STUDIES ON THE FORMATION OF 4-AMINOTRIAZOLE DERIVATIVES FROM ACYL HYDRAZINES

Thesis for the Degree of M. S.

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James Arthur Garrison

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By

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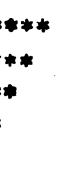
The author would like to express his gratitude to Dr. Robert M. Herbst, under whose direction this research was carried out and without whose inspiration and helpful suggestions this thesis would not have been possible.



STUDIES ON THE FORMATION OF 4-AMINOTRIAZOLE DERIVATIVES FROM ACYL HYDRAZINES

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In the course of study of high nitrogen compounds it was of interest to prepare a series of 3,5-dialkyl-4-amino-1,2,4-triazoles. A search of the literature disclosed the facts that no one person had prepared a continuous series of these compounds and that no single method had been applied to their synthesis. It was, therefore, desirable to find a shorter and a simpler method of preparation. This thesis and the experiments discussed herein are the results of investigations toward this goal.

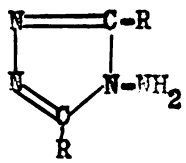
A convenient method of preparation of 3,5-dialkyl-4-amino-1,2,4-triazoles has been found. When the alkyl groups are below three carbon atoms, it is possible to prepare the triazoles from the free fatty acid and hydrazine hydrate solution in an ordinary distillation apparatus. Higher molecular weight aminotriazoles can be prepared by heating the diacyl hydrazine and hydrazine hydrate in a sealed tube. In Table I are compared the yields of 3,5-dialkyl-4-amino-1,2,4-triazoles obtained by the distillation method and the interaction of the diacyl hydrazines and aqueous hydrazine hydrate in sealed tubes.

A mechanism for the formation of aminotriazoles has been proposed. The mechanism involves (1) formation of a hydrazinium salt, (2) the dehydration of the hydrazinium salt to form the monoacyl hydrazine, (3) decomposition of the monoacyl hydrazine to form a diacyl hydrazine

and liberate hydrazine, (4) rearrangement of the diacyl hydrazine to the "lactim" form and reaction of the lactim form and hydrazine in one or more of three ways; direct formation of the aminotriazole; formation of a dihydrotetrazine which rearranges to the aminotriazole; or formation of an acyl hydrazidine followed by formation of the aminotriazole or of a dihydrotetrazine which subsequently rearranges to the aminotriazole.

TABLE I

FORMATION OF 3,5-DIALKYL-4-AMINO-1,2,4-TRIAZOLES



R	% Yield	
	Distillation Technique	Sealed Tube Technique
H	89	--
CH_3	75	--
C_2H_5	68	64
C_3H_7(n)	48	59
C_3H_7(iso)	0	62
C_6H_5	10	58

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INTRODUCTION

INTRODUCTION

In the course of study of high nitrogen compounds it was of interest to prepare a series of 3,5-dialkyl-4-amino-1,2,4-triazoles. A search of the literature disclosed the facts that no one person had prepared a continuous series of these compounds and that no single method had been applied to their synthesis. The most general reaction was the condensation of two molecules of a monoacyl hydrazine to give the amino triazoles and water (Reaction 1). This reaction was used by Pellizzari (6), Stollé (9) (10), and Silberrad (13). However, this

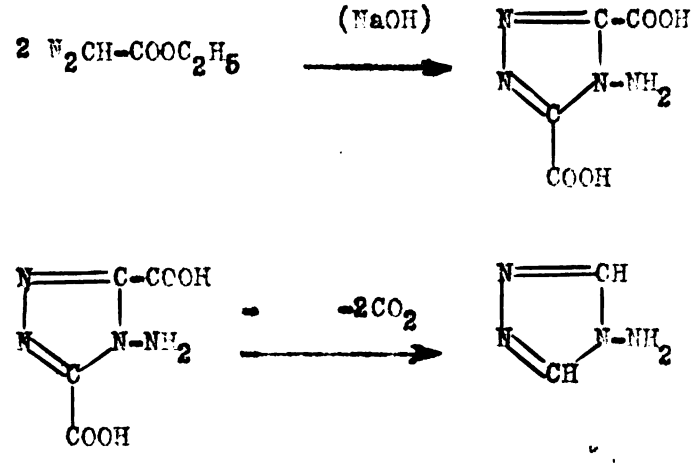
Reaction 1.

method was undesirable because the preparation of the monoacyl hydrazines involved long periods of refluxing. It was, therefore, desirable to find a shorter and a simpler method of preparation. This thesis and the experiments discussed herein are the results of investigations toward this goal.

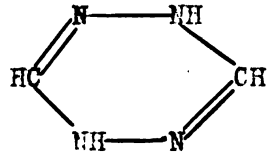
HISTORICAL

HISTORICAL

The first 4-amino-1,2,4-triazole derivative was described by Curtius and Lang (1) in 1888. It was prepared from ethyl diazoacetate in aqueous alkali.

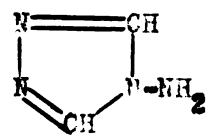


Curtius, however, through faulty molecular weight determinations, assigned the empirical formula $C_3H_6N_6$ to the compound. Several years later Hantzsch and Silberrad (2) found that the salts of this compound contained 1.5 moles of acid for each mole of base. This cast some doubt on the molecular weights as determined by Curtius. Upon redetermination of the molecular weight, Hantzsch found the correct formula to be $C_2H_4N_4$, to which he assigned the name N-dihydrotetrazine (Structure I).



