HETEROCYCLIC NITROGEN COMPOUNDS

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PART I. PENTACYCLIC COMPOUNDS[1]

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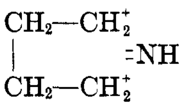
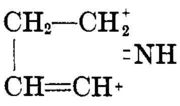
[1] Part II is to appear in a later issue.

I. INTRODUCTION

In the first part of this paper the attempt is made to contribute something to our knowledge of the structure of the pentacyclic compounds containing one, two, three, and four nitrogen atoms in the ring. In the second part hexacyclic compounds containing nitrogen will be discussed. It will be shown that all these compounds may be regarded as belonging to the nitrogen system of compounds (41).

Making use of the formulas, RCH_2^{+}, $RCH^{\ddagger}$, $RC^{\ddagger}$, and $^{\ddagger}C^{\ddagger}$, to indicate the augmentation state of carbon as it may be assumed to exist in the primary alcohols, the aldehydes, the carbylic acids, and the carbonic acids—thereby ignoring the carbon to carbon and the carbon to hydrogen polarities—and the symbols, $N^{\equiv}$, $^{=}N:N^{=}$, $^{-}N::N^{-}$, and $N^{\ddagger}$, to represent nitrogen as it may be assumed to be present in ammonia, hydrazine, the azo compounds, and the nitrous acids respectively (41), we venture to write the following formulas.[2]


Pyrrolidine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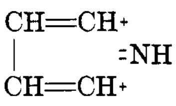
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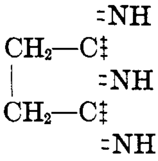
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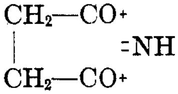
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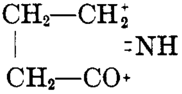
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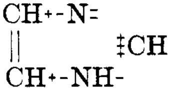
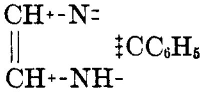
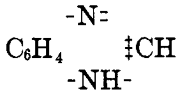
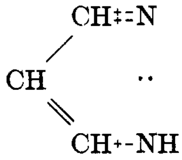
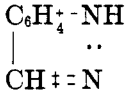
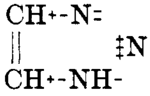

Imidazole


2-Phenylimidazole


Benzimidazole


Pyrazole


Indazole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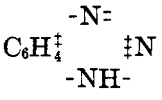
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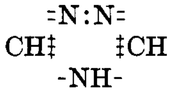
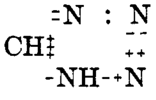
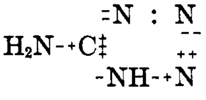

1,2,4-Triazole


Tetrazole


5-Aminotetrazole

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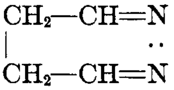
[2] The small plus and minus signs are used to represent covalent bonds which are more or less polar. They do not indicate ionization. For example, in the formulas, $C_2H_5^{-}Na^{+}$ (106b), $CH_3^{-+}H$, $CH_3:CH_3$, $CH_3^{+-}Cl$, $CH_3^{+-}NH_2$, $CH_3^{+-}OH$, and $CH_3^{+-}F$,

which respectively represent pyrrolidine as a saturated ammono alcohol, pyrroline and pyrrole as unsaturated ammono alcohols, succinimidine as an ammonosuccinic acid, succinimide as an aquo-ammonosuccinic acid, pyrrolidone[3] as a carboxazylic acid ester, imidazole as an ammonoformic acid ester of an unsaturated diatomic alcohol, 2-phenylimidazole as an ammonobenzoic acid ester, benzimidazole as *o*-phenylene ammonoformate, pyrazole as a tautomeric form of a malondialdehyde hydrazone,



$$\begin{array}{l} CH_2\text{—}CH\text{=}N \\ | \qquad\qquad\quad \vdots \\ CH_2\text{—}CH\text{=}N \end{array}$$

indazole as a compound which is at the same time a phenylenehydrazine and an aldehyde hydrazone, 1,2,3-triazole as an ammononitrous acid ester, benzotriazole as *o*-phenylene ammononitrite, 1,2,4-triazole as a diformic acid hydrazide, tetrazole as a formic acid nitrous acid hydrazide, and 5-aminotetrazole as a carbonic acid nitrous acid hydrazide.

Since all covalent links between unlike atoms are more or less polar (71), it is reasonable enough to write the above formulas in which the carbon atoms are represented as positive in respect to the nitrogen atoms. However one can hardly say baldly that one of the nitrogen atoms in 1,2,3-triazole, for example, is positive to the other two, or that 5-aminotetrazole contains residues of nitrous acid and hydrazine, as represented by the

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the polarities indicated by the plus and minus signs vary all the way from sodium ethyl, in which the ethyl group is a negative ion, to methyl fluoride in which the methyl group is highly positive (71, 84a). The colons and double colons are used to represent non-polar bonds or unions concerning the polarity of which no assumptions are made.

Excepting that we shall consistently make use of the symbols $=N:N=$ and $-N::N-$ for keeping track of hydrazine and azo nitrogen we shall for the most part write formulas after the familiar practice of the organic chemist, making use of plus and minus signs only when it is deemed that clarity will thereby be enhanced. The word "augmentation" will be used from time to time to mean oxidation in the broad general sense (41). The term "carbylic acid" has been adopted as a group name to include the carboxylic acids, the carboxazylic acids or acid amides, and the carbazylic acids or acid amidines. Because of the trivalency of nitrogen, strict nitrogen analogs of the aquo aldehydes are impossible. The aldehyde-imines, $RCH=NH$, which are aldehydes and at the same time either alcohols or acids, we have chosen to call aldehyde-alcohols. Schiff bases, $RCH=NR$, we shall call aldehyde-ethers; compounds of the formulas, $RCH=N(RCO)$ and $RCH=N(RCNH)$, aldehyde-esters. We have taken the liberty of expanding the designation "acetal" to include hydrobenzamide, $(C_6H_5CH=N)_2CHC_6H_5$, and similar compounds such as trioxymethylene and paraldehyde. Hydrobenzamide we choose to call a dialdehydeacetal, paraldehyde a cyclic acetal (32, 41).

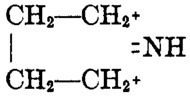
[3] The cyclic carbazylic acid ester in which the oxygen present in pyrrolidone is replaced by an imide group is unknown. In order to keep this paper within reasonable limits we shall only now and then mention cyclic compounds containing oxygen.

formulas given above. None the less we shall find as we proceed that, in so far as conclusions concerning the constitution of such cyclic compounds may be drawn from their methods of preparation, the formulas given receive a definite justification. Moreover we shall find that methods for opening many of these remarkably stable rings are known which lend support to the assumption that the nature of the compounds listed is, in a reasonable enough sense, represented by the respective formulas. One may perhaps say that the groups indicated are potentially present or that they are present in somewhat the same sense that ethylene unions are present in benzene. The formulas may be said to represent resonance phases of the respective compounds.

II. COMPOUNDS CONTAINING ONE NITROGEN ATOM IN THE RING

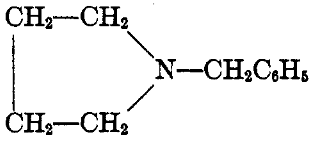
Three pentacyclic compounds containing one nitrogen atom in the ring are pyrrolidine, pyrroline, and pyrrole. These compounds are so obviously amines, or in other words ammono alcohols, as to make it unnecessary to discuss them in any considerable detail here.

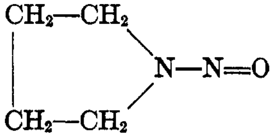
A. Pyrrolidine



$$\begin{array}{ll} CH_2{-}CH_2^{+} & \\ | & =NH \\ CH_2{-}CH_2^{+} & \end{array}$$

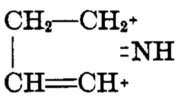
This formula represents a saturated cyclic primary ammono alcohol of which *N*-benzylpyrrolidine and *N*-nitrosopyrrolidine



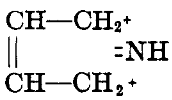


are respectively an ether and an aquo-ammononitrous acid ester.

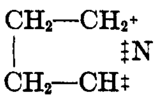
B. Pyrroline



$$\begin{array}{ll} CH_2{-}CH_2^{+} & \\ | & =NH \\ CH{=}CH^{+} & \end{array}$$

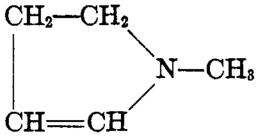


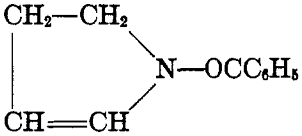
$$\begin{array}{ll} CH{-}CH_2^{+} & \\ \| & =NH \\ CH{-}CH_2^{+} & \end{array}$$



$$\begin{array}{ll} CH_2{-}CH_2^{+} & \\ | & \ddagger N \\ CH_2{-}CH\ddagger & \end{array}$$

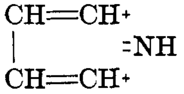
Of these tautomeric formulas the first two represent pyrroline as a cyclic unsaturated ammono alcohol. The third represents a cyclic aldehyde-ether. *N*-Methylpyrroline and *N*-benzoylpyrroline

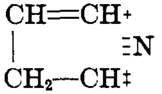


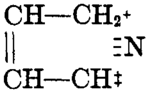


are respectively a pyrroline methyl ether and a pyrroline aquo-ammonobenzoate.

C. Pyrrole







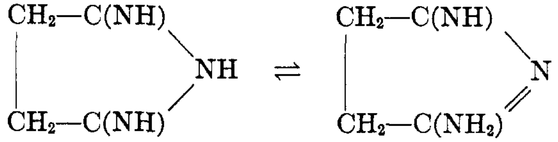
This compound is usually represented by the first formula without the plus and minus signs. It is, however, very probably a tautomeric compound and as such may be looked upon either as an unsaturated cyclic ammono alcohol (the first formula), or as an unsaturated cyclic aldehyde-ether as represented by the second and third formulas.

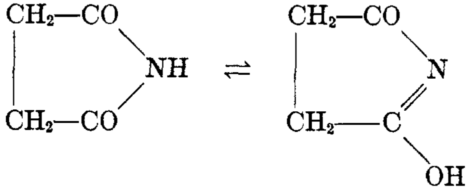
N-Alkylpyrroles are ammono ethers. *N*-Ethylpyrrole, for example, which has been prepared by the action of ethyl iodide on potassium pyrrole, remains unchanged under the action of potassium hydroxide and is decomposed by aqueous hydrochloric acid only at high temperatures. *N*-Acetylpyrrole, which is an acetic acid ester of pyrrole, has been obtained by the interaction of pyrrole and acetic anhydride and by the action of acetyl chloride on pyrrole potassium. As an ester acetylpyrrole is readily hydrolyzed by the action of potassium hydroxide solution to yield pyrrole and potassium acetate.

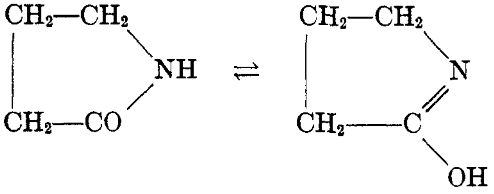
The first formula above, which represents pyrrole as an unsaturated ammono alcohol or, in other words, as a deammonation product of the tautomeric form of the succindialdehyde-alcohol represented by the formula, $H_2N—CH{=}CH—CH{=}CH—NH_2$, contains an imino group as a member of a ring in which two ethylene unions are present. In view of the negative influence of these double bonds it might well be expected that pyrrole would show properties distinctly more acid than do the saturated ammono alcohols. The following metallic salts of pyrrole have been obtained by means of reactions carried out in liquid ammonia solutions (40): sodium pyrrole, C_4H_4NNa, and $C_4H_4NNa \cdot NH_3$; calcium pyrrole, $(C_4H_4N)_2Ca$, and $(C_4H_4N)_2Ca \cdot 4NH_3$; magnesium pyrrole, $(C_4H_4N)_2Mg \cdot 2NH_3$; and silver pyrrole, $C_4H_4NAg \cdot NH_3$. In a similar manner potassium indole, C_8H_6NK, sodium indole, C_8H_6NNa, calcium indole, $(C_8H_6N)_2Ca \cdot 4NH_3$, magnesium indole, $(C_8H_6N)_2Mg \cdot 4NH_3$, silver indole, $C_8H_6NAg \cdot NH_3$, potassium carbazole, $C_{12}H_8NK$, $C_{12}H_8N \cdot NH_3$, and $C_{12}H_8NK \cdot 3NH_3$, silver carbazole, $C_{12}H_8NAg \cdot NH_3$ and $C_{12}H_8NAg \cdot 2NH_3$, and calcium carbazole $(C_{12}H_8N)_2Ca \cdot 4NH_3$ and $(C_{12}H_8N)_2Ca \cdot 7NH_3$, have been prepared (40).

D. Succinimidine, succinimide, and pyrrolidone

These compounds may be represented by the following respective pairs of tautomeric formulas





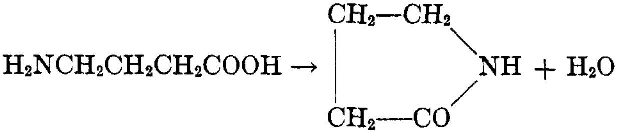


Concerning succinimidine and succinimide it will suffice present purposes to note that they are respectively an ammonosuccinic acid and an aquo-ammonosuccinic acid.

Some considerations which support the view that pyrrolidone is a cyclic carboxazylic acid ester are the following.

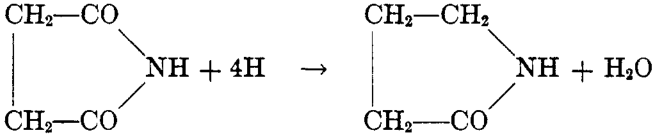
(1) It is formed by heating γ-aminobutyric acid and inversely is hydrolyzed to this aminocarboxylic acid under the action of alkalis or mineral acids (43).

The equation

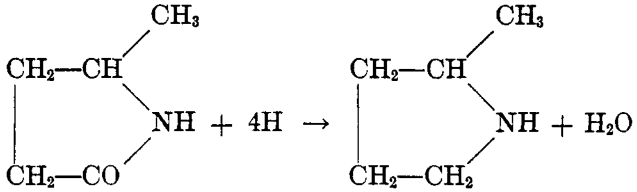


represents the intramolecular esterification of a compound which is at the same time an ammono alcohol and a carboxylic acid to form a cyclic carboxazylic acid ester. The inverse reaction consists in the hydrolysis of the cyclic ester to the open chain alcohol-acid.

(2) Pyrrolidone is formed also by the electrolytic reduction of succinimide (95), the action involved consisting in the conversion of a cyclic acid to a cyclic ester acid as represented by the equation



(3) While pyrrolidone apparently has not been reduced to pyrrolidine it does happen that 2-methylpyrrolidone has been reduced to 2-methylpyrrolidine (94, 14), as represented by the equation



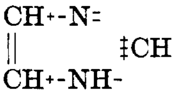
in accordance with which a cyclic carboxazylic acid ester is reduced to a cyclic ammono alcohol.

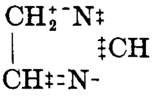
(4) Since pyrrolidone is formally an acid ester it should be capable of forming metallic salts. Accordingly a sodium salt, C_4H_6ONNa, is obtained as a crystalline precipitate when sodium hydroxide is added to a concentrated solution of pyrrolidone in alcohol or water (96). A hydrated mercuric salt, $(C_4H_6ON)_2Hg \cdot H_2O$, which loses its water of crystallization at 100°C., has also been prepared. Moreover pyrrolidone vigorously attacks the alkali metals with evolution of hydrogen.

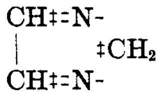
III. COMPOUNDS CONTAINING TWO NITROGEN ATOMS IN THE RING

The known pentacyclic compounds containing two nitrogen atoms in the ring are imidazole and pyrazole, together with their derivatives.

A. Imidazole







The first formula, which is the generally accepted one, represents imidazole as an ammonoformic acid ester of either the one or the other of the unsaturated alcohols, HOCH=CHOH[4] or $H_2NCH{=}CHNH_2$; the

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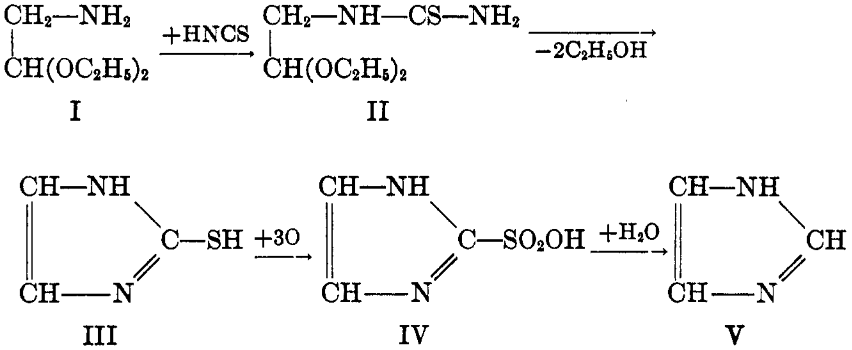
[4] This compound is unknown excepting in so far as it may exist in tautomeric equilibrium with glycol aldehyde. The nitrogen analog is quite unknown.

second represents it as a compound which is a formic acid ester in respect to the upper union of the formic acid group and a formic acid acetal of glycol aldehyde in respect to the lower. The third formula may be said to represent a cyclic acetal containing glyoxal and formaldehyde residues.

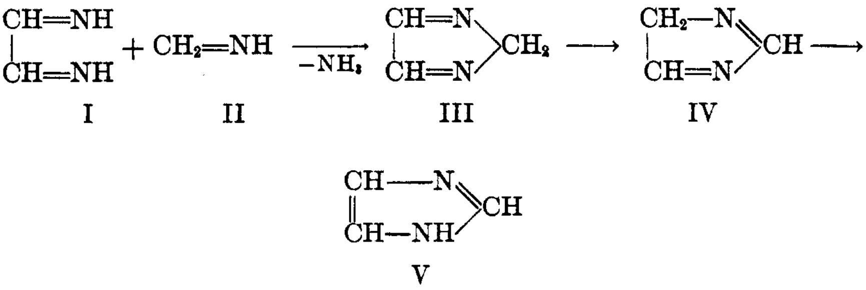
1. Formation. (a) Carrying out a series of reactions summarized by the scheme



Marckwald (67) prepared imidazole and concluded that its constitution must be represented by formula V.

