho[1,2]triazoles was tried by the action of hydrazine hydrate on impure 1-chloro-2-nitronaphthalene. The proposed steps are outlined below:



VI a. Action of phosphorus pentachloride on 2-nitro-1-naphthol, without solvent

A method similar to that of Jackson and Gazzolo²⁰ was used with approximately 2.5 g of phosphorus pentachloride to each gram of the 2-nitro-1-naphthol. A 500-cc Erlenmeyer flask was used with reflux on the water bath. The reaction began just as the water began to boil and was complete in a few minutes. Caution should be taken to use small quantities of reactants or a very large reaction flask, for the evolution of heat and the evolution of hydrogen chloride will carry both the reactants and the products out the condenser.

The products were washed with water and extracted with ether. The ether evaporated to leave much red oil which had almost the same properties as the oil obtained in the preparation of 2-bromo-1-nitronaphthalene (see page 27). Sodium fusion showed the presence of halogen and nitrogen. It was not possible to solidify the oil or to extract a solid from it. Hodgson and Kilner's¹⁶ proposed method of purification failed. In it the impure material was taken up in 50 cc of hot alcohol and poured into 100 cc of a 1 per cent solution of sodium hydroxide. It was found that the sodium hydroxide solution readily hydrolyzed whatever 1-chloro-2-nitronaphthalene that was present²⁶; for upon filtering the reddish

²⁶E. Wertheim, ibid., p. 417.

solution formed²⁵, none of the 1-chloro-2-nitronaphthalene was obtained. Acidification and steam distillation of the hydrolysis products gave over a gram of the original 2-nitro-1-naphthol. It is likely that the red-brown oil contained impure 1-chloro-2-nitronaphthalene, for the unreacted 2-nitro-1-naphthol would have precipitated upon acidification; it would also have been recrystallized from benzene and alcohol.

It was found that if the reaction products were allowed to stand overnight, and if ether was not used to extract, the mass solidified. Due to the instability of the reaction product²⁶ no method was devised to purify it without changing its composition.

b. Action of phosphorus pentachloride on 2-nitro-1-naphthol in carbon tetrachloride

The reaction was also tried in carbon tetrachloride solution to no avail. One-half gram of 2-nitro-1-naphthol was boiled for two minutes in carbon tetrachloride solution which had been saturated with phosphorus pentachloride. The carbon tetrachloride was evaporated off, and the excess phosphorus pentachloride hydrolyzed with water. The remaining material was recrystallized from benzene and proved to be the original naphthol (m.p. 128-129°C.)

c. Action of para-toluenesulfonyl chloride on
2-nitro-1-naphthol in presence of dimethyl aniline

The method of Ullmann and Bruck¹⁹ for the preparation of 2,4-dinitro-1-naphthalene was applied, with some changes, to the preparation of 2-nitro-1-chloronaphthalene.

A mixture of 5 g of 2-nitro-1-naphthol, 6 g of freshly distilled dimethyl aniline, and 5 g of para-toluenesulfonyl chloride was warmed under reflux on a water bath for two hours. The solid product was washed with warm dilute hydrochloric acid and then with dilute ammonium hydroxide. It was recrystallized from benzene.

The main residue upon the final recrystallization was the original 2-nitro-1-naphthol; it melted at 127-128°C. Hodgson and Kilner¹⁶ state that 1-chloro-2-nitronaphthalene does not lower the melting point of 2-nitro-1-naphthol. The desired 1-chloro-2-nitronaphthalene supposedly melts at 76°C.¹⁶ Besides the material which melted at 127-128°, there appeared a blackish-purple mass which caused the whole precipitate to give various colored solutions, from blue-green to purple and red, upon treatment with various reagents such as hydrochloric acid, ammonium hydroxide and benzene.

After repeated treatment with hydrochloric acid and recrystallization from benzene and alcohol, a yellow precipitate was obtained and shaken with a 2 per cent solution of hot sodium hydroxide. The red coloration due to the unreacted 2-nitro-1-naphthol appeared, and this treatment removed any

remaining traces of it. Upon filtration and recrystallization of the remaining material from alcohol, light tan crystals melting at 110°C . were isolated. Sodium fusion gave a positive test for sulfur and negative test for halogen. The material melting at $127-128^{\circ}$ also gave a negative test for halogen.