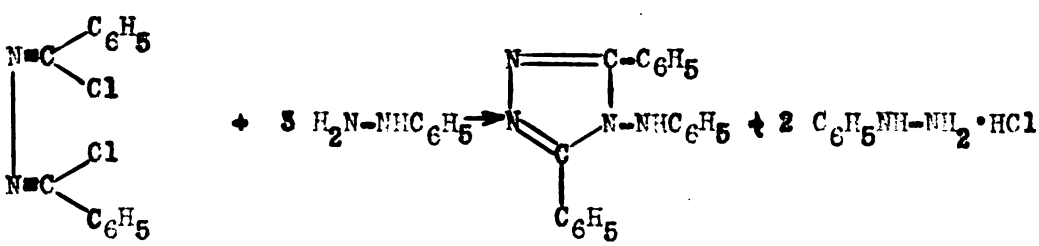
(I)

Pinner (3) considered the possibility that compounds of this type could be amino triazoles, but he did not attempt to prove their structure. In 1906, Bülow (4) proposed the 4-amino-1,2,4-triazole structure (Structure II) on the basis of the reactions with γ-diketones and aromatic aldehydes.

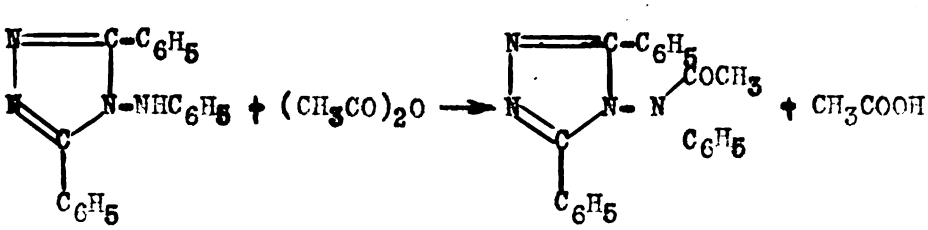


(II)

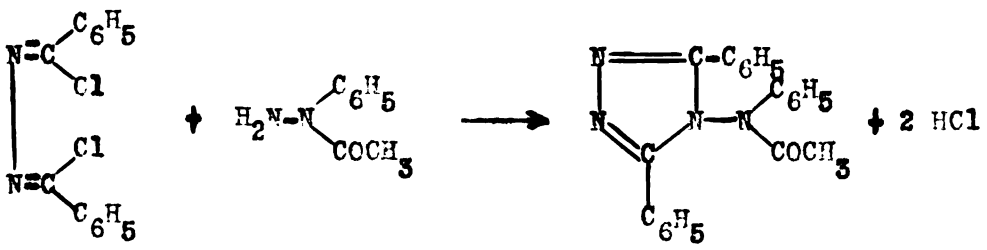
The controversy concerning the correct structure for these compounds was settled in 1907, when Stollé, who had been originally a vigorous supporter of the dihydrotetrazine structure (5), proved quite conclusively that the amino triazole structure was correct (6). The foundation of his proof rested on the following series of reactions:



Reaction 2a



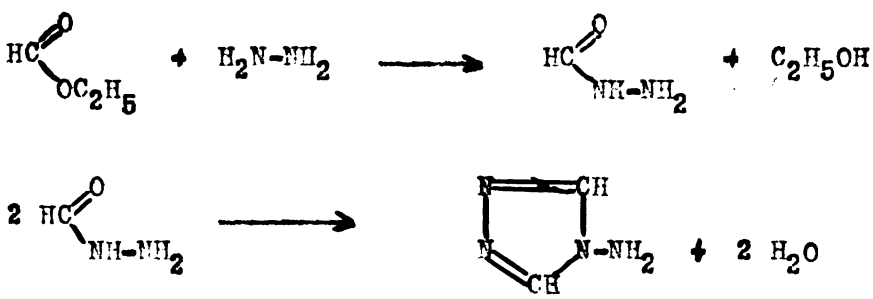
Reaction 2b



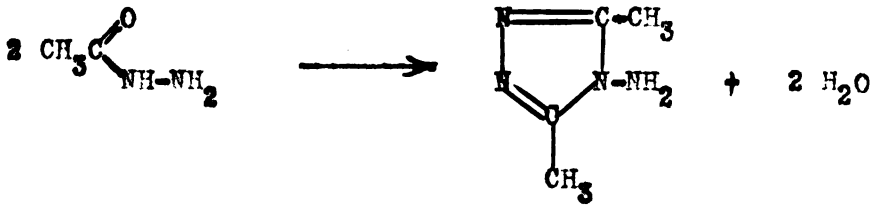
Reaction 3

The products of reaction 2b and reaction 3 were identical. If a structure analogous to structure I were correct, reaction 3 would not have taken place because there is no available hydrogen on the nitrogen carrying the phenyl group. Therefore, the 4-amino-1,2,4-triazole structure (II) was correct.

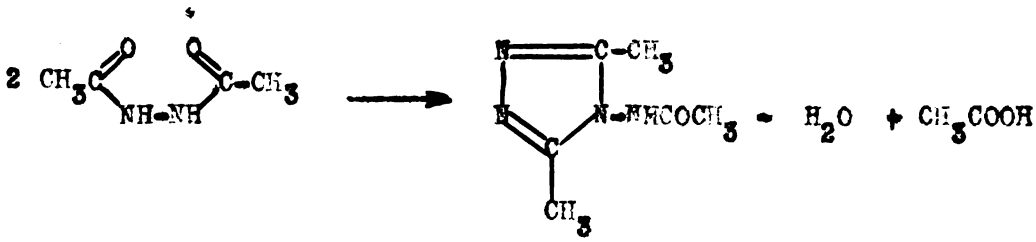
The synthesis of 4-amino-1,2,4-triazole, the first member of the series of 3,5-dialkyl-4-amino-1,2,4-triazoles discussed in this thesis, has been described in Organic Syntheses (7). The method described involves, first, the preparation of monoformyl hydrazine by refluxing ethyl formate and hydrazine hydrate on a steam bath for 18 hours. The monoacyl hydrazine was isolated and then heated to 180° C. for three hours. The yield of the amino triazole was about 80 percent.