When the hydrochloride of the aminoacetaldehyde-acetal (I) is treated with potassium thiocyanate the thiourea derivative (II), which was not analyzed, is formed. On heating this compound at 140°C. intramolecular ammonolysis takes place, forming ethyl alcohol and compound III, which Marckwald named imidazolylmercaptan. This ethylenyl thioammonocarbonate, when warmed in solution in 10 per cent nitric acid, yields imidazole (V) and sulfuric acid, presumably by way of the unknown sulfonic acid (IV).

(b) Assuming that imidazole is a cyclic ammonoformate its formation by the interaction of glyoxal, formaldehyde, and ammonia (78) may be represented by the scheme



in accordance with which the dialdehyde-diimine (I) and the formaldehyde-imine (II) formed, it may be surmised, by the action of ammonia on glyoxal and on formaldehyde, respectively, react with each other with the elimination of ammonia to form III. This hypothetical formaldehyde glyoxal acetal, undergoing an intramolecular Cannizzaro reaction, passes over into the formic acid ester acetal (IV) which, by intramolecular rearrangement identical in principle with the keto–enol transformation, is converted into imidazole (V).

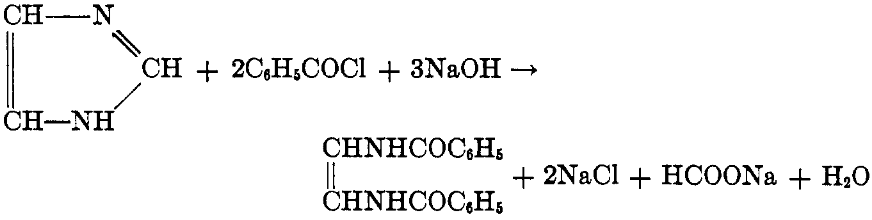
Of course the simplest interpretation of this method for the preparation of imidazole is to the effect that it is a cyclic acetal (formula III above).

2. Opening the ring. Assuming imidazole established as a cyclic ethylenyl ammonoformate, one might expect to find it hydrolyzable to aquoformic acid, ammonia, and perhaps glycolaldehyde

$$HOCH{=}CHOH \rightleftharpoons HOCH_2{-}CHO$$

As a matter of fact, imidazole resists the action of acids and alkalis. However, several methods are known whereby the opening of the imidazole ring has been effected.

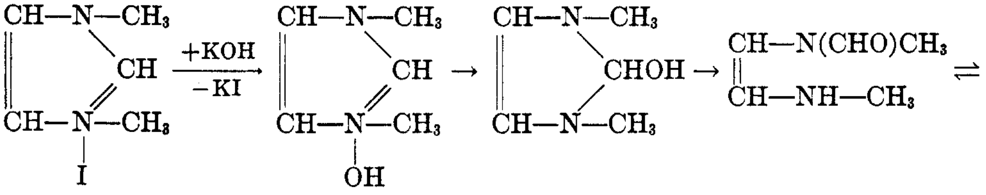
(a) When imidazole is treated with benzoyl chloride and sodium hydroxide (Schotten-Baumann reagent), even at temperatures as low as 0°C., dibenzoyldiaminoethylene and sodium formate are formed quantitatively (6).



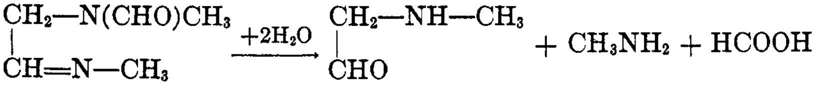
$$+ 2C_6H_5COCl + 3NaOH \rightarrow \begin{matrix}CHNHCOC_6H_5\\ \|\\ CHNHCOC_6H_5\end{matrix} + 2NaCl + HCOONa + H_2O$$

The reactions as thus represented consist in the conversion of a cyclic formic acid ester into an open chain aquo-ammonobenzoate of an unsaturated diatomic alcohol and sodium aquoformate. In principle an ammonoformic acid ester is hydrolyzed to an ammono alcohol and aquoformic acid.

(b) When the quaternary ammonium salt, I below, formed by the action of methyl iodide on 1-methylimidazole, is boiled with strong potassium hydroxide solution, good yields of methylamine and formic acid are obtained (82, 76). The successive reactions involved may be represented by the scheme



I II III IV

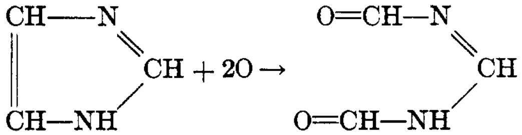


$$\begin{matrix}CH_2—N(CHO)CH_3\\ | \\ CH{=}N—CH_3\end{matrix} \xrightarrow{+2H_2O} \begin{matrix}CH_2—NH—CH_3\\ | \\ CHO\end{matrix} + CH_3NH_2 + HCOOH$$

IV′ V

and explained as follows. The quaternary ammonium hydroxide (II), formed by the action of potassium hydroxide on the iodide (I), rearranges to compound III in a manner resembling, in essence, the decomposition of tetramethylammonium hydroxide to form trimethylamine and methyl alcohol. Compound III is an ester of an aquo-ammonoorthoformic acid, $HC(NH_2)_2OH$. Such a compound, being an acid ester, should be unstable and therefore ready to pass over into the open chain compound IV. In the presence of potassium hydroxide solution the tautomeric form (IV′) of this compound, which is at the same time an aldehyde-ether (lower branch) and a formic acid ester (upper branch), should undergo hydrolysis to form methylamine, formic acid, and perhaps the unknown methylaminoacetaldehyde (V). The appearance of formic acid and methylamine among the reaction products supports the view that 1-methylimidazole is a cyclic ammonoformate. No one of the compounds represented by the formulas II, III, IV, IV′, and V was isolated.

3. Oxidation. Reducing agents are without action on imidazole. Wyss (108) identified carbon dioxide and formic acid as products of the action of potassium permanganate on imidazole. The formation of formic acid may be explained on the assumption that a cyclic formate is oxidized at the ethylene union, as represented by the equation



and that the unknown triformic acid thus formed undergoes hydrolysis to yield aquoformic acid and ammonia

$$OCH—N{=}CH—NH—CHO + 4H_2O \rightarrow 3HCOOH + 2NH_3$$

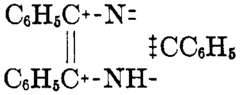
Wyss, however, does not mention ammonia as one of the reaction products (cf. p. 318).

Radzisewski (79) found oxamide among the products formed by the action of hydrogen peroxide on imidazole. His observation is readily interpreted as supporting any one of the formulas given above.

4. Metallic salts. Since imidazole is an acid ester it should be capable of forming metallic salts. A silver salt, obtained as an amorphous precipitate by adding silver nitrate to a water solution of imidazole, has long been known. Using liquid ammonia as solvent in which to carry out the necessary reactions Wenzel (102) prepared the imidazole salts listed herewith: $C_3H_3N_2Na\cdot NH_3$, $C_3H_3N_2K\cdot NH_3$, $(C_3H_3N_2)_2Mg\cdot 4NH_3$, $(C_3H_3N_2)_2Mg\cdot NH_3$, $(C_3H_3N_2)_2Ca\cdot 2.5NH_3$, $(C_3H_3N_2)_2Ca\cdot 1.5NH_3$, $C_3H_3N_2Ag$. The zinc and cobalt salts, $(C_3H_3N_2)_2Zn$ and $(C_3H_3N_2)_2Co$, have been prepared by the action of imidazole on salts of the respective metals in aqua ammonia solution (30).

Clearly the methods of preparation of imidazole and the reactions it undergoes lend support to the view that it is a cyclic ammonoformate.

B. Lophine, 2,4,5-triphenylimidazole

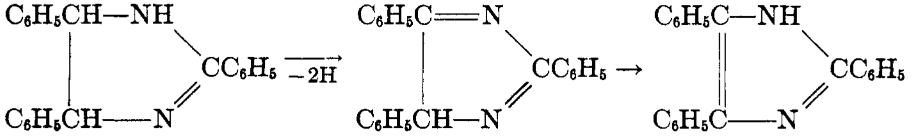


$$\begin{array}{l} C_6H_5C^{+}\text{-}N{=} \\ \quad\;\, \| \qquad\quad \ddagger CC_6H_5 \\ C_6H_5C^{+}\text{-}NH\text{-} \end{array}$$

Just as the preceding discussion has shown that imidazole may be regarded as a cyclic ammonoformic acid ester, so in harmony with the view that lophine is a cyclic ammonobenzoic acid ester are the methods for its preparation and the numerous reactions which it has been observed to undergo.

1. Formation. (a) By the action of oxidizing agents in water solution (38) and of iodine in liquid ammonia solution amarine, which is a dihydride of lophine, is converted into lophine. Also simply by heating amarine, or allowing it to stand in liquid ammonia solution in the presence of potassium amide, lophine is formed (92).

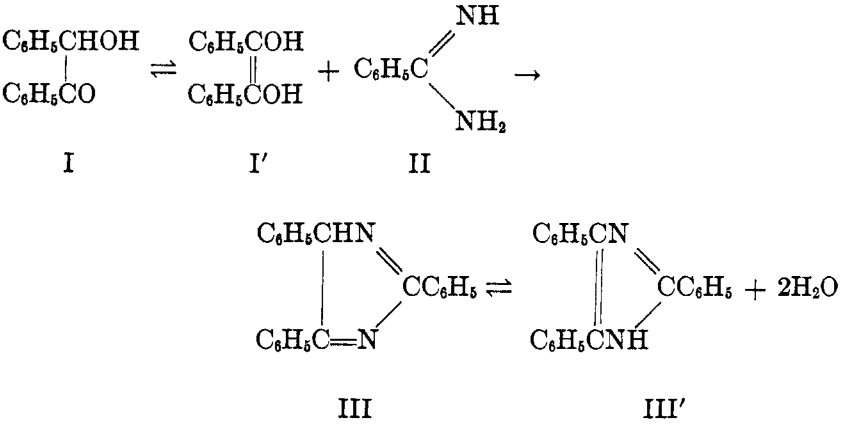
Making use of Japp and Moir's formulas for amarine and lophine (58), the augmentation of any one of the stereoisomeric forms of amarine to lophine may be represented by the scheme



I II III

The first step involves the augmentation (dehydrogenation) of one of the secondary alcohol groups present in amarine (I) to a ketone group in formula II; the second consists in an intramolecular rearrangement which is strictly analogous to the familiar keto–enol transformation.[5] It is of course possible that I is dehydrogenated directly to III, in which case a saturated carbon to carbon union is augmented to an ethylene union.

(b) In agreement with our assumption that lophine is a cyclic ammonobenzoate is its formation by the action of benzamidine (an ammonobenzoic acid) on benzoin (61) in accordance with the equation



Assuming that the constitution of lophine is as represented by formula III′, one may say either that the tautomer (III), formed by the interaction of benzamidine (II) and benzoin (I), undergoing a keto–enol transformation is converted into lophine (III′), or that the tautomeric form of benzoin (I′) reacts with benzamidine to give lophine directly. Formula III′

---

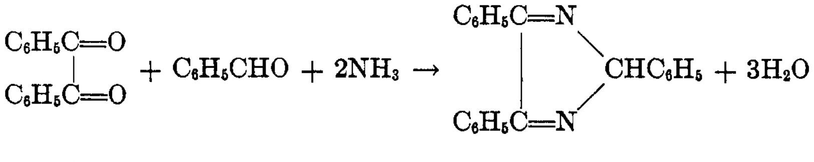
[5] Just as the keto–enol rearrangement takes place in accordance with the reversible equation, $RCOCHR_2 \rightleftharpoons RC(OH)CR_2$, so it is reasonable to expect analogous compounds belonging to the nitrogen system ready to undergo similar rearrangements. Diacetonitrile, for example, behaves under certain conditions in accordance with the first, under others with the second of the formulas,

$$CH_3C(NH)CH_2CN \rightleftharpoons CH_3C(NH_2)CHCN$$

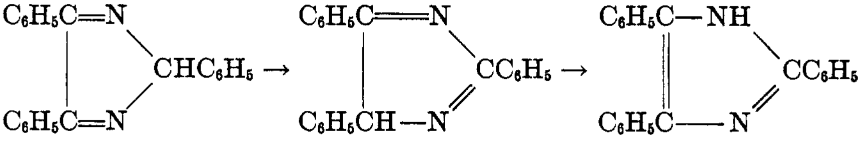
Indeed, as it seems, this compound has been established as existing in two isomeric forms as represented by the preceding formulas (69). Perhaps the most extensively investigated tautomeric compound known to exist in both the keto and enol forms is acetoacetic ester. The nitrogen analog of acetoacetic acid would be β-iminobutyramidine, $CH_3C(NH)CH_2C(NH)NH_2$, which is unknown. However diacetonitrile, $CH_3C(NH)CH_2CN$, which is the anammonide of β-iminobutyramidine, is formed from acetonitrile under much the same conditions as acetoacetic ester is formed by the aldol condensation of ethyl acetate, and in many respects resembles acetoacetic ester in its behavior.

represents lophine as a cyclic ammonobenzoate of an unsaturated diatomic alcohol. As represented by the formula III, it is at the same time a ketone benzoic acid acetal and an ammonobenzoic acid ester.

(c) Radzisewski (78) prepared lophine by heating equimolecular quantities of benzil and benzaldehyde with alcoholic or aqueous ammonia. As represented by the equation



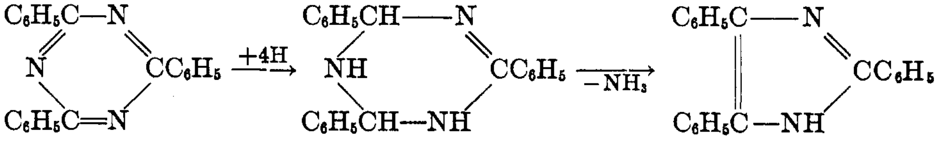
this method of preparation would seem to imply that lophine is a benzaldehyde diketone-acetal. Since, however, lophine is fairly certainly established (58) as a cyclic benzoate, it is to be concluded that the above-formulated product of the interaction of benzil, benzaldehyde, and ammonia undergoes rearrangement in accordance with the scheme,



I II III

which represents the intramolecular augmentation of the benzaldehyde group in I to the benzoic acid group in II, and the concomitant reduction of the one of the ketone groups to a secondary alcohol group and finally the enolization of II to III.

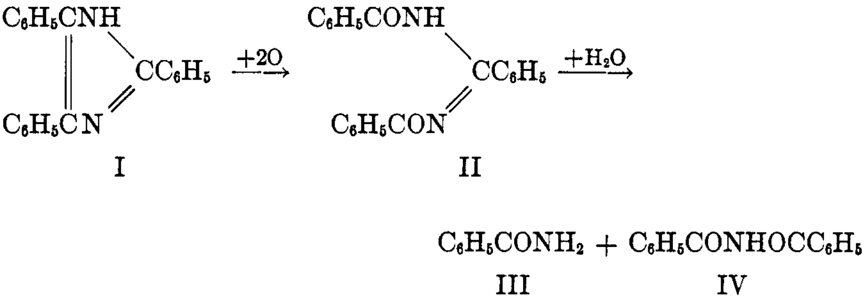
(d) Lophine has been obtained by the reduction of cyaphenine (77), the reactions involved probably taking place as represented by the scheme



I II III

in accordance with which two of the benzoic acid groups in the trimeric benzoic anammonide (I) undergo reduction to benzaldehyde groups in II, following which this dibenzaldehyde benzoic acid acetal loses ammonia to form lophine (III).

2. Oxidation. Lophine is very resistant to the action of reducing agents. Apparently it has not been reduced to amarine, from which it is formed by oxidation (11, 57) and by nitridation (p. 315). On the other hand it is readily attacked by oxidizing agents. On warming with chromic acid in dilute acetic acid solution lophine is quantitatively oxidized to benzamide and dibenzamide (38, 59) in a manner which may be represented by the scheme

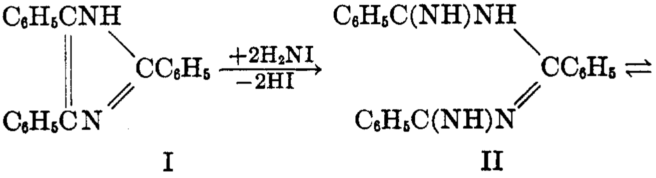

I II III IV

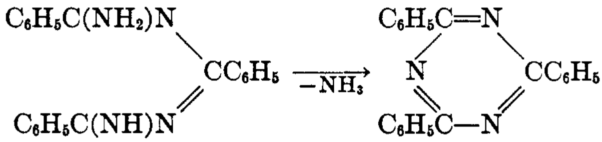
$C_6H_5CONH_2 + C_6H_5CONHOCC_6H_5$

It is assumed that oxidation at the double bond converts lophine into an unknown tribenzoic acid (II), which in turn is hydrolyzed to equimolecular quantities of the two aquo-ammonobenzoic acids III and IV. The imidazole ring in lophine is opened just as in imidazole itself under the action of potassium permanganate.

In aqueous alkaline solution lophine is converted into aquobenzoic acid and ammonia by the action of atmospheric oxygen (77). Here again it is fair to say that lophine is oxidized to dibenzoylbenzamidine, formula II above, which in the presence of strong alkali is hydrolyzed completely to aquobenzoic acid and ammonia.

3. Nitridation. If we are justified in our assumption that the primary product of the action of oxidizing agents on lophine is the tribenzoic acid represented by the formula II above, then it is reasonable to expect that nitridation agents will attack lophine in a similar manner to form the ammonotribenzoic acid, formula II below, which hypothetical compound may either take up ammonia to form benzamidine or lose ammonia to give benzonitrile or its trimer. As a matter of fact, by the nitridizing action of iodine in liquid ammonia solution lophine is converted into cyaphenine (91) as represented, let us say, by the scheme


I II

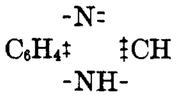


II′ III

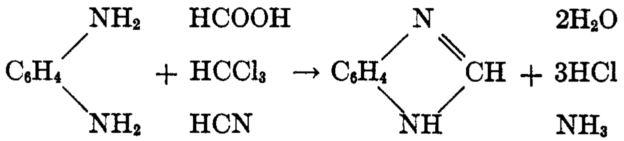
4. Metallic salts. Since lophine contains an ammonobenzoic acid hydrogen atom,[6] it is an acid ester and should in consequence thereof be capable of forming metallic salts.