Ullmann found¹⁹ that by treatment of the 2,4-dinitro-1-naphthol with diethyl aniline and para-toluenesulfonyl chloride in the cold, the para-toluenesulfonyl ester is formed (m.p. 159°C .) This reaction appears to dominate in the case of the 2-nitro compound under similar conditions with heat. The compound isolated above and melting at 110° must be the corresponding sulfonyl ester. It gave a positive test for sulfur; and when treated with sodium ethoxide and acidified, one of the hydrolysis products proved to be the original 2-nitro-1-naphthol (m.p. 128°C .). Before treatment with sodium ethoxide the characteristic color of the nitro-naphthol in weak base was noted, but after the hydrolysis it was plainly a yellow-red.

VII Reaction of alcoholic hydrazine hydrate with the product of the phosphorus pentachloride reaction

It was concluded that attempted purification of the 2-nitro-1-chloronaphthalene tended to change its composition; so it was deemed worthwhile to attempt to form the triazole from the impure product. A method by which Muller¹¹ prepared

the corresponding triazole in small yields from 2,4-dinitro-1-chloronaphthalene was tried, with some modifications.

The entire product from the reaction of phosphorus pentachloride on 2-nitro-1-naphthol (see page 19) was mixed with alcohol in a large Erlenmeyer flask and refluxed with an equal weight of hydrazine hydrate for seven hours. Upon filtering the hot reaction mass, several grams of a brown powdery material were left on the filter paper.

The brown solid was insoluble in hot alcohol, in hot water, and in base; it did not melt in the open flame. It was boiled with water for some time and filtered; the filtrate gave no precipitate upon cooling. This shows that little or none of the 2,2'-azonaphthalene was formed here. According to Muller¹¹, 4,4'-dinitro-2,2'-azonaphthalene is obtained from similar treatment of 2-4,dinitro-1-chloronaphthalene with hydrazine hydrate. They state that the triazole is derived from further treatment of any precipitated azo compound.

The original alcoholic filtrate gave a brown, gelatinous precipitate upon acidification. The precipitate was soluble in a solution of sodium hydroxide. Attempts to decolorize its sodium hydroxide solution with animal charcoal failed. Sodium fusion gave a positive test for nitrogen. The material was practically insoluble in alcohol and ether and left much residue on burning. The same or a similar

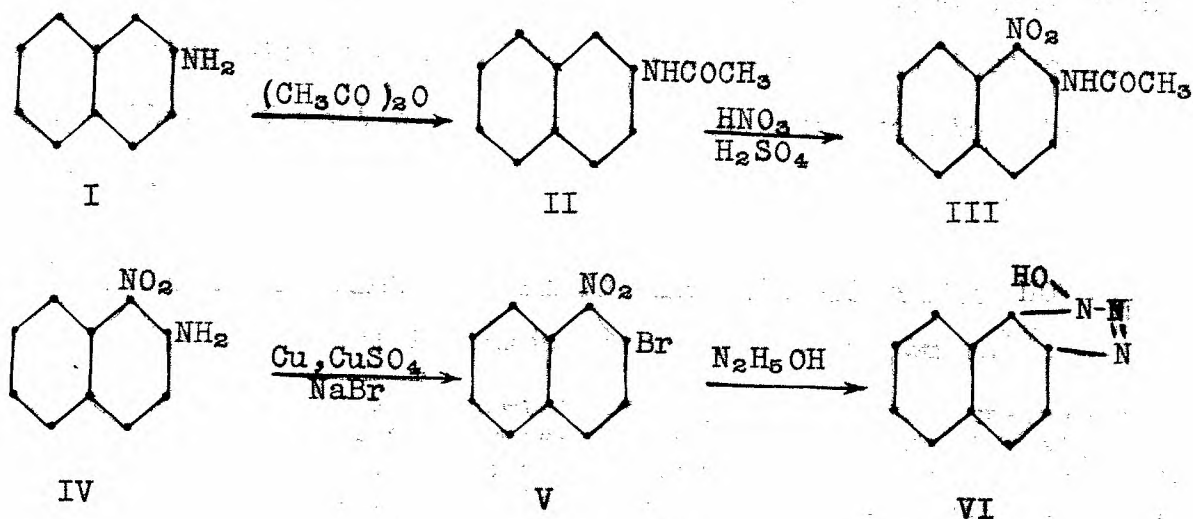
type precipitate was a product of the action of hydrazine hydrate on 2-nitro-1-naphthol (see page 16).