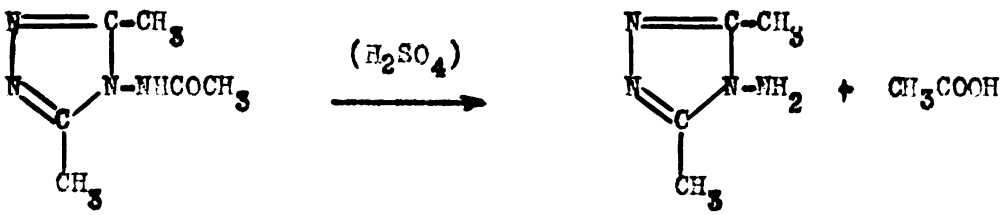


The 3,5-dimethyl-4-amino-1,2,4-triazole has been prepared by a variety of methods. It was first obtained by Pellizzari (8) by heating monoacetyl hydrazine for 7-8 hours at 180° C. Another method

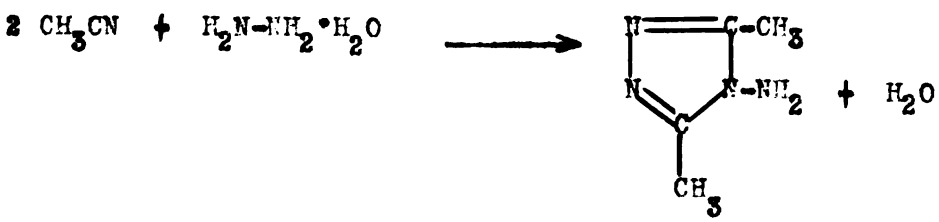


described in the same paper involved heating diacetyl hydrazine at 180-190° C. to form 4-acetylamino-3,5-dimethyl-1,2,4-triazole. The amide was hydrolyzed with sulfuric acid.

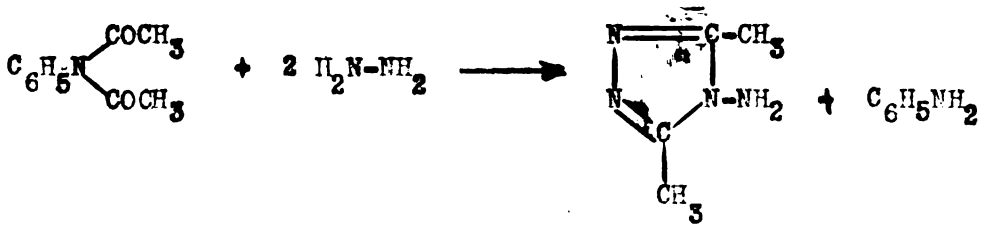




Dedichen (9) heated acetonitrile with hydrazine hydrate in a sealed tube at 180° C. for 48 hours to obtain the triazole.



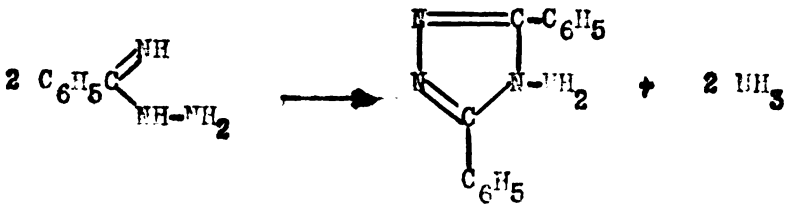
Silberrad (10) heated n-acetylacetanilide and hydrazine hydrate at 260° C. for four hours and got a good yield of the triazole.



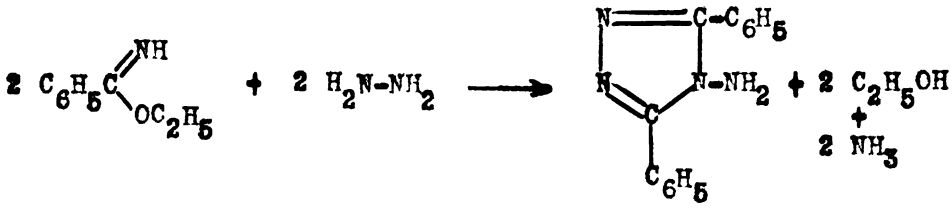
Dedichen (9) also prepared 3,5-diethyl-4-amino-1,2,4-triazole by the method mentioned above using propionitrile in place of acetonitrile.

The 3,5-di-n-propyl and di-isopropyl 4-aminotriazoles were prepared by Stollé and his students (11) (12) by refluxing an alcohol solution of the ethyl ester of the appropriate acid and hydrazine hydrate for three days on a steam bath. The product of this reaction is the monoacyl hydrazine. The acyl hydrazine was then placed in a bomb and heated to 270° C. The yield of triazole was not reported in either reaction.