Using liquid ammonia as solvent in which to effect the necessary reactions Strain (91) has prepared the salts listed herewith: $C_{21}H_{15}N_2K$, $C_{21}H_{15}N_2K \cdot 3NH_3$, $C_{21}H_{15}N_2Na$, $C_{21}H_{15}N_2Li$, $C_{21}H_{15}N_2Li \cdot xNH_3$, $(C_{21}H_{15}N_2)_2Ca$, $(C_{21}H_{15}N_2)_2Ca \cdot 6NH_3$, $(C_{21}H_{15}N_2)_2Mg \cdot 2NH_3$, $C_{21}H_{15}N_2Ag$, $C_{21}H_{15}N_2Ag \cdot 2NH_3$, $C_{21}H_{15}N_2Cu$, $(C_{21}H_{15}N_2)_2Cu$, and $(C_{21}H_{15}N_2)_2Cu \cdot xNH_3$. The potassium, sodium, and lithium salts were obtained by the action of lophine on the respective metallic amides; the calcium salt by the action of lophine on calcium amide and on metallic calcium; the magnesium salt by the action of lophine on metallic magnesium; the silver salt by the action of lophine on silver amide and also by the action of potassium lophine on silver nitrate; the cuprous salt by the action of lophine on ammonous cuprous nitride, $Cu_3N \cdot xNH_3$; the cupric salt by bringing together solutions of potassium lophine and cupric nitrate. Most of these salts were obtained well crystallized and of sharply definite composition. They are all hydrolyzed by the action of water to lophine and the respective metallic hydroxides or oxides.

C. Benzimidazole



Three reactions whereby this bicyclic compound has been prepared (107, 46, 22) may be summarized by means of the scheme



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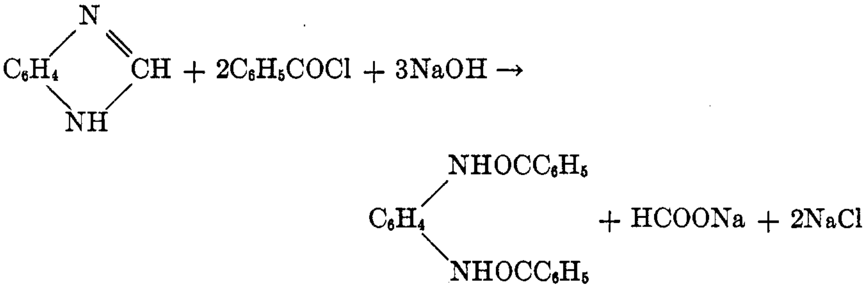
[6] This hydrogen atom may of course be looked upon as alcoholic hydrogen as well as acid hydrogen. Since, however, the acid group contributes much more to the mobility of the hydrogen atom than does the alcohol group, it is reasonable in this and other similar cases to speak of acid hydrogen.

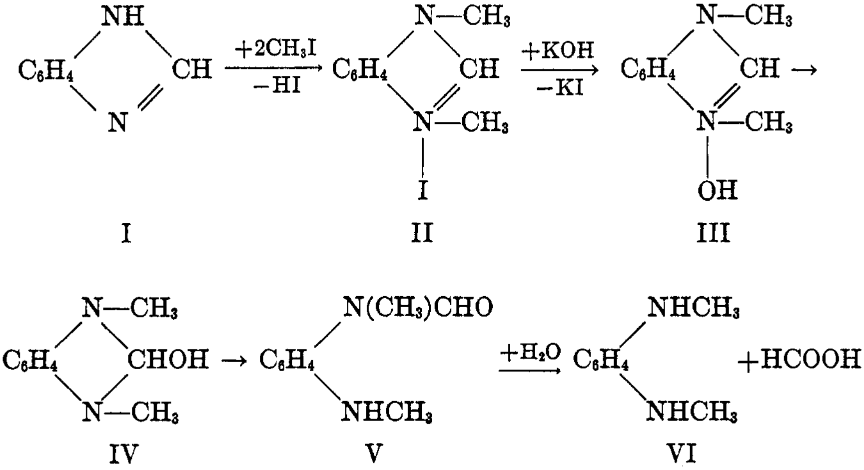
which represents the formation of an *o*-phenylene ester of ammonoformic acid by the action first, of aquoformic acid, second, of a formic acid chloride, and third, of formic anammonide on *o*-phenylenediamine. Dains used hydrocyanic acid in the form of the so-called hydrocyanic acid sesquichloride.

Benzimidazole has not been hydrolyzed directly to *o*-phenylenediamine and formic acid. However, by the action of benzoyl chloride in the presence of sodium hydroxide the imidazole ring is opened (6, 53, 105), just as is imidazole itself by similar treatment (p. 313). As represented by the equation



dibenzoyl-*o*-phenylenediamine and sodium formate are formed.

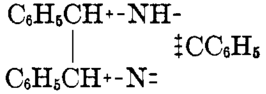
Furthermore, by way of the quaternary salt, II below, the imidazole ring in benzimidazole has been opened by a sequence of reactions represented by the scheme (34):



Neither the quaternary base (III) nor the aquo-ammonoformate represented by formula V was isolated. The identification of compound IV, which is a formic acid ester, and its hydrolysis, presumably by way of V, to *N*,*N'*-dimethyl-*o*-phenylenediamine (VI) and aquoformic acid supports the view that benzimidazole is a cyclic *o*-phenylene ammonoformate. Compound IV was also obtained by Fischer and Fussenegger (33) by heating *N*,*N'*-dimethylphenylenediamine with excess of formic acid.

Using liquid ammonia as solvent in which to carry out the reactions involved, the following formulated salts have been obtained (106a): $C_7H_5N_2Na$, $C_7H_5N_2Li \cdot 2NH_3$, $C_7H_5N_2Li$, $(C_7H_5N_2)_2Ba \cdot NH_3$, $(C_7H_5N_2)_2Ba$. Other salts of benzimidazole which have been prepared are $C_7H_5N_2Ag$, $(C_7H_5N_2)_2Cu$, $(C_7H_5N_2)_2Cd$, $(C_7H_5N_2)_2Co$, and $(C_7H_5N_2)_2Zn$. A mercury salt of the formula, $C_7H_5N_2HgCl$, is known (8, 30), as are also alkyl and acyl derivatives such as $C_7H_5N_2CH_3$ and $C_7H_5N_2OCC_6H_5$.

D. Amarine, 2,4,5-triphenyl-4,5-dihydroimidazole

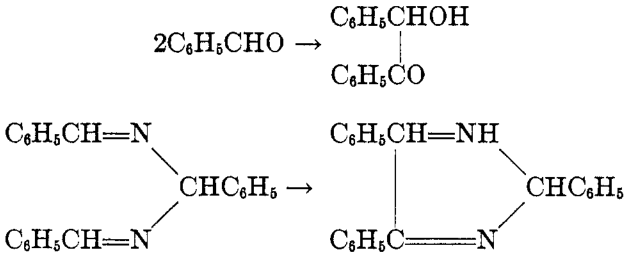


$$\begin{array}{ll} C_6H_5CH^{+}\text{-}NH\text{-} & \\ \quad | & \ddagger CC_6H_5 \\ C_6H_5CH^{+}\text{-}N= & \end{array}$$

This formula, which has been established by Japp and Moir (51), represents amarine as a cyclic hydrobenzoin ammonobenzoate.

1. Formation. (a) It has long been known that hydrobenzamide, when heated alone or with potassium hydroxide solution, is converted into an isomer known as amarine. More recently it has been found by Strain (91) that the same rearrangement takes place when hydrobenzamide is warmed in liquid ammonia solution with potassium amide.

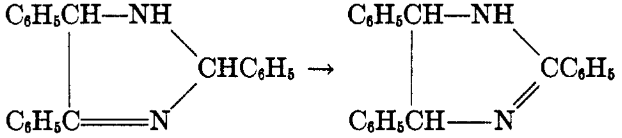
Since hydrobenzamide is a near analog of benzaldehyde it would be reasonable to expect it to undergo a benzoin condensation, just as benzaldehyde is known to condense to benzoin. The respective reactions involved may be represented by the equations



$$2C_6H_5CHO \rightarrow \begin{array}{l} C_6H_5CHOH \\ \quad | \\ C_6H_5CO \end{array}$$

In the first case with the establishment of a carbon to carbon union, two molecules of benzaldehyde are converted into a mixed ketone secondary alcohol. In the second, the same carbon to carbon union is established and at the same time a hydrogen atom from one of the aldehyde groups wanders to the nitrogen atom of the other, thereby converting the one aldehyde group into a secondary alcohol group and the other into a ketone group.

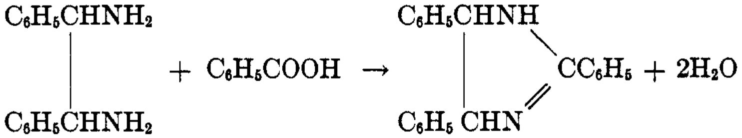
However, as has been shown by Japp and Moir, amarine has the constitution represented by the second formula herewith.



It follows therefore that the transformation of the assumed primary condensation product of hydrobenzamide into amarine involves an intramolecular Cannizzaro reaction, which is to say that the benzaldehyde group at the right-hand end of the first formula is augmented to a benzoic acid group as shown in the second, while concomitantly the ketone group is reduced to a secondary alcohol group.

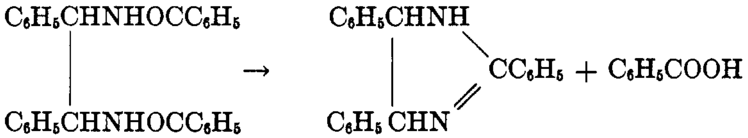
(b) Radzisewski (78) prepared amarine by the interaction of benzoin, benzaldehyde, and ammonia, and concluded that it should be represented by the first of the formulas above. Since, however, the second formula has been established (58) as representing amarine we must conclude that Radzisewski's assumed product undergoes intramolecular augmentation and reduction to form amarine.

(c) Japp and Moir (58) have shown that isoamarine is formed as represented by the equation



when the racemic form of diphenylethylenediamine is heated with aquobenzoic acid. The aquobenzoic acid acts on a diatomic ammono alcohol to form a cyclic ammonobenzoate.

(d) Isoamarine has also been obtained by heating the racemic form of dibenzoyldiphenylethylenediamine, formula I below, in a current of hydrochloric acid gas (31, 58). The reaction involved, which is represented by the equation

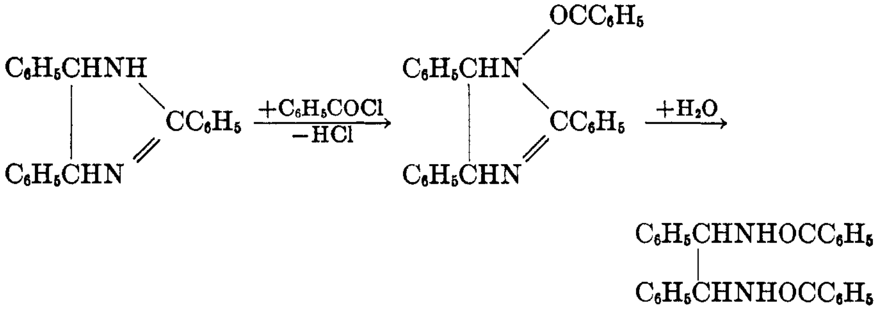


I II III

consists in the conversion of an open chain aquo-ammonobenzoate into a cyclic ammonobenzoate and aquobenzoic acid. By an intramolecular process one of the aquo-ammonobenzoic acid groups in I is ammonolyzed to an ammonobenzoic acid group in II, the other being simultaneously hydrolyzed to aquobenzoic acid. The reaction involved is similar to that which takes place when acetamide is converted into equimolecular quantities of acetic acid and acetamidine under the action of hot dry hydrochloric acid.

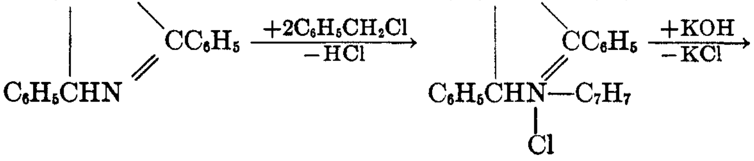
2. Opening the dihydroimidazole ring. Although amarine has not been hydrolyzed to diphenylethylenediamine and aquobenzoic acid, or to hydrobenzoin, aquobenzoic acid, and ammonia, as might perhaps be expected on the assumption that it is a benzoic acid ester of diphenylethylenediamine, it does happen that procedures for opening the amarine ring are known which are to be regarded as accomplishing such a hydrolytic decomposition.

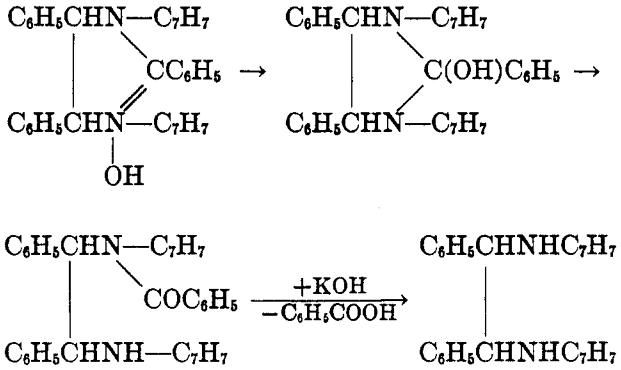
(a) When treated with a benzene solution of benzoyl chloride amarine yields benzoylamarine which in turn, under the action of alcoholic hydrochloric acid, is converted into dibenzoyldiphenylethylenediamine (58). As represented by the scheme (cf. p. 313),



a cyclic benzoate is first and last converted into an open chain aquo-ammonobenzoate. The first and second formulas represent cyclic benzoates; the last an open chain benzoate.

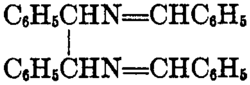
(b) Japp and Moir (58) converted amarine into symmetrical dibenzyldiphenylethylenediamine (last formula below) and aquobenzoic acid by means of a series of reactions represented by the scheme (cf. p. 320).





Compounds represented by the third and fourth formulas were not isolated. The amarine ring is opened to form an open chain derivative of diphenylethylenediamine, which is a diatomic ammono alcohol, and aquobenzoic acid. In principle amarine may be said to undergo hydrolytic decomposition.

3. Oxidation and reduction. The augmentation of amarine to lophine has already been discussed (p. 315). By the action of metallic sodium on amarine small yields (20 per cent) of a compound represented by the formula

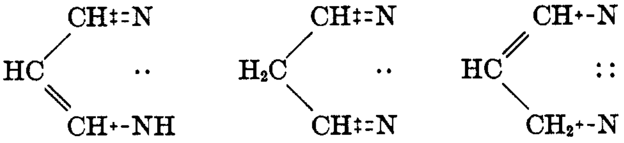


$$\begin{array}{l} C_6H_5CHN{=}CHC_6H_5 \\ \;| \\ C_6H_5CHN{=}CHC_6H_5 \end{array}$$

have been obtained (48, 58, 36). Whatever the mechanism of the reactions involved may be, which is not obvious, the net result, in so far as the formation of the above-formulated compound is concerned, consists in the reduction of an ammonobenzoic acid ester to a dibenzaldehyde-ether.

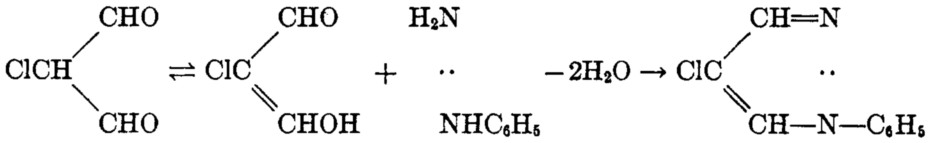
4. Metallic salts. Silver salts of both amarine and isoamarine, $C_{21}H_{17}N_2Ag$, are known (86, 19). A sodium salt of isoamarine has been isolated, though its composition has not been fixed by analysis (58).

E. Pyrazole

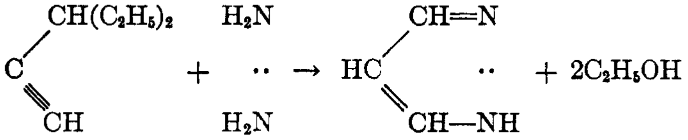


The first two formulas represent tautomeric forms of a cyclic malondialdehyde hydrazone; the third represents a cyclic azo compound. In the first formula one of the hydrazine nitrogen atoms is attached to aldehyde carbon, in the other to alcohol carbon. In the second formula both hydrazine nitrogen atoms are in combination with aldehyde residues. The first formula is the generally accepted one.

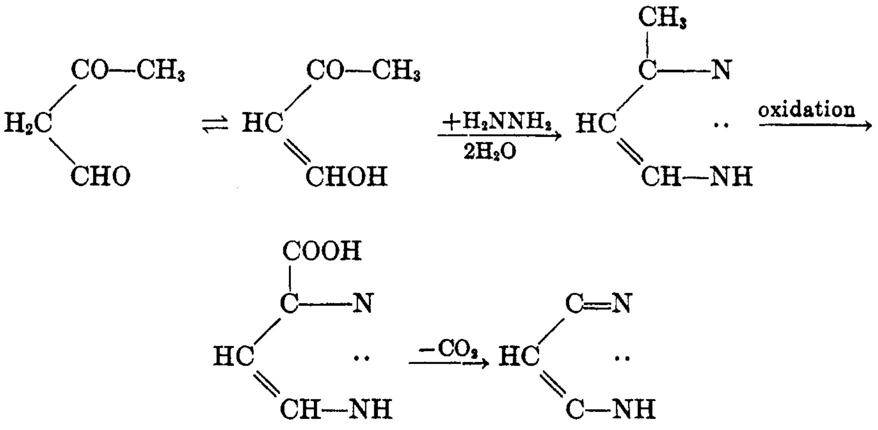
1. Formation. Regarding pyrazole as a cyclic malondialdehyde hydrazone, it would be reasonable to expect that it might be prepared by the interaction of malondialdehyde, a somewhat indefinitely known compound, and hydrazine. Now while such a reaction is unknown it does happen that 1-phenyl-4-chloropyrazole has been obtained by the action of phenylhydrazine on chloromalondialdehyde in alcohol solution (23) as represented by the equation



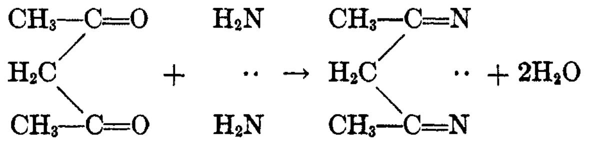
and that pyrazole itself has been prepared by the action of hydrazine on propargyldiethylacetal (18).