The triazole was not formed. It should be white and acidic, and it should melt at $222^{\circ}14$. It was not possible to isolate any substance from the above reaction products.

ATTEMPTED PREPARATION OF 1-HYDROXY-1-NAPHTHO [1,2] TRIAZOLE

A. From 2-bromo-1-nitronaphthalene

The possibilities of the preparation of triazole compounds of naphthalene through the preparation of 1-nitro-2-bromonaphthalene have been studied according to the scheme which follows:



I Beta-naphthylamine

The Baker Chemical Company's beta-naphthylamine of technical grade was used in these experiments.

II Preparation of acetyl derivative of beta-naphthylamine

The directions are according to Clary⁹.

'Under reflux, 343 g of beta-naphthylamine are heated with 1300 cc of dry benzene at 60° , and 250 g (231 cc) of acetic anhydride are added dropwise with stirring (use 3-necked 3-liter flask). After all of the acetic anhydride is

added, warm gradually to boiling; pour into a beaker while hot and allow to cool. Filter and wash with 200 cc of benzene. White crystals which melt at 131-132° are obtained.

Upon cooling the mother liquor in an ice bath, an additional 73 g are collected (m.p. 129-130°C.)

The above procedure was followed using 350 grams of technical beta-naphthylamine. Yields of over 90 per cent were obtained. Upon cooling the mother liquor, a steel-gray precipitate appeared which was purified by recrystallization and washing with benzene. No more product precipitated upon distilling off most of the mother liquor and cooling the residue.

III Preparation of 1-nitro-2-acetylaminonaphthalene

The procedure is taken from Hartman and Smith²⁷.

In a 2-liter flask equipped with a mechanical stirrer, a thermometer, and a dropping funnel, and clamped in such a position that it may be surrounded by water and ice when desired, are placed 300 g (1.62 moles) of acetyl-beta-naphthylamine (m.p. 132°) and 500 cc of glacial acetic acid. At room temperature the stirrer is set in motion and 200 g (143 cc of 2.1 moles) of concentrated nitric acid (sp gr 1.4) is added drop-wise over a period of forty-five minutes; the temperature is kept below 40° by immersion in cooling bath. After about one-tenth of the acid has been added, the reaction mixture solidifies. The addition of acid is stopped. In from three to five minutes it again becomes liquid. When one-fourth of the acid is added, it all becomes liquid again. Considerable

²⁷W. W. Hartmann, and L. A. Smith, Organic Syntheses, Vol. XIII, New York: John Wiley and Sons, 1933. pp. 72-73.

heat is evolved at this point, and much cooling is required to keep the temperature below 40°.''
 ''After addition is complete, stirring is continued for ten minutes. The flask is stoppered and cooled in ice-water bath for three hours. Crystals are collected on a Buchner funnel, washed with 200 cc of 50 per cent acetic acid and then 400 cc of ethyl alcohol. The yield is 270 to 290 g. The crude material is placed in a 3-liter flask and refluxed for twenty minutes with 1700 cc of benzene. The mixture is allowed to cool to 40-50° and filtered. The residue is a mixture of sparingly soluble isomers; on further cooling, 190 to 200 g of product is obtained which melts at 117-119°.''

Recrystallization of the above product from alcohol gave about 40 per cent yields of fine needles melting at 123-124° C.²⁷ The procedure was carried through using 330 g of acetyl-beta-naphthylamine (m.p. 132° C.) and 145 cc of chemically pure nitric acid. The acetic acid used melted at 15-16°. The color of the reaction mixture upon addition of the nitric acid was at first white as solid in the acetic acid, then canary yellow. The solid was converted into a reddish-brown liquid, which was allowed to cool.