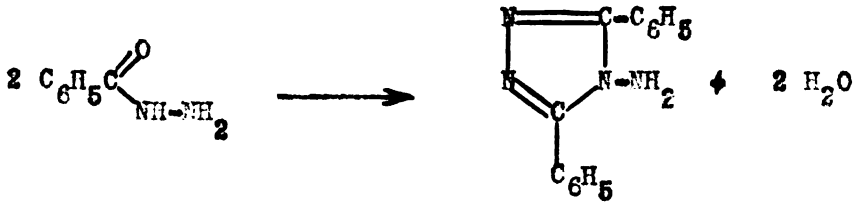
The 3,5-diphenyl-4-amino-1,2,4-triazole was prepared first by Curtius and Dedichen (13), who heated benzonitrile with hydrazine hydrate at 150° C. In 1897, Pinner (3) found that benzamidrazone on standing gave off ammonia and condensed to form the 3,5-diphenyl-4-aminotriazole.



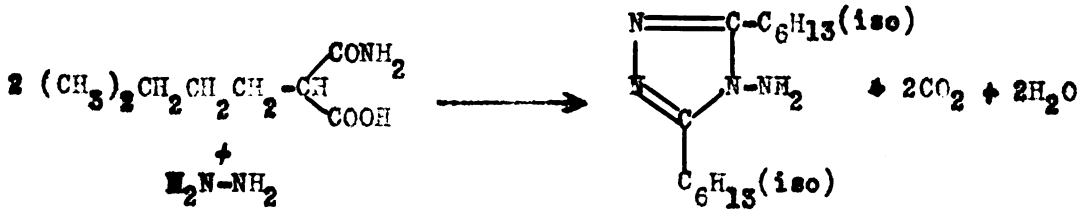
He also found that the ethyl benzimino ether on standing for eight days with hydrazine hydrate formed the triazole. Presumably the first step in this reaction is the formation of the amidrazone with the liberation of ethyl alcohol. The amidrazone then undergoes the elimination of



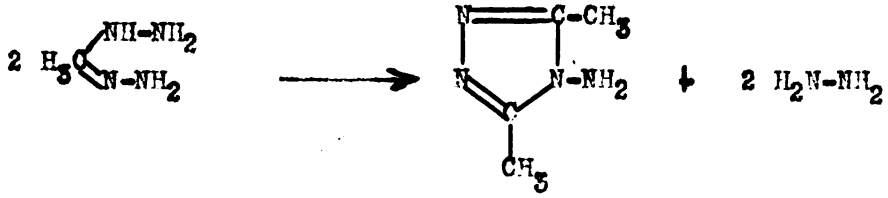
ammonia and condensation mentioned above. Silberrad (14) prepared this triazole in the best yield reported by any of the investigators for any of the compounds under discussion. He reported yields of 96 percent by heating monobenzoyl hydrazine at 230° C. with enough hydrazine hydrate to prevent formation of the dibenzoyl hydrazine.



More recently, Curtius and his co-workers (15) (16) prepared the 3,5-di-isobutyl, di-isoamyl, and a di-isohexyl-4-aminotriazole. They found that the triazoles could be prepared by heating the properly substituted malonylamidic acid with hydrazine at 150° C. for one day. In 1933, Oberhummer (17) used a



method similar to that described by Pinner to prepare 3,5-dimethyl-4-amino-1,2,4-triazole. This was the first preparation of



an aliphatic triazole by this method. In the same year, Aspelund and Augustson (18) heated ethyl acetate and hydrazine hydrate at 130° C. for only four hours and obtained a good yield of the dimethyl amino triazole.

DISCUSSION

DISCUSSION

The simplest procedure for the preparation of 4-aminotriazole derivatives involved simply heating a mixture of a lower fatty acid and hydrazine hydrate solution. The water originally present in the mixture and the water formed during the reaction were removed continuously by distillation. The successive steps in the reaction involved (1) formation of the hydrazinium salt, (2) dehydration of the hydrazinium salt, (3) decomposition of the monoacyl hydrazine, and (4) formation of the triazole. All the methods described in the historical section involving acyl hydrazines require the isolation of these compounds as intermediates, a step which is not essential in all instances.

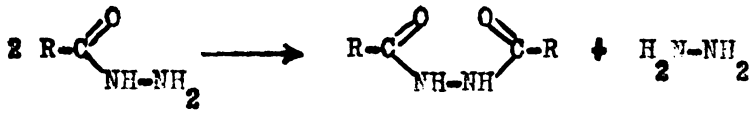
The distillation method of preparation of the triazoles gave good yields of the compounds in which the alkyl side chains were shorter than three carbon atoms. When the carbon chain contained three carbon atoms, or when the benzene ring replaced the alkyl side chain, the yields dropped considerably. In attempts to prepare the diisopropyl and diphenyl aminotriazoles by this technique the diacyl hydrazine was the principal product. This suggests the following mechanism:

Step 1. Formation of the hydrazinium salt.

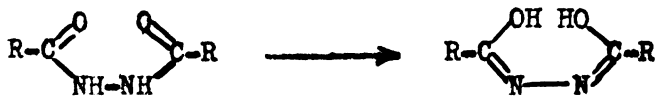
$$R\text{-}COOH + H_2N\text{-}NH_2 \longrightarrow R\text{-}COO^- \; {}^+H_3N\text{-}NH_2$$

Step 2. Dehydration of the hydrazinium salt to form the monoacyl hydrazine.

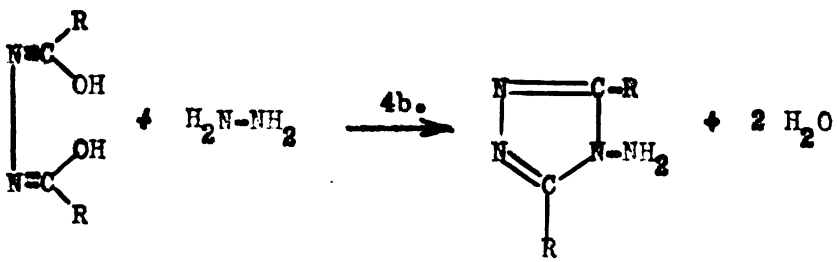
Step 3. Decomposition of the monoacyl hydrazine to form the diacyl hydrazine and liberate hydrazine.