Starting with acetoacetic aldehyde (18a) pyrazole has furthermore been made as represented by the scheme



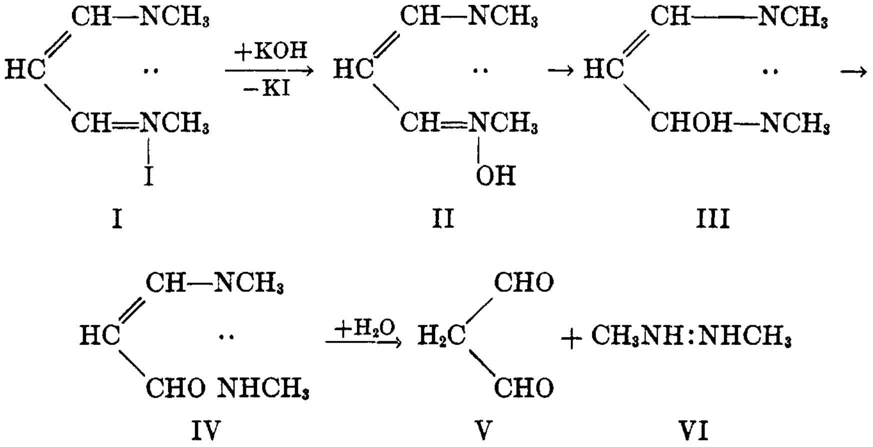
A quantitative yield of 3,5-dimethylpyrazole appears when acetylacetone, hydrazine sulfate, and sodium hydroxide are brought together in water solution (81). The reactions here involved take place in accordance with the equation



which represents the action of hydrazine on a diketone to form a cyclic diketone hydrazone.

2. Opening the ring. Pyrazole is a very stable compound. It is aromatic in character and shows but few of the properties of open chain derivatives of hydrazine. Nevertheless under certain conditions the hydrazine group, which we assume to be present (or potentially present) in the pyrazole ring, reveals itself, as the following discussion will show.

(a) The quaternary salt, I below, which is formed by the action of methyl iodide on 1-methylpyrazole, yields all of its nitrogen in the form of symmetrical dimethylhydrazine when heated with strong potassium hydroxide solution (59, 60). Symmetrical dimethylhydrazine is formed by the hydrolysis of the quaternary salt in accordance, let us say, with the scheme:

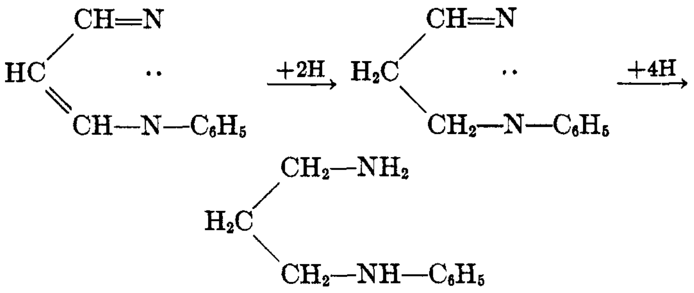


I II III

IV V VI

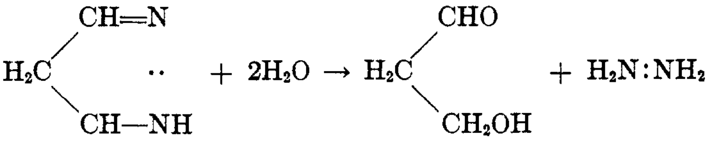
Formula III contains an aldehyde hydrazone hydrate group, RCH(OH)-NR:NR$_2$, which makes for the ready rearrangement of a compound of this formula into the open chain compound IV. It is assumed that by the action of aqueous potassium hydroxide on IV, symmetrical dimethylhydrazine and presumably malondialdehyde (V) are formed. None of the compounds represented by the formulas II, III, IV, and V was identified. Considerable amounts of formic acid were present in the reaction mixture.

(b) Pyrazole resists the action of reducing agents. However 1-phenylpyrazole has been reduced first to 1-phenylpyrazoline and thence to 1-amino-3-phenylaminopropane (3, 4) as represented by the scheme



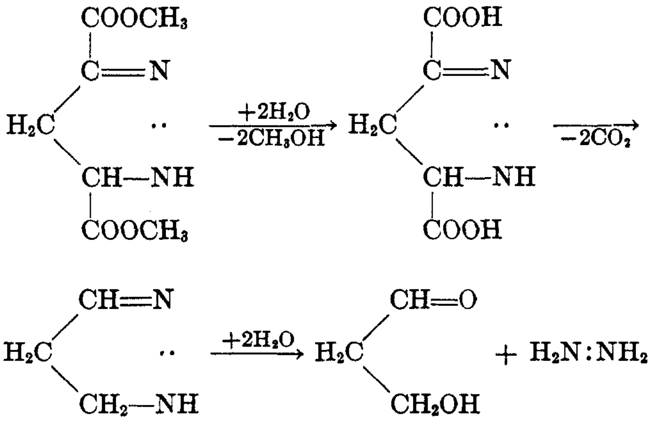
In so far as the opening of the ring is concerned, the action involved consists in the reduction of hydrazine nitrogen to ammonia nitrogen.

(c) A fair yield of hydrazine is obtained when pyrazoline is heated with concentrated hydrochloric acid, the reaction involved probably taking place as represented by the equation



though hydracrylaldehyde was not identified (21).

(d) The dimethyl ester of pyrazoline-3,5-dicarboxylic acid (first formula below) gives abundant yields of hydrazine when heated with dilute sulfuric acid (16). The reactions involved may be represented by the scheme



though the products formed other than carbon dioxide and hydrazine remain unknown.

3. Metallic salts. A sodium salt, which was not analyzed, a silver salt, $C_3H_3N_2Ag$, and a pyrazole mercuric chloride, $C_3H_3N_2HgCl$, have been prepared (15). Rosengarten (80) prepared a silver salt, $C_5H_7N_2Ag \cdot H_2O$, and a mercuric salt, which was not analyzed, of 2,5-dimethylpyrazole. It may be noted that, formally, neither pyrazole nor dimethylpyrazole is an ammono acid. It seems fair however to say that the hydrazine hydrogen atom becomes distinctly more acid under the negative influence of the pyrazole ring. It will be recalled that alkali metal derivatives of hydrazine are known.

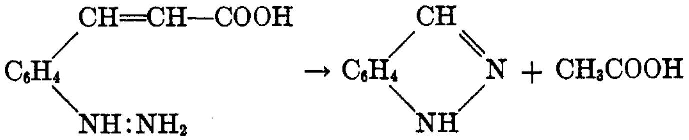
F. Indazole

$$\begin{array}{ll} C_6H_4{}^{+}\text{-}NH \\ | \quad \cdot\cdot \\ CH\ddagger{=}N \end{array} \qquad \begin{array}{ll} C_6H_4{}^{+}\text{-}N \\ | \quad \vdots \\ CH_2{}^{+}\text{-}N \end{array}$$

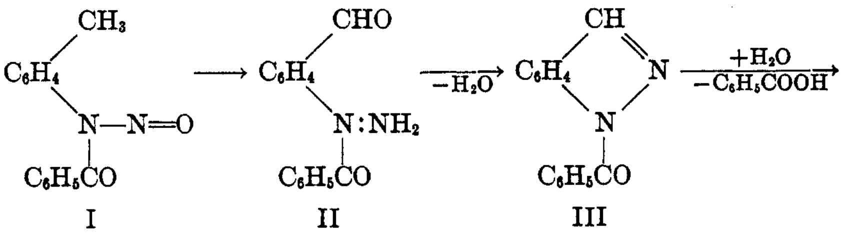
The first formula represents indazole as a cyclic hydrazinobenzaldehyde hydrazone, the second as a cyclic azo compound.

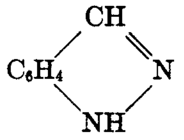
1. Formation. Methods for the preparation of indazole and 3-methylindazole, which are in agreement with the assumption that they are derivatives of hydrazine, are the following.

(a) Simply by heating hydrazinocinnamic acid indazole is formed (35), the reaction involved taking place as represented by the equation



(b) Indazole is formed in good yield when benzoyl-*o*-tolylnitrosamine, formula I below, which is a benzoyltolyl derivative of an aquo-ammononitrous acid, is warmed in contact with dry benzene (56). The reactions involved may be represented by the scheme

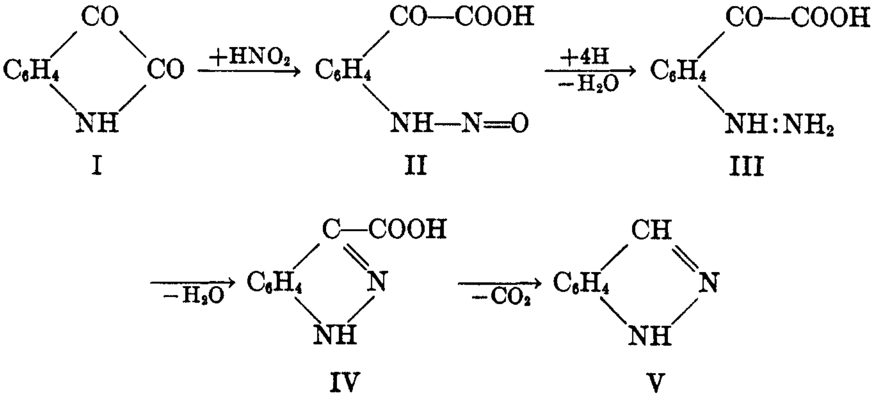




IV

which is to say that by an intramolecular reaction the methyl group in I is augmented to an aldehyde group in II, while at the same time the nitrous acid group is reduced to the hydrazine group. The unknown benzoylhydrazinobenzaldehyde (II) thus formed loses water to yield the likewise unknown benzoylindazole (III). It may be assumed that the water formed in the conversion of II into III hydrolyzes the latter to indazole (IV) and benzoic acid.

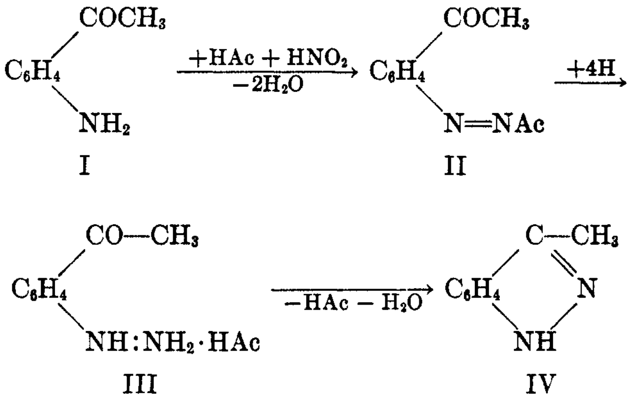
(c) When *o*-diazophenylglyoxylic acid, formula II below, formed by diazotizing isatin (I) in dilute sulfuric acid solution, is reduced by the action of sulfur dioxide and stannous chloride, the *o*-hydrazinophenylglyoxylic acid (III), which is formed, loses water and passes over into the indazolecarboxylic acid (IV). Simply by heating this compound somewhat above its melting point a quantitative yield of indazole is obtained (84). The successive steps may be represented by the scheme



By the action of the reducing agent the nitrous acid group present in II is converted into the hydrazine group in III which, it is fair to assume, persists as such in the final product (V).

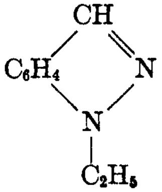
Imidazole is not known to enter into reactions which support the view that it contains a hydrazine residue.

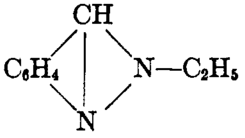
(d) 3-Methylindazole (IV) has been prepared from *o*-aminoacetophenone (34, 3, 4) by way of the diazo and hydrazine derivatives II and III as represented, in effect, by the scheme



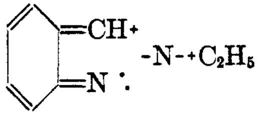
Under the action of nitrous acid the amino compound (I) is converted into the diazo compound (II), which latter compound on reduction yields III. With the elimination of water and acid this hydrazine derivative passes over into 3-methylindazole (IV).

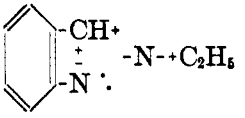
2. N-Alkylindazoles. Two *N*-ethylindazoles have been prepared, to which the formulas





have been given (1a, 2). The first formula may reasonably be said to represent a derivative of hydrazine. The second formula we must perforce let stand without comment other than to note that in a highly speculative way one may write the formulas





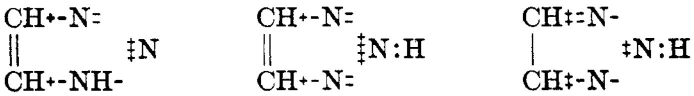
and say that they represent derivatives of hydrazine.

3. Metallic salts. Fischer and Tafel (37) prepared a silver and a mercury salt of indazole, which were later shown (56) to have the composition represented by the respective formulas $C_7H_5N_2Ag$ and $(C_7H_5N_2)_2Hg$.

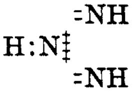
IV. COMPOUNDS CONTAINING THREE NITROGEN ATOMS IN THE RING

Compounds containing three nitrogen atoms in a pentacyclic ring are 1,2,3-triazole and 1,2,4-triazole, and their derivatives.

A. 1, 2, 3-Triazole[7]



The first formula represents an ethylenyl ester of the one tautomeric form of ammononitrous acid, $HN{=}{\ddagger}N{+}{-}NH_2$, the second an ester of the other form,



$$H{:}N{\ddagger}\begin{matrix}{=}NH\\ {=}NH\end{matrix}$$

Indulging in a little wishful thinking it is perhaps not altogether unreasonable to say that the third formula represents a cyclic glyoxal hyponitrous acid acetal.[8]

Some of the methods for the preparation of 1,2,3-triazole and its derivatives are readily interpreted as supporting the view that they are derivatives of an ammononitrous acid; others, while not forbidding such a view, are perhaps better explained as resulting in the formation of compounds

---

[7] A colon is printed between the nitrogen and hydrogen atoms in the second and third formulas, as well as in others to follow, as a convenient means of indicating that no assumptions are made concerning the polarity of these unions. The NH group in the first formula represents an ammonia residue in which of course the nitrogen atom is negative in respect to the hydrogen atom. For a reasonable justification of the symbol representing pentapositive nitrogen as given in the second formula, see Franklin, The Nitrogen System of Compounds, p. 44 (reference 41).

[8] Franklin (41) has shown that Stieglitz' suggestion to the effect that the diazo compounds are derivatives of nitrous acid (93) is supported by a wealth of observations. Diazobenzene, in so far as it may be represented by the formulas,

$$C_6H_5{-}N{=}N{-}OH \rightleftharpoons C_6H_5NH{-}N{=}O$$

is a phenyl ester of an aquo-ammononitrous acid, $HN{=}N{-}OH \rightleftharpoons H_2N{-}N{=}O$. If we accept Angeli's formula, $C_6H_5N(NH)O$, diazobenzene may even be looked upon as a phenyl derivative of the tautomeric form of aquo-ammononitrous acid represented by the formula, $H{:}N(NH)O$, or in other words it may be said to be nitrobenzene in which one of the oxygen atoms is replaced by an imido group.

Since nitrous acid is generally assumed to be a tautomeric compound to which the formulas $HO{-}N{=}O$ and $H{:}NO_2$ may be given, one may speculate to the effect that aquo-ammononitrous acid, known in liquid ammonia solution (83), exists in the tautomeric forms represented by the formulas,

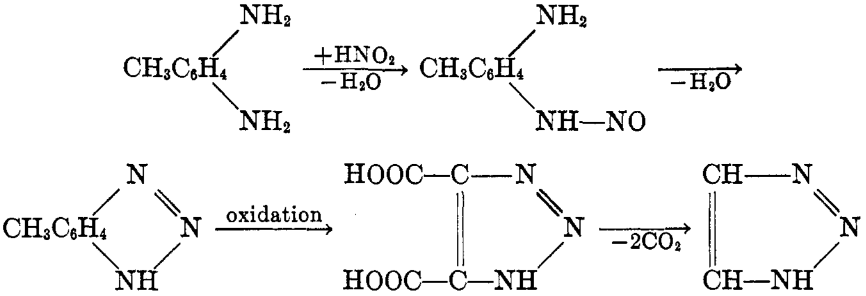
$$H_2N{-}N{=}O \rightleftharpoons HN{=}N{-}OH \rightleftharpoons H{:}N(NH)O$$

and that to the ammononitrous acid, known only in the form of esters, the formulas, $H_2N{-}N{=}NH \rightleftharpoons H{:}N(NH)_2$, may be given. For the reason that they are not available in this type face these above formulas are perforce printed without the small plus and minus signs.

containing nitrogen atoms linked together by non-polar bonds. So also certain of the reactions which 1,2,3-triazole and its derivatives undergo are in agreement with the assumption that they contain an ammononitrous acid group; others that they are rather derivatives of an unknown triazene, HN::N:NH_2.