IV Preparation of 1-nitro-2-naphthylamine

The method by which Hodgson and Kilner¹⁶ hydrolyzed 1-nitro-2-acetylaminonaphthalene is straightforward and yields practically 100 per cent of the product before recrystallization and about 90 per cent afterwards.

'Hydrolysis is effected by boiling a solution of aceto-b-naphthalide (125 g) in alcohol (500 cc) with concentrated hydrochloric acid (125 cc) for four hours; the treatment is repeated if necessary. The mixture is then poured into 4 liters of cold water and filtered off, dried, and recrystallized

from twice its weight of hot alcohol. Its melting point is 122° (Atterberg gives $124-125^{\circ}$ and Meldola $126-127^{\circ}$).''

V Gattermann reaction on 1-nitro-2-naphthylamine

According to Vesely²⁸.

''The 2-bromo-1-nitronaphthalene was prepared in the following manner: 5 g of 1-nitro-2-naphthylamine were mixed with 25 cc of hydrochloric acid (sp gr 1.18) and 50 cc of water added, whence the nitronaphthylamine separated out in needles. Nitrogen trioxide was led into the cooled mixture until everything had dissolved with a brown-red color. At that time a mixture of 5.4 g of copper sulfate, 40 g of water, 15 g of sodium bromide and 1.4 g of powdered copper were added. The reaction mass which separated out was extracted with ether and washed first with dilute sodium hydroxide and then with water. The ether was driven off and the residue recrystallized from alcohol. The yield was 2.6 g.

''The product so formed was of yellow needles with red metallic lustre, which melted at $102-103^{\circ}$. It was soluble in ether, benzene, acetone and acetic acid and distilled at 360° .''

In the first two trials to duplicate the above results, the first was with copper turnings brightened by heating with 9M sulfuric acid. The next used copper as precipitated from a copper sulfate solution by zinc in the presence of hydrochloric acid. Nitrogen trioxide was made by dropping hydrochloric acid on sodium nitrite. In both cases above, the reaction mixture solidified with much ebullition of freed nitrogen oxides and nitrogen. The color was first

²⁸V. Vesely, Ber., 38: 138, 1905.

yellow, then gray, and finally almost black on standing.

The reaction mass, when heated and stirred in ether, continued to liberate gas slowly and retained its dark color. After long heating, the ether became red; upon filtering and evaporating the ether extract, the only residue was a small amount of dark red material which partially crystallized, on standing, to flimsy red crystals. The amount obtained was too small to attempt recrystallization. It gave a positive Beilstein test.

After the extraction with ether, the reaction products became darker in color. In both cases the residual reaction mass was heated with alcohol; and after the evolution of much colorless and odorless gas, a dark solution was formed. The higher temperature at which alcohol boils caused the decomposition of the diazonium compound, the boiling point of ether is too low for this to take place²⁹. The expected reaction here is that of alcohol with the diazonium compound to produce 1-nitronaphthalene.

The solutions obtained by heating the diazonium compound with alcohol were filtered and allowed to stand. In both cases tan colored crystals appeared in the red oil. After recrystallization they melted at 55-75°C. and did not

²⁹E. E. Reid, College Organic Chemistry, New York: D. van Nostrand, 1930. p. 595.

give a positive Beilstein test. They were characterized as 1-nitronaphthalene. The red oil would not all crystallize and probably contained 1-nitro-2-bromonaphthalene.

The oil left from recrystallization of the 1-nitronaphthalene failed to solidify in an ice-salt bath. The residue, after evaporation of the alcohol extract and decantation from the above-mentioned crystals, remained in some water. It was stable to steam distillation for when removal by distillation was attempted, droplets of red oil came over in the distillate of water. The oil gave a positive Beilstein test. There must have been some of the 1-nitro-bromonaphthalene formed during the heating process and which was not decomposed by the alcohol.

In the third trial the diazotization was carried out much in the same manner as above; however, after addition of the mixture of sodium bromide, copper sulfate and precipitated copper, the reaction flask was removed from the ice bath and allowed to stand over-night at room temperature. The reaction mass was insoluble in ether. It had not given up its nitrogen; so it was heated and allowed to froth until it was evident that no more gas escaped. Upon cooling and extracting with ether, a dark red solution was obtained. This time a larger amount of red oil and crystals was left after evaporation of the ether. This oil gave a positive Beilstein test and was soluble in ether, alcohol, benzene, and acetic

acid. Its alcohol or acetic acid solution gave a milky color when diluted with water, and the oil always reappeared upon evaporation or standing. Finally, the alcohol solution was evaporated to small volume and the oil decanted from and put on ice. It solidified to an impure red-brown mass which melted slightly above room temperature.