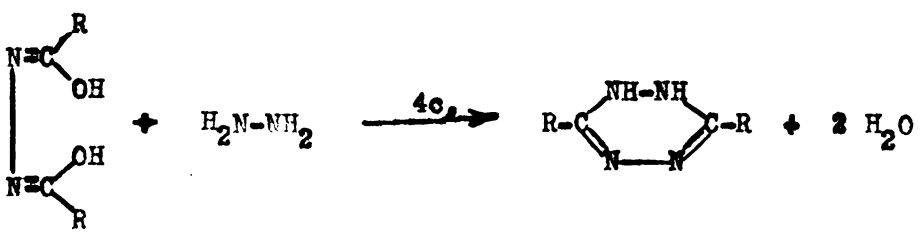


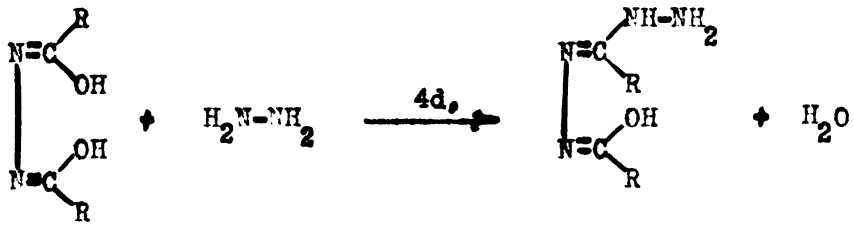
Step 4. (a) The rearrangement of the diacyl hydrazine to the "lactim" form.



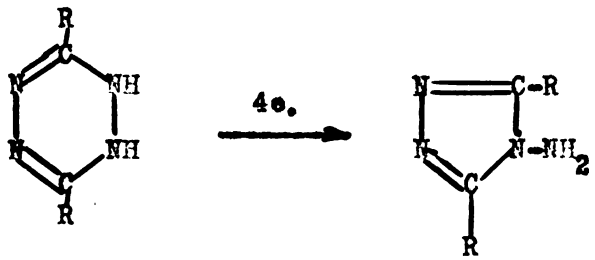
This is supported by the fact that on treatment with phosphorus pentachloride the diacyl hydrazine forms a diimino chloride.(6). The reaction of the lactim form of the diacyl hydrazine with hydrazine may follow one or more of the paths indicated.



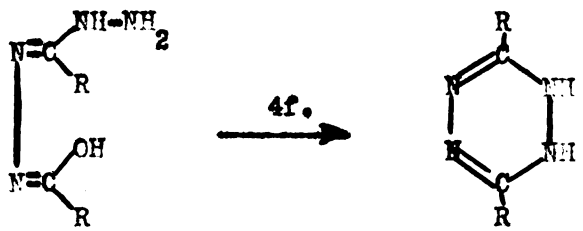




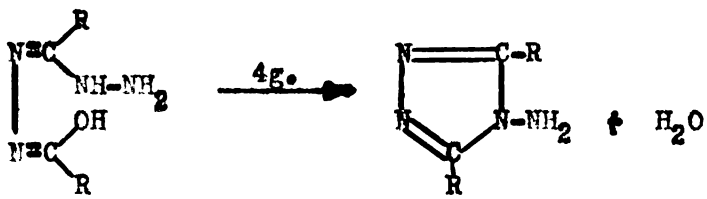
If path 4b. is followed, the product is formed directly. If path 4c. is followed, the next step would be a rearrangement of the dihydrotetrazine to the aminotriazole (4e).



If path 4d is followed, the next step could be one of two reactions,



either formation of the dihydrotetrazine (4f) followed by rearrangement of the dihydrotetrazine to the aminotriazole as in path 4e above, or direct cyclisation to the aminotriazole (4g).



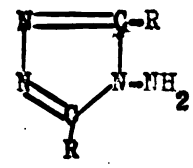
Apparently Step 4 does not take place readily with the higher molecular weight diacyl hydrazines formed from iso-butyric acid and benzoic acid. This may be due to several factors. Possibly the rate at which the reactions involved in Step 4 take place is not sufficiently rapid at the temperature at which Step 3 occurs to prevent loss by distillation of the hydrazine formed. Steric factors may also influence the ease of triazole formation. In a Fisher-Hirschfelder model of 3,5-diisopropyl-4-amino-1,2,4-triazole the substituent groups fail to rotate freely.

Attempts to prepare the diisopropyl and diphenyl compounds by heating the monoacyl hydrazines in a sealed tube at 180° C. for 48 hours were unsuccessful. The product was, in each case, the diacyl hydrazine. The odor of hydrazine was present when the tubes were opened. The lack of success in these reactions may have been due to the fact that the temperature was too low, (Compare Stollé and Gutmann (12)) or possibly due to the absence of the solvent effect of water. (See next paragraph.)