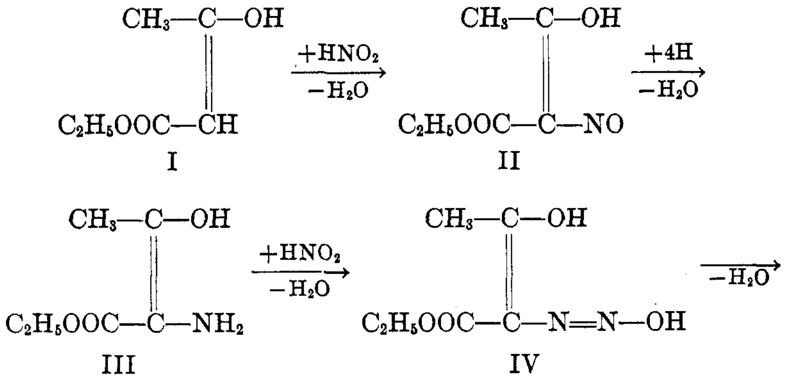
1. Formation. The following described methods for the preparation of 1,2,3-triazole and some of its derivatives lend support to the assumption that they are, at least potentially, so to say, cyclic ammononitrites.

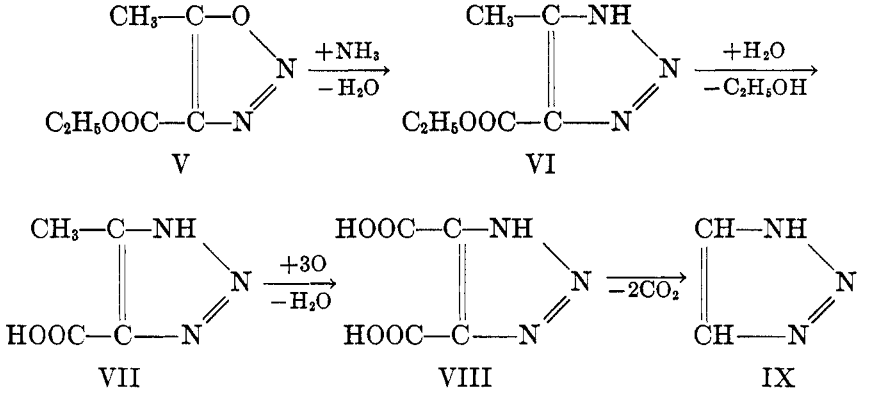
(a) Ladenburg (62) found that a toluotriazole, third formula below, is formed by the interaction of potassium nitrite and 3,4-diaminotoluene sulfate. When this cyclic ammononitrite is warmed with alkaline potassium permanganate solution it is oxidized to a triazoledicarboxylic acid, which, on heating somewhat above its melting point, yields carbon dioxide and 1,2,3-triazole (13). The reactions involved are represented by the scheme



It is interesting to note that the triazole ring, which we assume to contain a nitrous acid residue, is more resistant to the action of oxidizing agents than is the benzene ring.

(b) Starting with acetoacetic ester good yields of 1,2,3-triazole have been obtained (103) by means of reactions summarized by the scheme

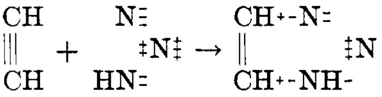




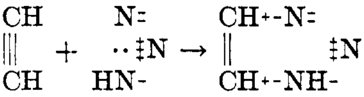
V VI VII VIII IX

By the action of nitrous acid on acetoacetic ester (I) the nitroso compound (II) is formed, which on reduction gives III. It is assumed that this aminoacetoacetic acid ester, under the action of nitrous acid, is converted into the diazo compound (IV). This unknown compound loses water to form the cyclic aquo-ammononitrite (V), which is ammonolyzed to the triazole derivative (VI) by the action of ammoniacal ammonium acetate solution. Compound VI on hydrolysis yields the carboxylic acid (VII), which has been oxidized to VIII. Bladin (13) observed the decomposition of this dicarboxylic acid to form 1,2,3-triazole (IX) and carbon dioxide.

(c) The formation of 1,2,3-triazole by the interaction of acetylene and hydrazoic acid (27) may be explained as involving the augmentation of acetylene to an ethylene derivative, and the concomitant reduction either of nitric acid nitrogen to nitrous acid nitrogen or of hydrazine nitrogen to ammonia nitrogen as represented by the equations



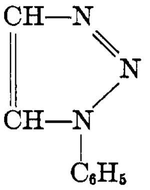
$$\begin{array}{c}\mathrm{CH}\\ \equiv\\ \mathrm{CH}\end{array} + \begin{array}{l}\quad\mathrm{N}\vdots\\ \qquad\ddagger\mathrm{N}\ddagger\\ \mathrm{HN}\colon\end{array} \rightarrow \begin{array}{ll}\mathrm{CH}^{+}\text{-}\mathrm{N}\colon & \\ \| & \ddagger\mathrm{N}\\ \mathrm{CH}^{+}\text{-}\mathrm{NH}\text{-} & \end{array}$$



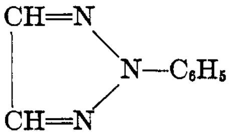
$$\begin{array}{c}\mathrm{CH}\\ \equiv\\ \mathrm{CH}\end{array} + \begin{array}{l}\quad\mathrm{N}\colon\\ \cdot\cdot\ddagger\mathrm{N}\\ \mathrm{HN}\text{-}\end{array} \rightarrow \begin{array}{ll}\mathrm{CH}^{+}\text{-}\mathrm{N}\colon & \\ \| & \ddagger\mathrm{N}\\ \mathrm{CH}^{+}\text{-}\mathrm{NH}\text{-} & \end{array}$$

B. Phenyl-1,2,3-triazoles

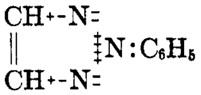
Two phenyl-1,2,3-triazoles have been prepared, to which the respective formulas



and

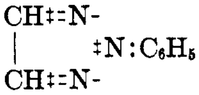


have been given (24, 72a). The first formula may clearly be said to represent a cyclic ethylenyl phenyl ammononitrite. For the second isomer, named *N*-phenylosotriazole by von Pechmann (72a), the formulas



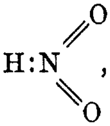
$$\begin{array}{ll} CH^{+}\text{-}N^{=} & \\ \| & \ddagger N:C_6H_5 \\ CH^{+}\text{-}N^{=} & \end{array}$$

and



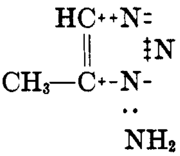
$$\begin{array}{ll} CH\ddagger{=}N\text{-} & \\ | & \ddagger N:C_6H_5 \\ CH\ddagger{=}N\text{-} & \end{array}$$

may be written and in a highly speculative way be said to represent derivatives of nitrobenzene and nitrosobenzene, respectively; which is to say that they are derivatives of the tautomeric form of nitrous acid,

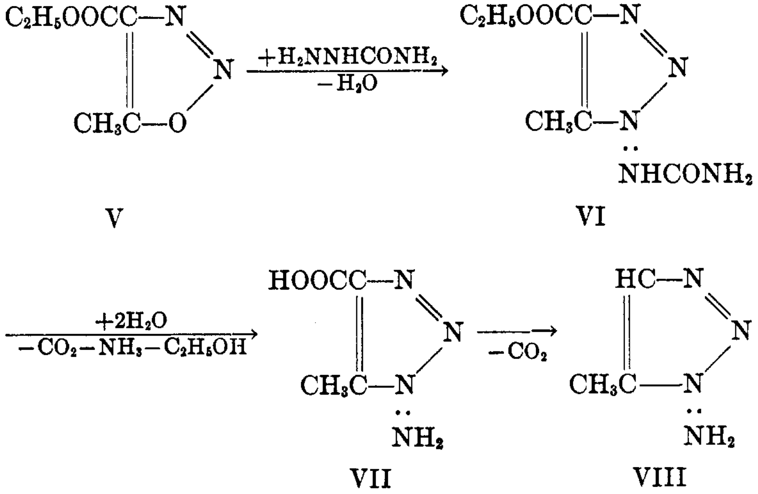


, and of hyponitrous acid, $H:N{=}O$.

C. 1-Amino-3-methyl-1,2,3-triazole

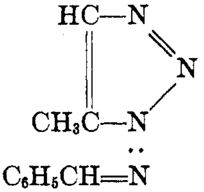


1-Amino-1,2,3-triazole is not known. However, starting with the anhydride of diazoacetic acid ester, formula V (p. 333 and below), Wolff and Hall (106), following processes represented herewith,



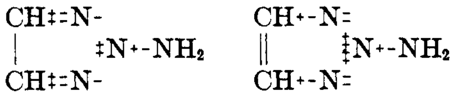
V VI VII VIII

prepared 1-amino-5-methyl-1,2,3-triazole (VIII). The reactions involved may reasonably be said to result in the formation of a cyclic compound which is a derivative of an unknown nitrous acid hydrazide, $H_2N{-}{}^{+}N{\ddagger}{=}N{:}NH_2$. The formation of a benzaldehyde hydrazone



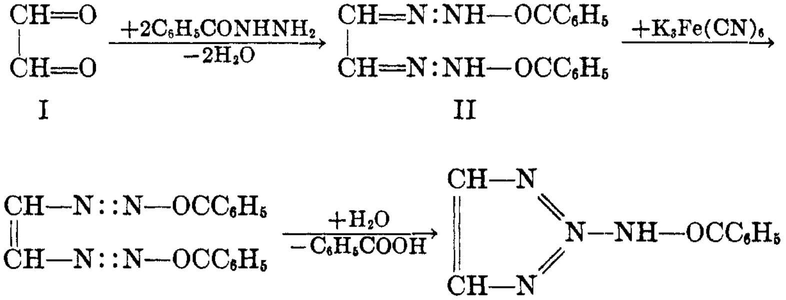
by the action of benzaldehyde on this aminotetrazole supports the view that it contains a hydrazine residue, as represented by formula VIII above.

D. 2-Amino-1,2,3-triazole



$$\begin{array}{lll} CH{\ddagger}{=}N{-} & & CH{+}{-}N{=} \\ | \qquad {\ddagger}N^{+}{-}NH_2 & & \| \qquad {\ddagger}N^{+}{-}NH_2 \\ CH{\ddagger}{=}N{-} & & CH{+}{-}N{=} \end{array}$$

As represented by these formulas this compound, to which von Pechmann gave the name *N*-aminoösotriazole, is either a glyoxal nitrous acid acetal or an ethylenyl ammononitrate. It has been prepared by a sequence of reactions (72, 88, 89), summarized by the scheme



I II

III[9] IV

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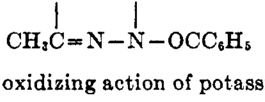
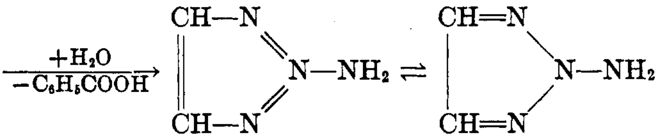
[9] This compound has not been isolated. However, its dimethyl homolog, to which von Pechmann gave the formula



$$\begin{array}{l} CH_3C=N-N-OCC_6H_5 \\ \qquad\quad\ |\quad\ \ | \\ CH_3C=N-N-OCC_6H_5 \end{array}$$

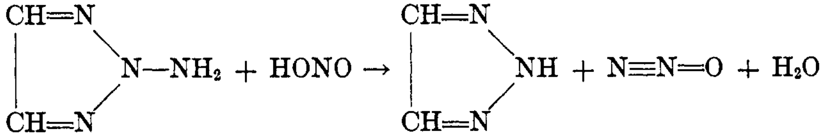
has been prepared (72) by the oxidizing action of potassium ferricyanide on diacetyldibenzoyl osazone.



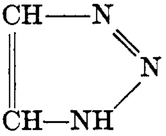
V V′

The glyoxal dibenzoylosazone (II), formed by the action of benzoylhydrazine on glyoxal (I), is represented as undergoing oxidation to the azo compound (III). In the presence of warm sodium hydroxide solution this compound yields IV,[10] which on warming with dilute hydrochloric acid is hydrolyzed to V, V′, and benzoic acid.

von Pechmann and Bauer (72) found that nitrous acid acts on this *N*-aminoösotriazole to form osotriazole



Dimroth (25) later showed that von Pechmann's osotriazole is identical with Bladen's (13) triazole represented by the formula



1. Opening the ring. 1,2,3-triazole in comparison with the open chain ammononitrous acid esters, with diazoaminobenzene, for example, is a remarkably stable compound which resists the action of hydrolyzing agents. None the less the ring in a number of 1,2,3-triazole derivatives has been opened by methods which show that such compounds may be regarded as cyclic ammononitrous acid esters. Two procedures whereby the 1,2,3-triazole ring has been opened are as follows.

(a) Dimroth (26) found that 1-phenyl-5-amino-1,2,3-triazole (formulas I and I′ below) under the action of hot dilute sulfuric acid yields nitrogen and glycolic acid phenylamidine (III below), just as by similar treatment diazoaminobenzene yields nitrogen, phenol, and aniline. It appears in accordance with the scheme

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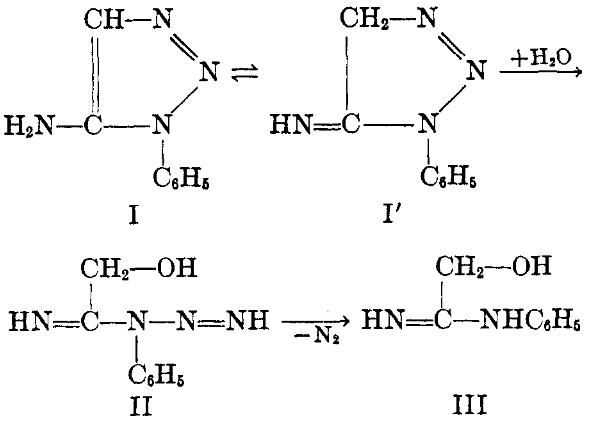
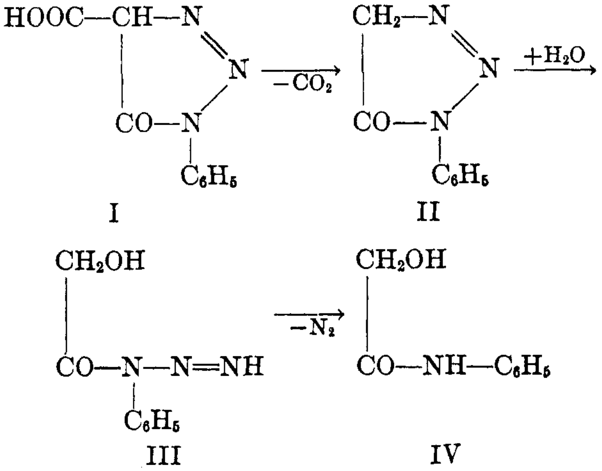
[10] The mechanism of the conversion of III into IV is not clear. It may be said, however, that of the four azo nitrogen atoms contained in III, three are reduced to ammonia nitrogen and the fourth is augmented to nitric acid nitrogen.



that 1-phenyl-5-amino-1,2,3-triazole is first hydrolyzed to the open chain diazo compound (II), and second, that this hypothetical ammononitrous acid derivative loses nitrogen (nitrous anammonide) to form glycolic acid phenylamidine (III).[11] This compound was identified by hydrolyzing it to glycolic acid anilide and ammonia. Noting that the group $^{+}CH_2C\ddagger$ characterizes the glycolic acids it may be said that the formulas I, I', and II represent respectively a cyclic and an open chain glycolic acid nitrous acid phenyl ester.

(b) When phenyltriazolonecarboxylic acid (formula I) is heated with water, glyoxylic acid anilide (formula IV), nitrogen, and carbon dioxide are formed (25a) in accordance with the scheme



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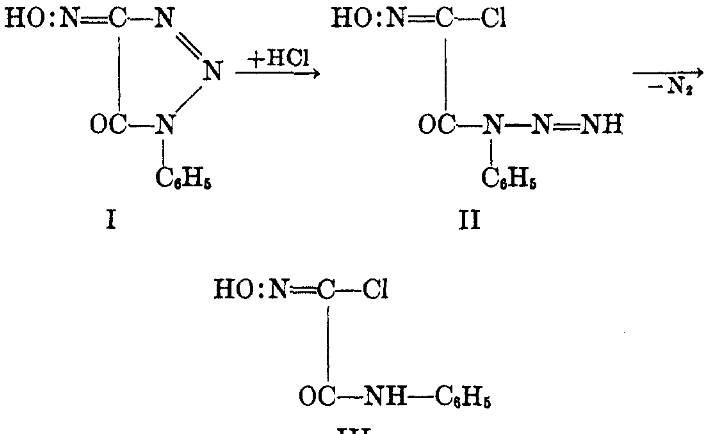
[11] Alternately it may be that II is hydrolyzed to III and the very unstable aquoammonitrous acid, HO—N=NH, which decomposes to form nitrogen and ammonia (83).

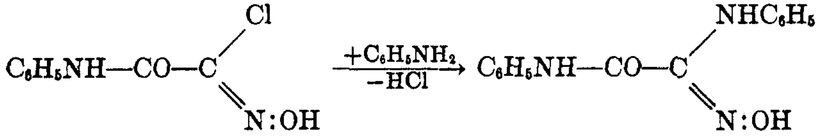
in which formulas II and III represent hypothetical compounds. It is assumed that the nitrogen results from the decomposition of the ammononitrous acid residue contained in compound III.

(c) A similar opening of the triazole ring takes place when the 1,2,3-triazole derivative known as 1-phenyl-4-isonitroso-5-triazolone (formula I below) is treated with fuming hydrochloric acid (29). The reactions involved may be represented by the scheme



I II III

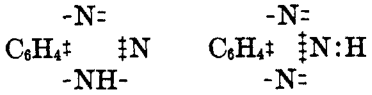
in accordance with which the compound I, which is at the same time an oxalic acid oxime and an ammonoöxalic ammononitrous acid phenyl ester, is opened to form II. This hypothetical diazo compound loses nitrogen to form the compound III, which is an oxalic acid oxime-chloride and at the same time an oxalic acid phenyl ester. Dimroth and Traub established the constitution of III by converting it into oxanilide



$$\xrightarrow[-H_2NOH]{+H_2O} C_6H_5NH—CO—CO—NHC_6H_5$$

2. Metallic salts. 1,2,3-Triazole shows distinct acid properties just as does diazoaminobenzene. Baltzer and von Pechmann (5) prepared a silver salt, $C_2H_2N_3Ag$, and a triazole mercuric chloride, $C_2H_2N_3HgCl$. A blue precipitate, which was assumed to be a cupric salt, was obtained by adding cupric sulfate to a water solution of triazole. Calcium hydroxide was observed to dissolve in a triazole solution. In ether solution 1,2,3-triazole attacks metallic sodium to form a sodium salt.