In the fourth trial, the diazotization was modified only by using an excess of precipitated copper and by mixing the reactants at 0°C. The flask was immediately heated to decompose the diazonium compound. The mass was allowed to stand at 45°C. over-night.

Upon extraction with ether and evaporation, much red oil was obtained. The oil was partially soluble in alcohol. The insoluble portion gave a large residue upon ignition over an open flame; the ash was not affected by concentrated nitric acid. A test for copper was negative. A similar spongy material was noted in the work on the preparation of 1-chloro-2-nitronaphthalene.

The alcoholic solution of the red oil above was concentrated by evaporation. It solidified when cooled in an ice bath. The Beilstein test was positive. The literature on 2-bromo-1-nitronaphthalene (see Introduction) is very uncertain and misleading. The literature gives two widely difference melting points, 80°¹⁸ and 102-103°²⁸.

VI a. Action of hydrazine hydrate on product of Gattermann-type reaction, without solvent

One gram of the 1-nitro-2-bromonaphthalene (the impure red oil) and 5 g of hydrazine hydrate were refluxed on the water bath for five hours. The oily substance had practically the same appearance at the end of the treatment as at the beginning. It was insoluble in sodium hydroxide solution. Hydrochloric acid acted on the reaction products to give hydrazine hydrochloride, a white precipitate soluble in water.

The oil was allowed to stand for three weeks at room temperature. It was extracted with ether and the ether allowed to evaporate slowly. Well-formed, almost white crystals appeared which, when recrystallized, melted at 51-54°C. They gave positive test for halogen and negative test for nitrogen and were characterized as 2-bromo-naphthalene. The appearance and analysis of these crystals proved to be almost exactly the same as that of those formed from the oily product of the action of hydrazine hydrate on 1-nitro-2-bromonaphthalene in an alcoholic solution. It appears that the same reaction takes place between the above materials whether or not alcohol is present.

VI b. Action of hydrazine hydrate on Gattermann-type reaction product, with alcohol as solvent

The procedure by which Muller¹¹ claims to have prepared a triazole from 2,4-dinitro-1-chloronaphthalene was repeated

with some modifications in another attempt to prepare the corresponding triazole from 2-nitro-1-bromonaphthalene (see page 27). Fifteen grams of that material which was thought to be impure 1-nitro-2-bromonaphthalene was mixed with alcohol and refluxed for six hours with an alcoholic solution of hydrazine hydrate on the water bath. No precipitate appeared when the mixture was filtered hot. Upon cooling the filtrate an oil separated out which was lighter in color than the beginning material--more separated on dilution.

Acidification of the diluted filtrate with hydrochloric acid produced hydrazine hydrochloride, and the oil remained unchanged. It was extracted with ether; and the ether extract, on slow evaporation from an open container, left light-brown crystals. When recrystallized from alcohol and ether, they melted at 51-56°C. and showed halogen present but nitrogen absent. They were concluded to be 2-bromonaphthalene. The same or similar crystals were produced from the same reaction without the use of the alcohol solvent. This seems to show that the halogenated nitro compound has been present. It also brings out the fact that the halogen or other group in the one-position is activated by the nitro group in the four-position.

SUMMARY

The preparation of 3-hydroxy-3-naphtho[1,2]triazole has been attempted by the use of several types of beginning materials and reactions.