When the diacyl hydrazines were heated in a sealed tube with at least an equimolar amount of 85% hydrazine hydrate solution, the yields of the aminotriazoles were excellent. In Table I are compared the yields of 3,5-dialkyl-4-amino-1,2,4-triazoles obtained by the distillation method and by interaction of the diacyl hydrazines and aqueous hydrazine hydrate in sealed tubes. The comparison of these data lends weight to the proposed mechanism, since in the sealed tube reactions the hydrazine is confined and does not escape before the cyclization reaction (Step 4) can take place. The importance of water as a medium

TABLE I

FORMATION OF 3,5-DIALKYL-4-AMINO-1,2,4-TRIAZOLES



R	% Yield	
	Distillation Technique	Sealed Tube Technique
H	89	--
CH_3	75	--
C_2H_5	68	64
C_3H_7(n)	48	59
C_3H_7(iso)	0	62
C_6H_5	10	58

for the reaction between the diacyl hydrazines and hydrazine is also emphasized by these results.

In conclusion, it can be said that a convenient method of preparation of 3,5-dialkyl-4-amino-1,2,4-triazole has been found. When the alkyl groups are below three carbon atoms, it is possible to prepare the aminotriazoles from the carboxylic acids and hydrazine hydrate solution in an ordinary distillation apparatus. Higher molecular weight aminotriazoles can be prepared by heating the diacyl hydrazine and hydrazine hydrate solution in a sealed tube. In all cases the yields are over fifty percent.

EXPERIMENTAL

EXPERIMENTAL

Hydrazine: The commercially available 85% solution of the hydrate was used in all experiments.

Formic acid: The 90% aqueous solution commonly available was used.

Acetic acid: Glacial acetic acid was used.

Propionic, n-butyric, and iso-butyric acids: Obtained from Eastman Kodak Company.

Benzoic acid: This reagent was obtained from General Chemical Company.

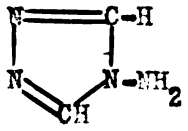
Isopropyl alcohol: The 99% material commonly known as "absolute" isopropyl alcohol was used in all instances.

Monoisobutyryl and monobenzoyl hydrazine: Prepared according to the method used by Stollé and Gutmann (12).

Dipropionyl and di-n-butyryl hydrazine: Obtained from Miss Wu, formerly of this department (19).

Diisobutyryl and dibenzoyl hydrazine: Obtained by the interaction of acid and hydrazine as described in subsequent sections of the experimental part of this thesis.

Preparation of 4-Amino-1,2,4-triazole



To one mole of formic acid in a round-bottomed flask was added 1.5 moles of hydrazine as an 85% solution of the hydrate. Since there was considerable heat evolved, the hydrazine was added slowly and the mixture kept cold, about 5° C. When the addition was complete, the flask was arranged for distillation and heated slowly to 200° C. The bulb of the thermometer was immersed in the reaction mixture so that the temperature of the melt could be determined. (Caution: It is important that the temperature does not rise above 220° C. as decomposition is very rapid above this temperature.) The weight of water and excess hydrazine hydrate distilled from the mixture were recorded as a measure of the extent of reaction. (Table II) It can be observed from the data in Table II that the temperature of the reaction mixture rose rather slowly until the water originally present and the water liberated by hydrazide formation had been eliminated. Thereafter, it rose rapidly and the distillate collected only slowly. After three hours at 200° C., the heating was stopped and the mixture allowed to cool. If the reaction mixture becomes pink or red on cooling, the conversion to the triazole is incomplete and the mixture should be reheated for about one hour. The product was taken up in 75 ml. of 95% ethyl alcohol and 75 ml. of ethyl ether added. Upon cooling, the oily product solidified. The amino triazole was recrystallized from a 1:1 mixture

TABLE II

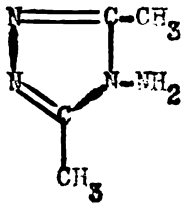
EXPERIMENTAL DATA FOR PREPARATION OF 4-AMINO-1,2,4-TRIAZOLE

Time (Hr.)	Time (Min.)	Flask Temp. (Degrees C.)	Weight of Distillate (Grams)
0	00	116	0.0
0	17	115	6.6
0	27	118	15.5
0	32	116	20.4
0	42	117	29.7
0	56	119	40.9
1	04	120	48.0
1	12	123	50.5
1	22	127	62.6
1	32	131	68.7
1	42	136	75.5
1	47	144	80.3*
1	57	163	85.4
2	07	185	88.9
2	12	205	89.5
2	22	198	89.5
6	12	200	90.9

* The formyl hydrazine is completely formed.

of 95% ethyl alcohol and ethyl ether. The recrystallized product was quickly transferred to a vacuum desiccator and dried overnight. The yield was 89%, m.p. 79-80.5° C. (uncorrected)

Preparation of 3,5-Dimethyl-4-amino-1,2,4-triazole



One mole of glacial acetic acid was placed in a round-bottomed flask and cooled in an ice bath to about 5° C. then one and a half moles of 85% hydrazine hydrate solution was added with cooling. The rate of addition was slow enough to prevent boiling of the mixture. The flask was then arranged for distillation in an all glass apparatus. The bulb of the thermometer was immersed in the reaction mixture in order to determine the temperature of the melt. The mixture was heated slowly, in an oil bath, to 220-230° C. The temperature was held in this range for five hours. The approximate extent of reaction was followed by measuring the amount of water and hydrazine hydrate which was distilled out of the mixture (Table III). At the end of the heating period, the mixture was allowed to cool to approximately 100° C. and then taken up in 150 ml. of isopropyl alcohol. The product crystallized from the alcohol on cooling as colorless prisms. The 3,5-dimethyl-4-amino-1,2,4-triazole was recrystallized from isopropyl alcohol. Since the triazole has appreciable solubility in ispppropyl alcohol, the mother liquors were concentrated to a rather small volume and the triazole