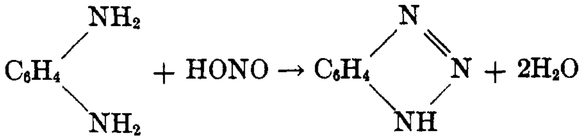
E. Benzotriazole



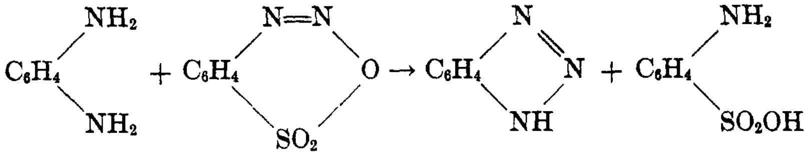
$$C_6H_4\begin{matrix}-N=\\ \ddagger\qquad\ddagger\\ -NH-\end{matrix}N \qquad C_6H_4\begin{matrix}-N=\\ \ddagger\quad\ddagger\\ -N=\end{matrix}N:H$$

It is reasonable to say that these formulas represent tautomeric forms of *o*-phenylene ammononitrite.

Benzotriazole has been prepared by the action of nitrous acid (62) and of *p*-diazobenzenesulfonic acid (47) on *o*-phenylenediamine. In accordance with the equation



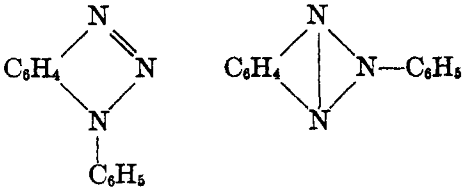
a cyclic *o*-phenylene ammononitrite is formed. As represented by the equation



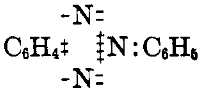
the same compound is formed by the action of a derivative of aquo-ammononitrous acid on *o*-phenylenediamine.

Benzotriazole is a very stable compound which shows none of the reactions of the open chain ammono and aquo-ammononitrous acid esters.

Two phenyl derivatives of benzotriazole are known, to which the respective formulas



have been ascribed (44, 82a, 45). As represented by the first formula, 1-phenylbenzotriazole may obviously be regarded as a cyclic phenyl o-phenylene ammononitrite. We venture to give 2-phenylbenzotriazole the formula

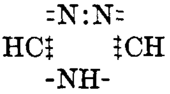


$$\begin{array}{c} \text{-N=} \\ C_6H_4\ddagger \quad \ddagger N{:}C_6H_5 \\ \text{-N=} \end{array}$$

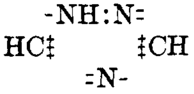
which represents it as nitrobenzene in which the two oxygen atoms are replaced by an o-phenylenediamine residue (41). In harmony with the assumption that o-phenylbenzotriazole is a derivative of nitrobenzene is its ready reduction to o-phenylenediamine and aniline (44). However, it must be said in this connection that attempts to prepare 2-phenylbenzotriazole by the interaction of o-phenylenediamine and nitrobenzene have not been successful.

Metallic salts of benzotriazole are apparently unknown. Zincke and Lawson (109) observed the formation of the sodium, $C_7H_6N_3Na$, silver, $C_7H_6N_3Ag$, mercury, $(C_7H_6N_3)_2Hg$, lead, copper, zinc, and cadmium salts of 6-methylbenzotriazole, though the latter four compounds were not analyzed. According to Hofmann (55) 5-nitrobenzotriazole is an acid of sufficient strength to redden sharply a water solution of litmus.

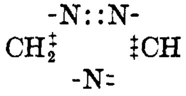
F. 1,2,4-Triazole



$$\begin{array}{c} \text{=N:N=} \\ HC\ddagger \qquad \ddagger CH \\ \text{-NH-} \end{array}$$



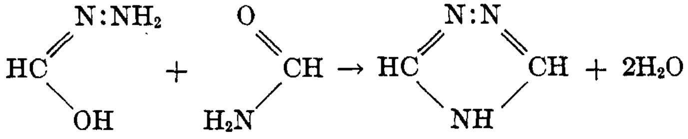
$$\begin{array}{c} \text{-NH:N=} \\ HC\ddagger \qquad \ddagger CH \\ \text{=N-} \end{array}$$



$$\begin{array}{c} \text{-N::N-} \\ CH_2^{\ddagger} \qquad \ddagger CH \\ \text{-N=} \end{array}$$

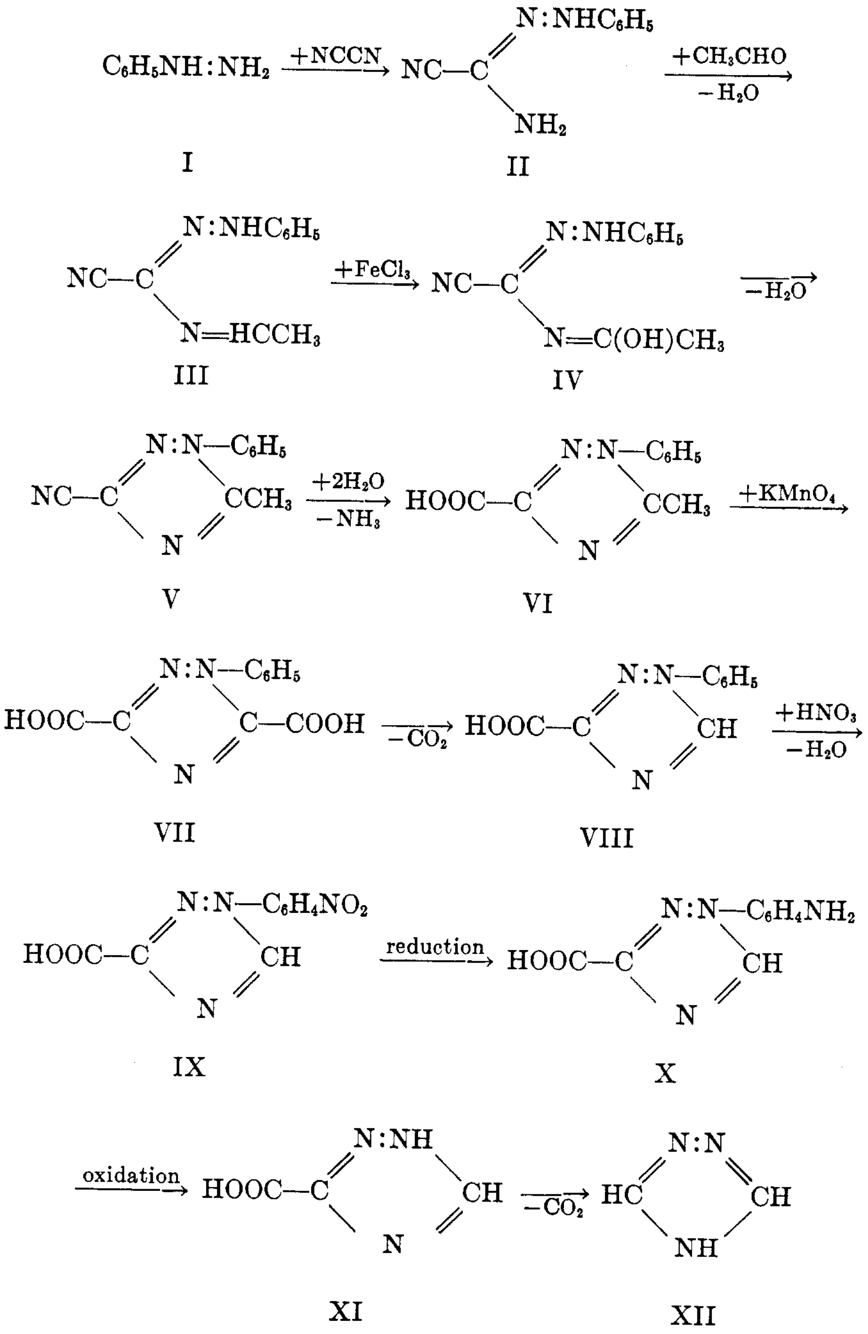
The first two formulas represent assumed tautomeric forms of a cyclic diformic acid hydrazide, the third a cyclic azo compound. The rearrangement of the first and second formulas into the third involves the intramolecular augmentation of hydrazine nitrogen to azo nitrogen and the concomitant reduction of one of the formic acid carbon atoms to formaldehyde carbon.

1. Formation. (a) 1,2,4-Triazole is formed by heating a mixture of formylhydrazine and formamide (73, 74). The equation



represents the action of an aquo-ammonoformic acid on a formic acid hydrazide to form a cyclic diformic acid hydrazide.

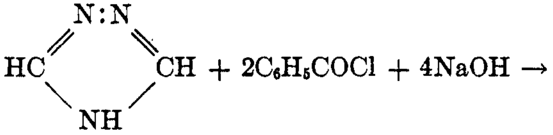
(b) The reactions involved in a second procedure for the preparation of 1,2,4-triazole are summarized by the scheme (11a, 12a, 12b, 12c)


C6H5NH:NH2
+NCCN
NC—C N:NHC6H5 NH2
+CH3CHO
−H2O
I
II
NC—C N:NHC6H5 N=HCCH3
+FeCl3
NC—C N:NHC6H5 N=C(OH)CH3
−H2O
III
IV
NC—C N:N—C6H5 CCH3 N
+2H2O
−NH3
HOOC—C N:N—C6H5 CCH3 N
+KMnO4
V
VI
HOOC—C N:N—C6H5 C—COOH N
−CO2
HOOC—C N:N—C6H5 CH N
+HNO3
−H2O
VII
VIII
HOOC—C N:N—C6H4NO2 CH N
reduction
HOOC—C N:N—C6H4NH2 CH N
IX
X
oxidation
HOOC—C N:NH CH N
−CO2
HC N:N CH NH
XI
XII

Excepting that the compound represented by formula IV has not been isolated, all the reactions represented are known. Since it appears from the above that the hydrazine residue, $=N:N=$, remains intact in the successive compounds indicated, it is reasonable to conclude from this method of preparation that 1,2,4-triazole is a cyclic diformic acid hydrazide.

2. Metallic salts. Using liquid ammonia as solvent Strain (91) prepared metallic salts of 1,2,4-triazole represented by the following formulas: $C_2H_2N_3Na$, $C_2H_2N_3Ag$, $C_2H_2N_3Ag \cdot NH_3$, $(C_2H_2N_3)_2Mg$, $(C_2H_2N_3)_2Mg \cdot 4NH_3$, $(C_2H_2N_3)_2Ca$, $(C_2H_2N_3)_2Ca \cdot xNH_3$, and $C_2H_2N_3Cu$. The cupric salt, $(C_2H_2N_3)_2Cu$, is also known.

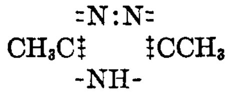
3. Opening the ring. 1,2,4-Triazole is a stable compound which, resisting the action of acids and alkalis, has not been hydrolyzed to formic acid, hydrazine, and ammonia as might be expected on the assumption that it is a formic acid hydrazide. However, when 1,2,4-triazole is heated on a water bath with benzoyl chloride and the reaction mass is treated with sodium hydroxide solution, symmetrical dibenzoylhydrazine is obtained in good yield (54). Moreover the reactions involved may be represented by the equation (cf. pp. 313, 320, 323),



$$C_6H_5CO{-}NH:NH{-}OCC_6H_5 + 2HCOONa + 2NaCl + H_2O + NH_3$$

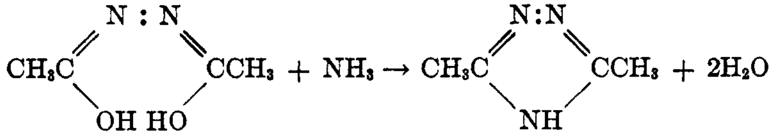
though formic acid and ammonia were not reported among the reaction products.

G. 3,5-Dimethyl-1,2,4-triazole



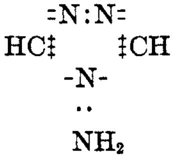
$$\begin{array}{c} {=}N:N{=} \\ CH_3C\ddagger \qquad \ddagger CCH_3 \\ {-}NH{-} \end{array}$$

The view that this compound is a cyclic diacetic acid hydrazide is in agreement with its formation in accordance with the equation

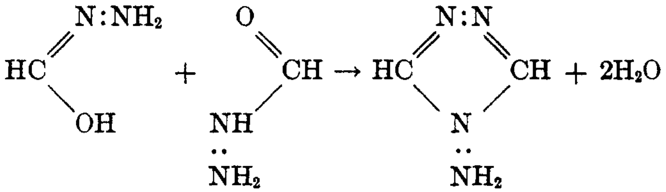


by the ammonolytic action of alcoholic ammonia on diacetylhydrazine at 200°C. (87). A silver salt of this acid hydrazide has been prepared.

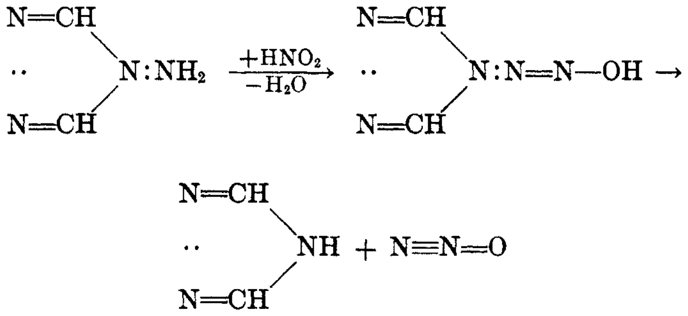
H. 4-Amino-1,2,4-triazole



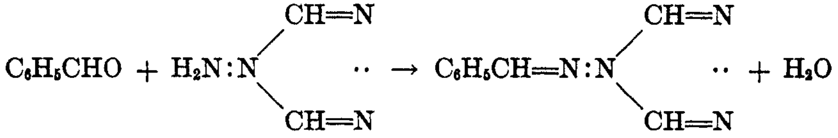
This cyclic formic acid hydrazide has been obtained by heating formylhydrazine at 150°C. (49, 17, 70), the reaction taking place in accordance with the equation



As represented by the above formula, 4-amino-1,2,4-triazole contains two hydrazine residues. The presence of the hydrazine group, which is partly extracyclic, is shown by the conversion of this aminotriazole into 1,2,4-triazole and nitrous oxide by the action of nitrous acid

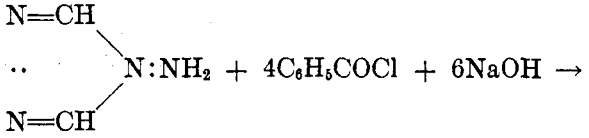


and by its interaction with aldehydes to form hydrazones. Benzaldehyde, for example, acts on 4-amino-1,2,4-triazole as represented by the equation



to form a compound which is at the same time a benzaldehyde hydrazone and a formic acid hydrazide (20, 17).

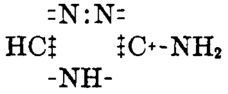
The two hydrazine residues and the two formic acid groups, which we assume to be present in this aminotriazole, are revealed when, under the action of benzoyl chloride and sodium hydroxide (cf. pp. 313, 320, 323, and 342), both hydrazine groups appear as dibenzoylhydrazine and the formic acid residues as sodium formate (49). The reactions involved are represented by the equation



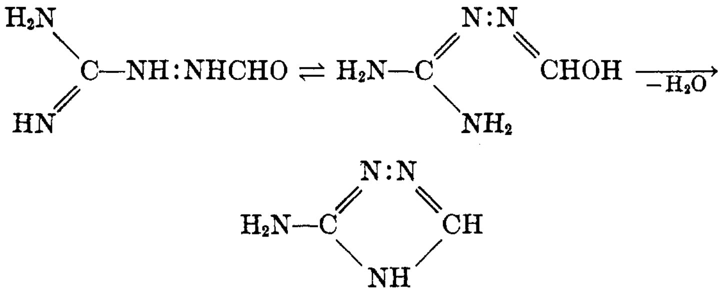
$$N{=}CH,\ N{=}CH \rangle N{:}NH_2 + 4C_6H_5COCl + 6NaOH \rightarrow$$

$$2C_6H_5CONH{:}NH{-}OCC_6H_5 + 2HCOONa + 4NaCl + 2H_2O$$

I. *3-Amino-1,2,4-triazole*



On treating formylaminoguanidine nitrate[12] with aqueous sodium carbonate it is converted into 3-amino-1,2,4-triazole (98, 100). The reactions involved, which are represented by the scheme



consist in the elimination of water from the open chain carbonic acid formic acid hydrazide thereby converting it into the cyclic hydrazide. Thiele and Manchot (100) had the silver salt of this compound in their hands, but did not analyze it.

Apparently the triazole ring in this cyclic acid hydrazide has not been opened. It happens however that 3-amino-5-methyl-1,2,4-triazole (first

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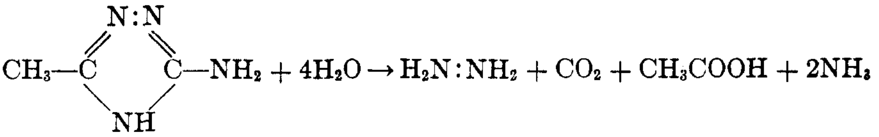
[12] Formylaminoguanidine, first and second formulas below, is a mixed carbonic acid formic acid hydrazide and not in any proper sense an amino compound.

formula below) has been hydrolyzed quantitatively in accordance with the equation,

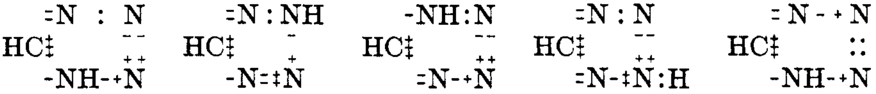


when heated with dilute sulfuric acid at 180°C. (98, 100). This equation may be read as representing the hydrolysis of a cyclic carbonic acid acetic acid hydrazide to hydrazine, carbonic anhydride, aquoacetic acid, and ammonia.

V. COMPOUNDS CONTAINING FOUR NITROGEN ATOMS IN THE RING

The one known pentacyclic ring containing four nitrogen atoms is present in tetrazole and its many derivatives.