Good yields of 2-nitro-1-naphthol have been prepared from alpha-naphthol. The previously untried reaction of phosphorus pentachloride with 2-nitro-1-naphthol gave no pure product. The impure 1-chloro-2-nitronaphthalene did not give the desired reaction with hydrazine hydrate to form 3-hydroxy-3-naphtho[1,2]triazole. These results are not surprising when it is noted that Muller¹¹ was able to obtain only small yields of a similar product, 4-nitro-2-hydroxy-3-naphtho[1,2]triazole, by means of blocking the 4-position with a nitro group and thereby increasing the activity of the one-position. Likewise, the closed 4-position enabled the same experimenters¹¹ to produce a more nearly pure product of the 1-chloro compound through the Ullmann method. Upon application of the Ullmann method to the synthesis of 1-chloro-2-nitronaphthalene (note the open 4-position which seems to reduce the activity of the one-position to some reagents) from 1-hydroxy-2-nitronaphthalene, an ester was formed instead of the desired chloro substitution product. This is presumably due to the absence of the activating group

in the 4-position, and hence the decreased activity of the hydroxyl group in the one-position.

The same difficulty was encountered in the attempted substitution of the hydroxyl group in 2-nitro-1-naphthol by chlorine through the use of phosphorus pentachloride. This type of replacement works well in the case of picric acid and fairly well in the case of 2,4-dinitrophenol, but the replacement of the hydroxyl group in ortho-nitrophenol by phosphorus pentachloride (see Introduction) gives only very small yields of the desired substitution product. By comparison, the difficulty of preparation of 1-chloro-2-nitronaphthalene in any quantities by the phosphorus pentachloride reaction is easily seen.

Without some group in the 4-position, both the Ullmann- and the phosphorus pentachloride-type reactions seem to produce no appreciable amount of 1-chloro-2-nitronaphthalene from 2-nitro-1-naphthol. If formed, the 1-chloro-2-nitronaphthalene lacked sufficient activation to produce the triazole structure in the presence of hydrazine hydrate.

In the attempted production of 3-hydroxy-3-naphtho [1, 2] triazole directly from 2-nitro-1-naphthol by the use of hydrazine hydrate with solvent under reflux, the failure to product the desired material is attributed to the same causes as above--chiefly the lack of activating groups in strategic ring positions. Neither was the triazole formed by the

heating of 2-nitro-1-naphthol in an aqueous solution of potassium hydroxide.

The synthesis of 1-hydroxy-1-naphtho [1,2] triazole has been attempted through the problematical preparation of 2-bromo-1-nitronaphthalene. The 1-nitro-2-naphthylamine was synthesized from beta-naphthylamine. The chief difficulties in the formation of 1-hydroxy-1-naphtho [1,2] triazole by this chain of reactions are those encountered in the substitution of a halogen into the correct ring position and in leaving it in a state active enough to react with the hydrazine hydrate reagent.

No pure product resulted from the attempted Gattermann-type reaction for the production of 2-bromo-1-nitronaphthalene from the corresponding 1-nitro-2-naphthylamine, and this impure product did not give the desired triazole when treated with hydrazine hydrate under reflux, either with or without alcohol as solvent.

In every case above when the reaction did not proceed as desired, the desired product was proved not to be present; and in practically every case those products which were formed were identified.

CONCLUSIONS

From a study of this work and the various references given, it is noted that if a triazole compound is to be formed in any appreciable yields by the treatment of 1-(or 2-) halogeno-2-(or-1-) nitronaphthalene with hydrazine hydrate, there must be an activating group (or groups) placed at an activating point (or points) on the rings -- preferably at the number four position. Even under these conditions the reported yield is small.

One of the chief problems lies in the preparation of the 1- (or 2-) halogeno-2-(or -1-)nitronaphthalenes themselves, for attempts to purify these intermediates seem to fail due to their instability and their tendency to revert to the naphthols.

Hydrazine hydrate may be synthesized in good yields from hydrazine sulfate.

The replacement of the hydroxyl group of the 2-nitro-1-naphthol with chlorine by the use of phosphorus pentachloride gives a more vigorous reaction than the reported action of the same reagent on the corresponding derivatives of phenol.

Hydrazine hydrate refluxed in an alcoholic medium for several hours with 2-nitro-1-naphthol may yield some 2-nitro-1-hydrazonaphthalene; but if so, it is unstable in acid medium.

Reid²⁹ has been confirmed in his statement that some diazonium derivatives of naphthalene are stable at room conditions for long periods of time.

As a possible suggestion to future workers in this field, it seems that the desired naphthotriazole may be formed by substitution of such activating groups in the rings that may be removed after activating the formation of the triazole ring.

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