TABLE III

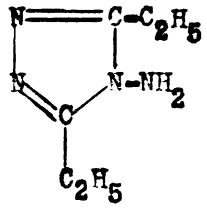
EXPERIMENTAL DATA FOR PREPARATION OF
3,5-DIMETHYL-4-AMINO-1,2,4-TRIAZOLE

Time (Hr. Min.)	Oil Bath Temp. (degrees C.)	Flask Temp. (degrees C.)	Wgt of Distillate (grams)
0 00	155	125	3.7
0 10	172	131	24.6
0 25	174	140	46.5
0 40	170	134	62.9*
1 10	230	211	82.5
2 40	220	216	85.8
3 10	234	231	86.8
4 10	230	227	87.3
5 30	236	236	87.3
7 50	230	225	87.3

* The acetyl hydrazine formation is complete.

allowed to precipitate before the mother liquors were discarded. The over-all yield, based on the acid, was 75%, m.p. 196.5-197.5 (corrected).

Preparation of 3,5-Diethyl-4-amino-1,2,4-triazole



One mole of propionic acid was placed in a round-bottomed flask and cooled in an ice bath. One and a half moles of 85% hydrazine hydrate solution was added in such a manner that the mixture did not boil. The flask was arranged for distillation with the bulb of the thermometer immersed in the reaction mixture and the mixture heated slowly to 220-230° C. The temperature was maintained in this range for five hours. The extent of reaction was followed, as before, by measuring the amount of water and hydrazine hydrate which was distilled out of the reaction mixture (Table IV). Upon completion of the heating, the product was allowed to cool and was taken up in ethyl acetate. When the ethyl acetate was cooled, the 3,5-diethyl-4-amino-1,2,4-triazole crystallised out in a very pure state. The yield was 47.9 grams (68%), m.p. 165.5-166.5° C. (corrected).

Preparation of 3,5-Di-n-propyl-4-amino-1,2,4-triazole

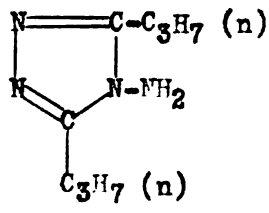


TABLE IV

EXPERIMENTAL DATA FOR PREPARATION OF
3,5-DI-N-PROPYL-4-AMINO-1,2,4-TRIAZOLE

Time (Hr.	Min.)	Oil Bath Temp. (degrees C.	Flask Temp. (degrees C.	Weight of Distillate (grams)
0	00	146	123	0.0
0	10	157	126	8.5
0	30	163	137	31.9
0	40	170	140	48.0
0	55	171	148	62.2*
1	10	175	159	72.1
1	25	210	186	80.9
1	40	222	214	85.6
2	10	235	228	86.0
6	55	220	220	87.0

* The formation of n-propionyl hydrazine is complete.

Normal butyric acid (one mole) and an 85% solution of hydrazine hydrate (1.5 moles) were mixed with cooling in a round-bottomed flask. The flask was then arranged for distillation and heated slowly to 270° C. The temperature rose slowly from the temperature at which distillation began until the monoacylhydrazine was formed. After the hydrazide formation was complete, the temperature rose rather quickly and rate of distillation decreased. After heating for 5-6 hours, the mixture was allowed to cool and then taken up in boiling ethyl acetate. The product crystallized as colorless needles on cooling. The 3,5-di-n-propyl-4-amino-1,2,4-triazole was recrystallized from ethyl acetate. The yield was 47%, m.p. 182-183° C. (corrected).

Reaction of Isobutyric Acid and Hydrazine

One mole of isobutyric acid and one and a half moles of hydrazine, as an 85 % solution of the hydrate, were mixed in a round-bottomed flask with cooling and then heated slowly to 270° C. After heating for 5-6 hours, the mixture was allowed to cool to about 100° C. The product was taken up in isopropyl alcohol. The first batch of crystals separated as colorless needles and melted at 238-239° C. (uncorrected). This product was only slightly soluble in water and alcohol and insoluble in ether. The melting point and the solubility properties correspond to those reported for di-isobutyryl hydrazine (12). The second crop of crystals melted over the range of 190-210° C. Repeated efforts to raise the melting point were unsuccessful. This product was considered

to be a mixture of the di-isopropylaminotriazole and di-isobutyryl hydrazine. The yield of di-isobutyryl hydrazine varied from 25-50%.

One reaction of isobutyric acid and hydrazine, under the condition described above, resulted in a 51% yield of the di-isopropylaminotriazole. However, repeated attempts to reproduce this result were unsuccessful.

Reaction of Benzoic Acid and Hydrazine

One mole of benzoic acid and 1.5 moles of 85% hydrazine hydrate solution were mixed, with cooling, in a round-bottomed flask. The mixture was then heated slowly to 270° C. After heating for a period of five hours at this temperature, the mixture was allowed to cool and then extracted several times with dilute hydrochloric acid (2-4N.). The acid solution was filtered and the filtrate neutralized with aqueous ammonia. The precipitate formed on neutralization was filtered off and recrystallized from 95% ethyl alcohol. The product separated as lustrous plates which melted at 259-260° C. corresponding to 3,5-diphenyl-4-amino-1,2,4-triazole. The yield was less than ten percent.

The residue from the acid extractions were recrystallized from ethyl alcohol and gave a voluminous precipitate. The product, when filtered and dried, melted at 238-239° C. (uncorrected) corresponding to dibenzoyl hydrazine. The yield was over fifty percent.