A. Tetrazole[13]



$$\begin{array}{lllll}
\text{=N : N} & \text{=N : NH} & \text{-NH:N} & \text{=N : N} & \text{= N - + N} \\
\text{HC}\ddagger \quad \overset{--}{\underset{++}{}} & \text{HC}\ddagger \quad \overset{-}{\underset{+}{}} & \text{HC}\ddagger \quad \overset{--}{\underset{++}{}} & \text{HC}\ddagger \quad \overset{--}{\underset{++}{}} & \text{HC}\ddagger \quad :: \\
\text{-NH-+N} & \text{-N=}\ddagger\text{N} & \text{=N-+N} & \text{=N-}\ddagger\text{N:H} & \text{-NH-+N}
\end{array}$$

The first four formulas represent hypothetical tautomeric forms of a mixed formic acid nitrous acid hydrazide, the fourth being related to the first as the formula $H:N(NH)_2$, for an hypothetical ammononitrous acid, is related to the formula $H_2N\text{-+}N\ddagger\text{=}NH$. It is reasonable to say that these formulas represent tautomeric forms or resonance phases of tetrazole. Certainly no one of them has been established to the exclusion of the others. A fifth possible formula representing tetrazole as a cyclic ammonoformic acid ammonohyponitrous acid is the last one given above.

While the writing of formulas in which one of the nitrogen atoms is represented as ammonia nitrogen, the second as nitrous acid nitrogen, and the remaining two as existing in the state in which nitrogen is present in hydrazine may perhaps appear somewhat naive, we shall nevertheless find that such formulas will be helpful in the following discussion of tetrazole and its derivatives. On the one hand we shall find that the methods of preparing these compounds are in agreement with such formulas. On the other hand, however, it happens that but one of them, namely 5-aminotetrazole, has been observed to enter into reactions which lend substantial support to our assumptions concerning the nature of the tetrazole ring.

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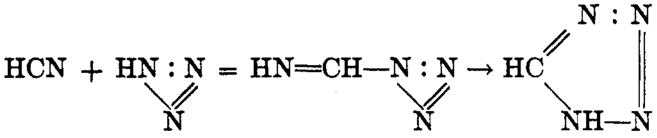
[13] Cf. footnote 7 concerning the use of the colon and double colon in these formulas.

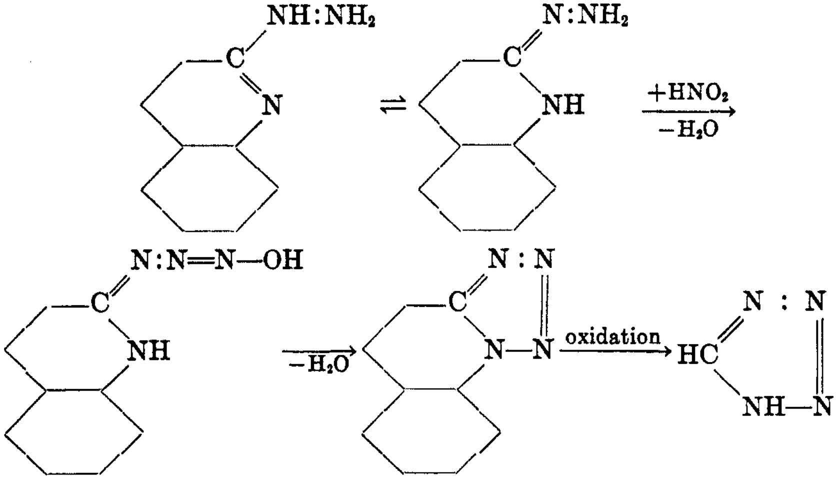
1. *Preparation.* (a) Tetrazole is obtained in excellent yield by heating hydrazoic acid in alcohol solution with hydrocyanic acid at 100°C. for a period of two or three days (27). Assuming hydrazoic acid and hydrocyanic acid to act respectively as a nitrous acid hydrazide and a formic anammonide, it is reasonable to say that as represented by the equation



$$\mathrm{HCN} + \underset{\mathrm{N}}{\mathrm{HN:N}} = \mathrm{HN{=}CH{-}}\underset{\mathrm{N}}{\mathrm{N:N}} \rightarrow \mathrm{HC}\begin{array}{l}\mathrm{N:N}\\ \mathrm{NH{-}N}\end{array}$$

an unknown mixed formic acid nitrous acid hydrazide is first formed which, undergoing rearrangement, in principle intramolecular ammonation, passes over into tetrazole.[14]

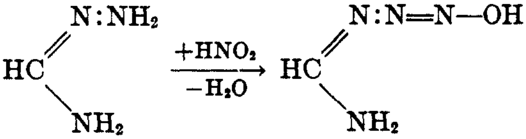
(b) An interesting method for the preparation of tetrazole which involves the action of nitrous acid on a hydrazine derivative, and which furthermore shows the remarkable resistance of the tetrazole ring to the action of oxidizing agents, is due to Marckwald and Meyer (68). By the action of nitrous acid on α-quinolylhydrazine (first and second formulas below), naphtetrazole, which is represented by the fourth formula, is formed quantitatively. This compound, when treated in a hot dilute acetic acid solution with potassium permanganate, is quantitatively oxidized to tetrazole. The reactions involved may be represented by the scheme



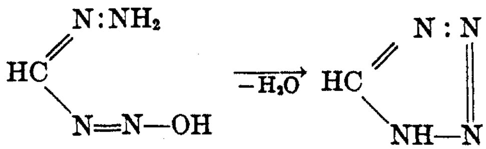
[14] Alternately it may be that hydrocyanic acid, acting as an ammonocarbonous acid, unites with hydrazoic acid to form a carbonous acid azide which arranges to the formic acid azide formulated above.

Since it appears impossible to formulate tetrazole as a derivative of an ammono-in which the third formula represents an unknown open chain quinolyl nitrous acid hydrazide.

(c) Looking upon tetrazole as a cyclic formic acid nitrous acid hydrazide, it would be reasonable to expect its formation by the interaction of a formic acid hydrazide and nitrous acid, say, as represented by the scheme



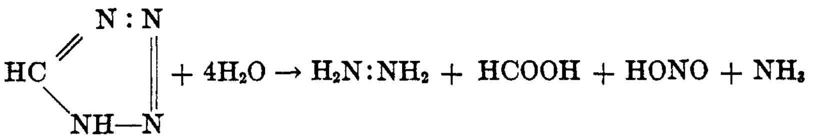
or



While such a reaction is unknown, it does happen that 5-phenyltetrazole has been prepared by the action of nitrous acid on a benzoic acid hydrazide (p. 353), and that 1-phenyltetrazole is formed by the interaction of diformylhydrazine and diazobenzene, which latter compound is a derivative of nitrous acid (p. 354).

2. Properties. Tetrazole resists to a remarkable degree the action of acids and alkalis, oxidizing and reducing agents. It is a moderately strong acid, as might be expected of a compound containing an imide group held in common by two acid residues. Its water solution reddens litmus sharply. In solution in water and in liquid ammonia (91) it is a good conductor of electricity. Water solutions of the sodium salt are neutral.

3. Opening the ring. (a) Under the action of aqueous hydrochloric acid at 200°C. tetrazole is slowly decomposed to form carbon dioxide, ammonia, and nitrogen (99) instead of undergoing hydrolysis in accordance with the equation



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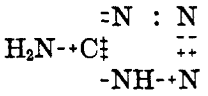
nitric acid, $HN{=}N{\equiv}N$, it is important to observe that this method of preparing tetrazole as well as other reactions discussed later, lend substantial support to the view developed elsewhere (41) to the effect that hydrazoic acid is a compound which is capable of acting either as an ammononitric acid or as a nitrous acid hydrazide.

as it might be expected to do on the assumption that it is a formic acid nitrous acid hydrazide. Nitrous acid would of course appear in the form of its anammonide, that is to say, as free nitrogen, as the result of the interaction of nitrous acid and ammonia, while observations made in this laboratory have shown that carbon dioxide and ammonia are formed when sodium formate and hydrazine sulfate are heated together either in the dry state or in solution in water. It follows therefore that the failure of tetrazole to hydrolyze in accordance with the above equation finds a reasonable explanation on the assumption that the formic acid and hydrazine formed interact at the elevated temperature to yield carbon dioxide and ammonia.

4. Metallic salts. Salts of sodium, $CHN_4Na \cdot H_2O$, barium, $(CHN_4)_2Ba \cdot 3.5H_2O$, and silver, CHN_4Ag, have long been known (89). Strain (91) obtained the ammonium salt, CHN_4NH_4, by the action of ammonia on tetrazole, and the calcium salt, $(CHN_4)_2Ca$, by the action of tetrazole in liquid ammonia solution on metallic calcium and on calcium amide.

B. 5-Aminotetrazole

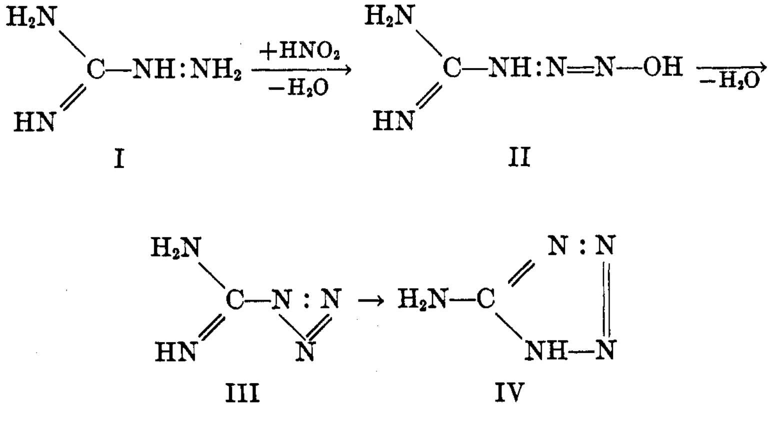


$$\begin{array}{lll} & {}^{=}N & : N \\ H_2N\text{-}^{+}C\ddagger & & \overset{--}{\underset{++}{\ }} \\ & \text{-}NH\text{-}^{+}N & \end{array}$$

This formula represents 5-aminotetrazole as a cyclic carbonic acid nitrous acid hydrazide.

1. Formation. Two methods whereby this compound has been made are in harmony with this view concerning its constitution.

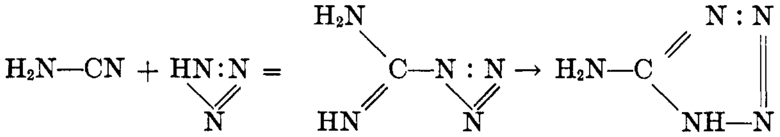
(a) By the action of nitrous acid on guanylhydrazine guanylazide is formed which latter compound in turn readily rearranges to 5-aminotetrazole (97). As represented herewith



(1)

one may say that nitrous acid acts on the carbonic acid hydrazide (I) to form the open chain carbonic acid nitrous acid hydrazide (II), that this compound, known in the form of its nitrate, loses water to form guanylazide (III) which, by intramolecular ammonation of the azide group, isomerizes to 5-aminotetrazole (IV). The compounds II, III, and IV thus appear as carbonic acid nitrous acid hydrazides.

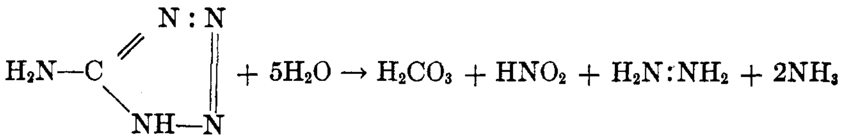
(b) The preparation of 5-aminotetrazole is also readily accomplished by the interaction of hydrazoic acid and cyanamide in water solution (50). Assuming that hydrazoic acid acts as a nitrous acid hydrazide the reactions involved may be represented by the equation



(2)

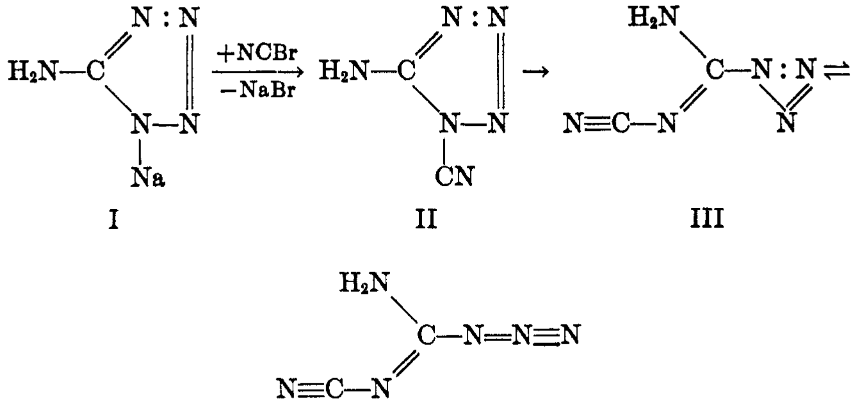
Cyanamide and hydrazoic acid unite to form guanylazide, which, as noted above, readily rearranges to 5-aminotetrazole. The reader will have observed that, as represented by equation 1 above, 5-aminotetrazole is formed by the action of nitrous acid on a carbonic acid hydrazide, while in accordance with equation 2 it results from the interaction of a nitrous acid hydrazide and an ammonocarbonic acid.

2. Opening the tetrazole ring. Regarding 5-aminotetrazole as a mixed hydrazide of carbonic acid and nitrous acid it might be expected that its complete hydrolysis would result in the formation of aquocarbonic acid, nitrous acid, hydrazine, and ammonia in accordance, let us say, with the equation



As a matter of fact, when heated with concentrated hydrochloric acid at temperatures around 200°C., 5-aminotetrazole gives quantitative yields of carbon dioxide, hydrazine, ammonia, and nitrogen (99). The absence of nitrous acid and the appearance of nitrogen among the hydrolytic products is explained when it is recalled that ammonium nitrite readily decomposes to form nitrogen and water. 5-Aminotetrazole hydrolyzes as if it were a carbonic acid nitrous acid hydrazide.

A second method for opening the tetrazole ring is due to Hart (52), who has shown that dicyanamidazide (III) is formed in accordance with the following equation

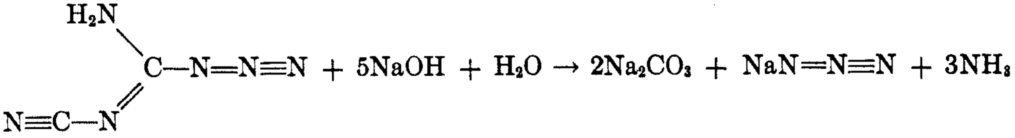


I II III

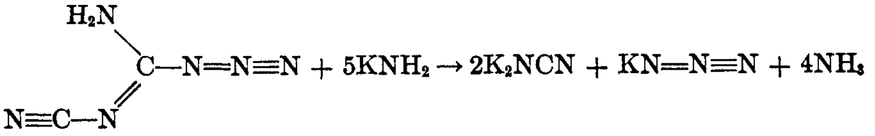
III′

when the sodium salt of 5-aminotetrazole (I) is treated with cyanogen bromide, which is a carbonic acid bromide. The 1-cyano-5-aminotetrazole (II) which one might expect to obtain is for some reason unstable. The ring opens up to form the dicarbonic acid azide represented by the formula III.

Hart observed furthermore (51) that dicyanamidazide is hydrolyzed by the action of warm sodium hydroxide solution to form sodium aquocarbonate, sodium azide, and ammonia,



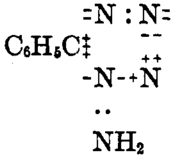
and that it is ammonolyzed to dipotassium cyanamide (an ammonocarbonate), potassium azide (an ammononitrate), and ammonia when warmed with potassium amide in liquid ammonia solution



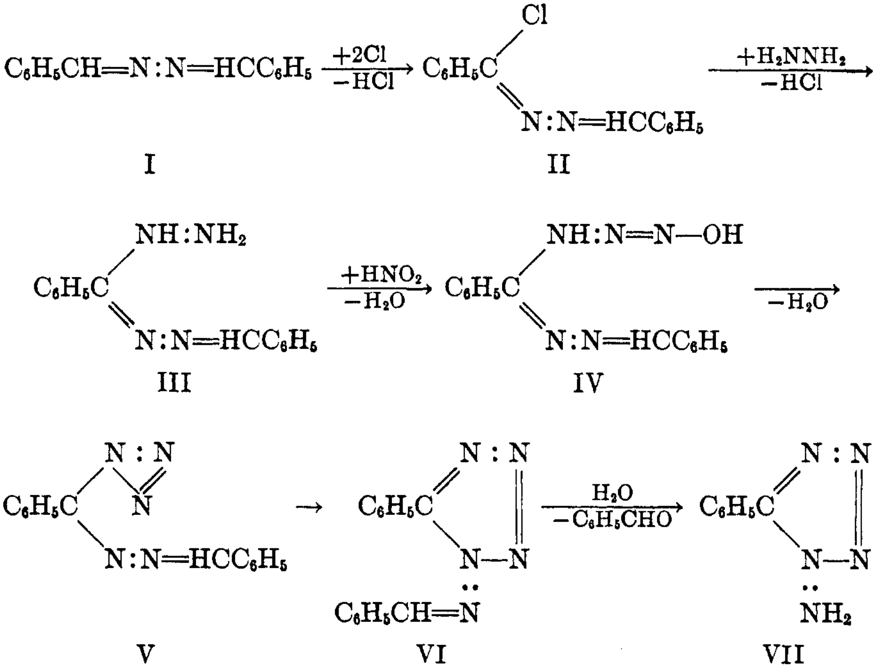
3. Metallic salts. Although weaker than tetrazole, 5-aminotetrazole is distinctly an acid of which the salts of silver, CH_2N_5Ag, sodium, $CH_2N_5Na \cdot 3H_2O$, and barium, $(CH_2N_5)_2Ba \cdot xH_2O$, have been prepared

(91). Thiele observed the formation of aluminum, zinc, manganese, cadmium, mercury, cobalt, nickel, iron, and copper salts but did not analyze them.