Formation of Diisobutyryl Hydrazine from Monoisobutyryl Hydrazine

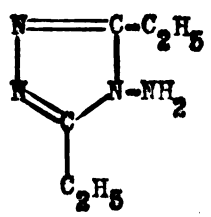
Five grams of monoisobutyryl hydrazine were placed in a combustion tube. The sealed tube was heated for 24 hours at 180° C. The tube was allowed to cool and then opened. The product was crystallized from

isopropyl alcohol. The yield of di-isobutyryl hydrazine was 50-60%, m.p. 237-239° C. (uncorrected).

Formation of Dibenzoyl Hydrazine from Monobenzoyl Hydrazine

Ten grams of monobenzoyl hydrazine were sealed in a combustion tube and heated for 24 hours at 180° C. The tube was allowed to cool and then opened. The product was crystallized from 95% ethyl alcohol. The crystals were very fluffy and voluminous. The yield of dibenzoyl hydrazine was 50-60%, m.p. 237-238° C. There was no isolatable quantity of the dibenzoylaminotriazole present.

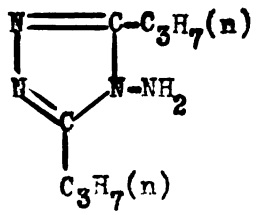
Preparation of 3,5-Diethyl-4-amino-1,2,4-triazole



Dipropionyl hydrazine (0.1 moles) was mixed with 85% hydrazine hydrate solution (0.1 moles) in a Pyrex combustion tube and the tube was sealed and heated for a period of 48 hours at 180 ± 5° C. After allowing about six hours for the tube to cool, it was opened with the aid of a flame, since the pressure in the tube was great enough to blow through the glass when the glass was heated until soft. The product was an oily liquid. The oil was dissolved in toluene and the water in the reaction mixture removed by azeotropic distillation. The 3,5-diethyl-4-amino-1,2,4-triazole precipitated from the toluene. It was

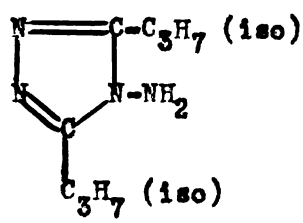
recrystallized twice from ethyl acetate. Yield was 64%, m.p. 165.5-166.5° C. Analysis. Calculated for $C_6H_{12}N_4$: N, 40.0. Found: N, 39.9

Preparation of 3,5-Di-n-propyl-4-amino-1,2,4-triazole



One tenth mole each of di-n-butyryl hydrazine and 85% hydrazine hydrate solution was placed in a Pyrex combustion tube and the tube was sealed and heated for a period of 48 hours at 180° C. The cooled tube was opened by the method described above. The product of the reaction was a white crystalline solid. The product was recrystallized from ethyl acetate. The yield of 3,5-di-n-propyl-4-amino-1,2,4-triazole was 59%, m.p. 182-183° C. (corrected). Analysis. Calculated for $C_8H_{16}N_4$: N, 33.3. Found: N, 33.1

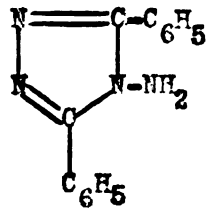
Preparation of 3,5-Di-isopropyl-4-amino-1,2,4-triazole



Di-isobutyryl hydrazine (0.1 mole) and 85% hydrazine hydrate solution (0.1 mole) were mixed in a Pyrex combustion tube and the tube was sealed. After heating the tube for 48 hours at 180° C., it was opened as previously described. The white crystals were taken up in hot

isopropyl alcohol. The 3,5-di-isopropyl-4-amino-1,2,4-triazole crystallized out as white plates on cooling. Yield 62%, m.p. 228.5-230 (corrected). Analysis. Calculated for $C_8H_{16}N_4$: N, 33.3. Found: N, 33.2

Preparation of 3,5-Diphenyl-4-amino-1,2,4-triazole



One tenth mole of dibenzoyl hydrazine and 0.2 moles of 85% hydrazine hydrate solution were mixed in a Pyrex combustion tube and the tube was sealed. After heating the sealed tube for 48 hours at 180° C., it was opened as described previously. The product was a white solid which darkened on standing. The solid was taken up in hot ethyl alcohol and decolorized with charcoal. On cooling a tan solid precipitated. This solid was recrystallized from ethyl alcohol and gave lustrous plates on cooling. The yield of the diphenyl triazole was 58%, m.p. 259-260° C. Analysis. Calculated for $C_{14}H_{12}N_4$: N, 23.7. Found: N, 23.8

In reactions in which only 0.1 mole of 85% hydrazine hydrate solution was used the yield of diphenylaminotriazole was considerably lower. This was probably due to the physical properties of dibenzoyl hydrazine.

SUMMARY

A convenient method of preparation of 3,5-dialkyl-4-amino-1,2,4-triazoles has been found. When the alkyl groups are below three carbon atoms, it is possible to prepare the triazoles from the free fatty acid and hydrazine hydrate solution in an ordinary distillation apparatus. Higher molecular weight aminotriazoles can be prepared by heating the diacyl hydrazine and hydrazine hydrate in a sealed tube. In all cases the yields are over fifty percent.

A mechanism for the formation of aminotriazoles has been proposed. The mechanism involves (1) formation of a hydrazinium salt, (2) the dehydration of the hydrazinium salt to form the monoacyl hydrazine, (3) decomposition of the monoacyl hydrazine to form a diacyl hydrazine and liberate hydrazine, (4) rearrangement of the diacyl hydrazine to the "lactim" form and reaction of the lactim form and hydrazine in one or more of three ways; direct formation of the aminotriazole; formation of a dihydrotetrazine which rearranges to the aminotriazole; or formation of an acyl hydrazidine followed by formation of the aminotriazole, or of a dihydrotetrazine which subsequently rearranges to the aminotriazole.

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