C. 1-Amino-5-Phenyltetrazole



1-Aminotetrazole, a possible isomer of 5-aminotetrazole, would be a cyclic formic acid nitrous acid hydrazide containing two hydrazine residues. While such a compound is not known its benzoic acid analog, namely 1-amino-5-phenyltetrazole, has been prepared (90). The reactions involved in the formation of this compound, which are in harmony with our assumption that it is a cyclic benzoic acid nitrous acid hydrazide, may be summarized by means of the scheme

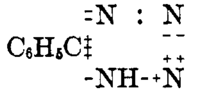


By the action of chlorine on dibenzalhydrazine (I) one of the benzaldehyde groups is augmented to a benzoic acid group, thereby forming II.

This acid chloride reacts with hydrazine to form III (named benzal-benzenyl-hydrazon-hydrazid by Stollé and Hellwerth (90)), which is at the same time a benzoic acid dihydrazide and a benzaldehyde hydrazone. On treating III with nitrous acid the compound IV, containing a nitrous acid group, a benzoic acid group, two hydrazine residues, and a benzaldehyde group is presumably formed. This unknown compound loses water to yield V (benzal-benzhydrazid-azid). Gently heated in alcoholic solution V rearranges to VI, which in turn, under the action of hot aqueous hydrochloric acid, is hydrolyzed to 1-amino-5-phenyltetrazole (VII) and benzaldehyde. It is noted that two molecules of hydrazine and one of nitrous acid enter into the reactions represented above. It is reasonable to say that they persist in the final product. The ready conversion of 1-amino-5-phenyltetrazole into 5-phenyltetrazole by the action of nitrous acid is in agreement with the assumption that the extracyclic NH_2 group is a part of a hydrazine residue. The tetrazole ring in this compound has apparently not been opened.

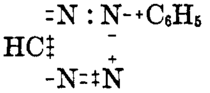
D. Phenyltetrazoles

As will be shown in the following discussion, the methods of preparation of the three known phenyltetrazoles lead logically to the formulas



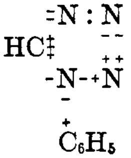
$$\begin{array}{ll} & {=}N : N \\ C_6H_5C\ddagger & \qquad \begin{smallmatrix}-\,-\\+\,+\end{smallmatrix} \\ & {-}NH{-}{+}N \end{array}$$

I



$$\begin{array}{ll} & {=}N : N{-}{+}C_6H_5 \\ HC\ddagger & \qquad \begin{smallmatrix}-\\+\end{smallmatrix} \\ & {-}N{=}\ddagger N \end{array}$$

II

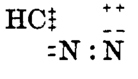


$$\begin{array}{ll} & {=}N : N \\ HC\ddagger & \qquad \begin{smallmatrix}-\,-\\+\,+\end{smallmatrix} \\ & {-}N{-}{+}N \\ & \quad \begin{smallmatrix}-\\+\end{smallmatrix} \\ & \quad C_6H_5 \end{array}$$

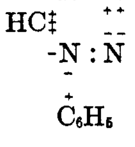
III

which may be read as representing respectively a benzoic acid nitrous acid hydrazide, a formic acid nitrous acid phenylhydrazide, and a compound which is at the same time a formic acid hydrazide, a nitrous acid hydrazide, and a phenyl ester of a mixed formic nitrous acid. However, beyond the methods whereby they have been synthesized, little or nothing is known which supports the view that the tetrazole ring in these compounds has the constitution represented by the above formulas.

Written as containing formic acid, nitrous acid, and hydrazine residues are two further purely speculative formulas



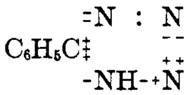
$$\begin{array}{ll} & {-}N{=}\ddagger N{:}C_6H_5 \\ HC\ddagger & \qquad \begin{smallmatrix}+\,+\\-\,-\end{smallmatrix} \\ & {=}N : N \end{array}$$



$$\begin{array}{ll} & {=}N{-}{+}N \\ HC\ddagger & \qquad \begin{smallmatrix}+\,+\\-\,-\end{smallmatrix} \\ & {-}N : N \\ & \quad \begin{smallmatrix}-\\+\end{smallmatrix} \\ & \quad C_6H_5 \end{array}$$

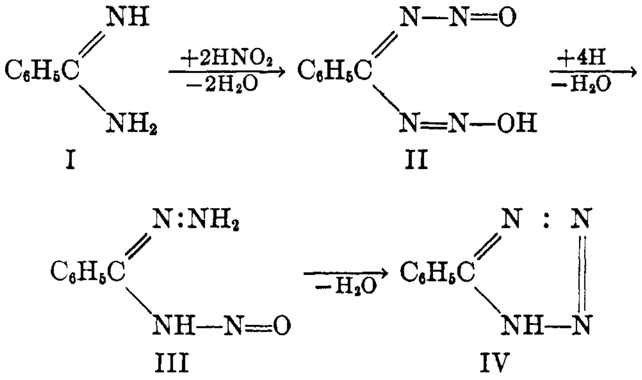
which, while possibly representing compounds not yet prepared, probably rather represent resonance phases, the one of compound II above, the other of III.

E. 5-Phenyltetrazole



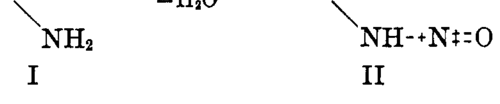
1. Formation. The formation of 5-phenyltetrazole from 1-amino-5-phenyltetrazole has already been noted (p. 352). Two further methods for obtaining this compound are here interpreted as showing that it may be regarded as a benzoic acid nitrous acid hydrazide.

(a) By treating benzamidine with nitrous acid and reducing the resulting diazo compound 5-phenyltetrazole has been obtained (64). The reactions involved may be represented by the scheme

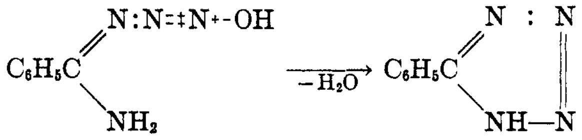


in accordance with which an ammonobenzoic acid (I) is diazotized to the compound II, which was isolated in the form of metallic salts and named benzenyldioxytetrazotic acid. On submitting this compound to the action of sodium amalgam the one or the other of the aquo-ammononitrous acid groups is reduced to a hydrazine group, as shown in the hypothetical formula III which, losing water as the result of the interaction of nitrous acid and hydrazine residues, yields 5-phenyltetrazole (IV).

(b) 5-Phenyltetrazole is formed quantitatively as represented by the scheme



or

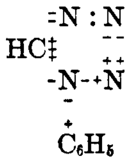

III IV

when the benzoic acid hydrazide (I), known in the form of its salts, is treated with nitrous acid (75). By way of II or III, compound I reacts with nitrous acid to form the cyclic benzoic acid nitrous acid hydrazide (IV) which is 5-phenyltetrazole. Whether nitrous acid first converts the amido group in I into a diazo group in II or the hydrazine residue in I into a nitrous acid hydrazide group in III is a matter of no concern in so far as the present argument is concerned. Neither of the compounds represented by formulas II and III is known.

When heated at 200°C. with concentrated hydrochloric acid 5-phenyltetrazole yields nitrogen, carbon dioxide, ammonia, and aniline; these results may be compared with those obtained by the action of hot aqueous hydrochloric acid on tetrazole and on 5-aminotetrazole. The benzoic acid hydrazide part of the molecule obviously undergoes the Lossen rearrangement.

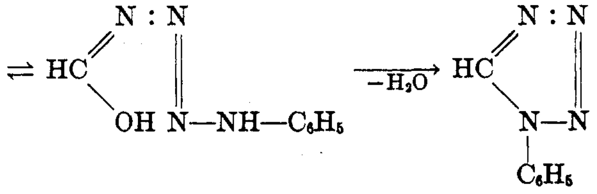
5-Phenyltetrazole is an acid of such strength as sharply to redden litmus. Clemens Lossen (65) prepared an ethyl ester, $C_7H_5N_4C_2H_5$, and the potassium, $C_7H_5N_4K$, barium, $(C_7H_5N_4)_2\ Ba \cdot 2H_2O$, and silver, $C_7H_5N_4Ag$, salts. The formation of a considerable number of other metallic salts was observed. They were, however, not analyzed.

F. 1-Phenyltetrazole



This phenyltetrazole has been obtained by the interaction of diformylhydrazine and diazobenzene in alkaline solution (28). Representing the reactions involved by the scheme

$$\underset{\text{I}}{\text{OHC—NH:NH—CHO}} \xrightarrow[-\text{HCOOH}]{+C_6H_5N{=}NOH} \underset{\text{II}}{\text{OHC—NH:NH—N}{=}\text{N—}C_6H_5}$$

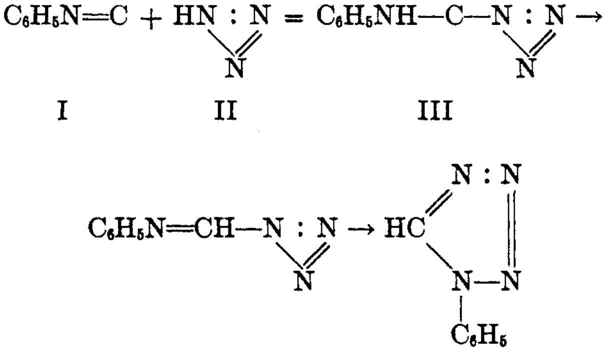


II′ III

it may be said that an open chain formic acid nitrous acid hydrazide (II, II′), which was isolated but not analyzed, is first formed. When this compound is boiled with aqueous hydrochloric acid it loses water, thereby passing over into the cyclic hydrazide (III), namely, into 1-phenyltetrazole.

Very interesting, in that thereby the tetrazole ring shows its remarkable stability toward hydrolyzing, oxidizing, and reducing agents, is the conversion of 1-phenyltetrazole first, into a nitrophenyltetrazole under the action of fuming nitric acid, second, the reduction of this nitrophenyltetrazole to aminophenyltetrazole, and finally the oxidation of this compound to tetrazole (42).

A second method for the preparation of 1-phenyltetrazole is found in the action of hydrazoic acid on phenylisocyanide (70). Assuming the reactions involved to take place as follows



I II III

IV V

it appears first, that phenyl ammonocarbonite (I) unites with hydrazoic acid (II) to form an unknown carbonous acid ester-azide (III); second, that this compound, after the manner of the transformation of the one tautomer of hydrocyanic acid into the other, rearranges to the formic acid ester-azide[15] (IV); and third, that IV, with the azide group acting as a

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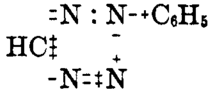
[15] The assumption that compound III is primarily formed is of course highly speculative.

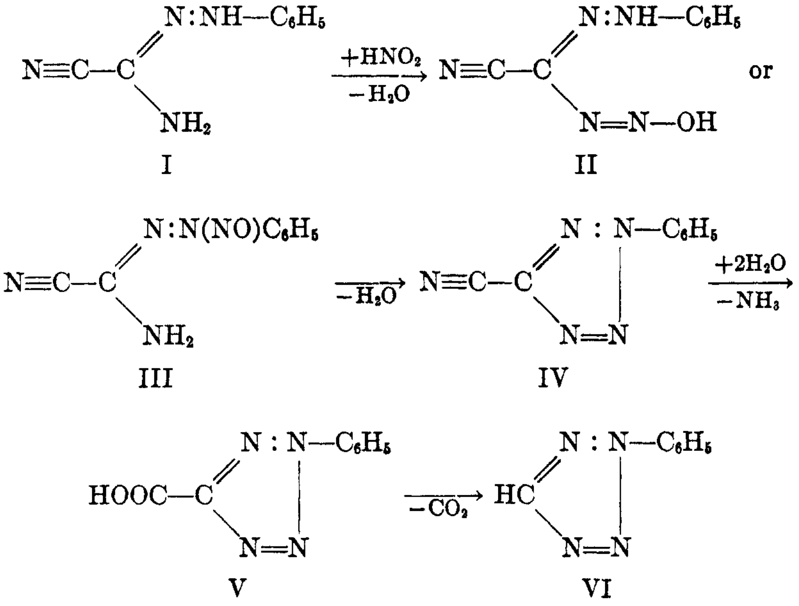
nitrous acid hydrazide group, passes over into 1-phenyltetrazole (V). Being a neutral ester this compound is incapable of forming metallic salts.

G. 2-Phenyltetrazole



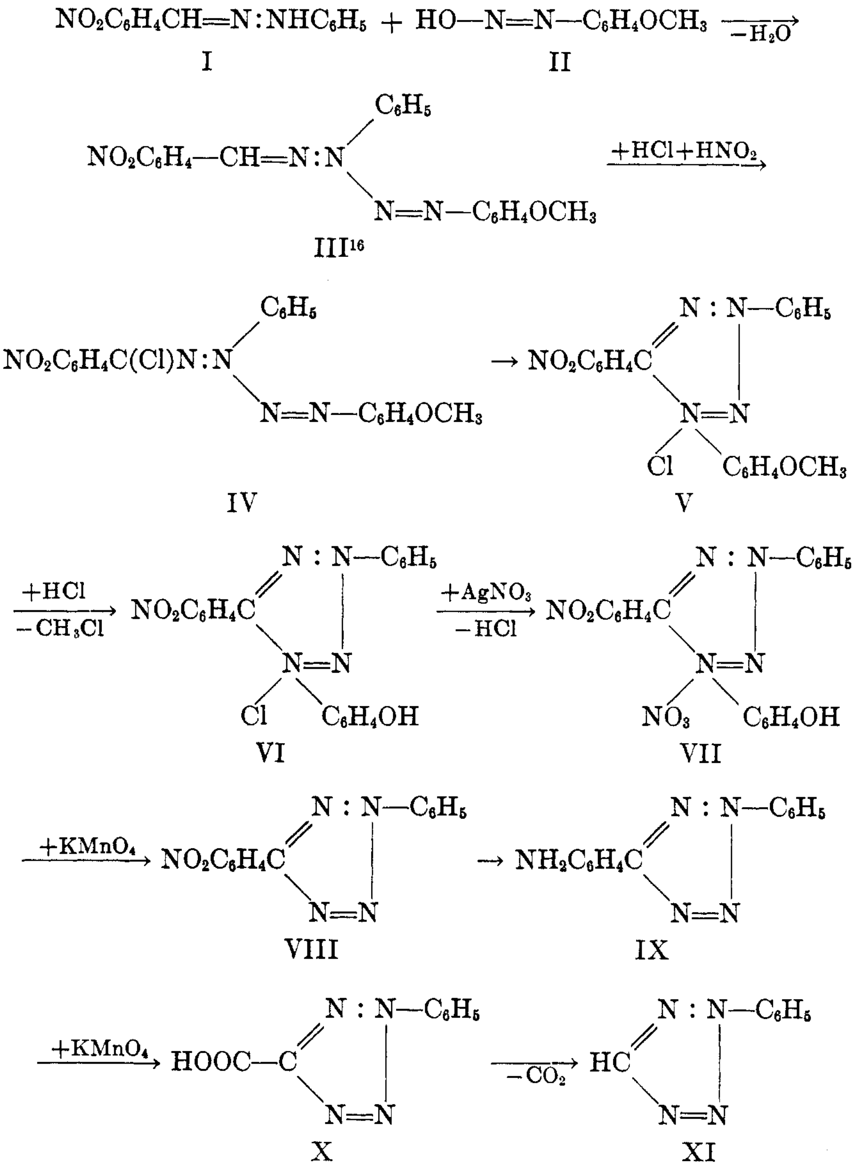
$$\begin{array}{l} \quad =N : N\text{-}{+}C_6H_5 \\ HC\ddagger \qquad \overset{-}{\underset{+}{}} \\ \quad -N=\ddagger\dot{N} \end{array}$$

Bladin (12) prepared this compound by means of the successive reactions summarized as follows: Cyanogen, which is the anammonide of oxalic acid, reacts with phenylhydrazine to form a compound (I below), which, in so far as the carbon to phenylhydrazine union is concerned, is a phenyl hydrazide of oxalic acid. By virtue of the presence of the amido group it is at the same time an ammonoöxalic acid. The other carbon atom of the cyanogen remains associated with nitrogen as an oxalic anammonide group. This compound (I) reacts with nitrous acid in accordance with the scheme



to form 2-phenyl-5-cyantetrazole (IV) which, by saponification of the nitrile group to a carboxyl group followed by the elimination of carbon dioxide, is converted into 2-phenyltetrazole (VI). Formulas II and III represent hypothetical compounds. As thus prepared 2-phenyltetrazole appears as a phenylhydrazide of a mixed formic nitrous acid which, containing no acid hydrogen, does not form metallic salts.

Wedekind (101) obtained 2-phenyltetrazole by following the somewhat elaborate sequence of reactions summarized by the scheme



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[16] Wedekind used the formula, $NO_2C_6H_4C(N-NH-C_6H_5)N=N-C_6H_4OCH_3$, to represent this so-called formazyl compound. We venture to give it formula III, which represents it as a derivative of an ammononitrous acid hydrazide, $H_2N:NH-N=NH$.

p-Nitrobenzaldehyde phenylhydrazone (I), which is formed by the interaction of *p*-nitrobenzaldehyde and phenylhydrazine, reacts with diazotized *p*-anisidine (II) to form III, which is at the same time a nitrobenzaldehyde hydrazone and a methoxyphenyl nitrous acid hydrazide. This compound, when acted upon by hydrochloric acid and nitrous acid in alcoholic solution, is augmented to the unknown acid chloride (IV), which rearranges to the quaternary salt (V). When heated with fuming hydrochloric acid V yields VI which, under the action of silver nitrate, is converted into the quaternary nitrate (VII). Treated with warm potassium permanganate solution this salt yields 2-phenyl-5-nitrophenyltetrazole (VIII). Reducing agents convert this nitro compound into the amino compound (IX), which under the action of potassium permanganate is augmented to the phenyltetrazolecarboxylic acid (X). Simply upon heating this acid loses carbon dioxide to yield 2-phenyltetrazole (XI). The sequence of reactions may be reasonably interpreted as resulting in the formation of a cyclic formic acid nitrous acid phenylhydrazide.

VI. CONCLUSION

Finally it may be said that the writers by no means claim that all the heterocyclic compounds containing nitrogen in the ring can certainly be formulated in accordance with the hypotheses upon which the many formulas given in this paper are based. Certainly the large majority of the formulas are reasonable enough; others are obviously highly speculative. Even with their shortcomings we deem it worth while to bring our speculations concerning the nature of the heterocyclic nitrogen compounds to the attention of fellow chemists.

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