Preparation and Properties of Alpha Nitrogen Derivatives of Furan.

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PREPARATION AND PROPERTIES OF ALPHA NITROGEN

DERIVATIVES OF FURAN

A DISSERTATION

SUBMITTED TO THE FACULTY

OF THE

LOUISIANA STATE UNIVERSITY

AND

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FOR

THE DOCTOR OF PHILOSOPHY DEGREE

BY

HENRY MARVIN SINGLETON

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Abstract

The Hofmann amide degradation reaction was shown to be unsuccessful as a means for preparing alpha amino furan.

A number of alpha nitrogen derivatives of furan were prepared and investigated in the course of a sequence of reactions based on a modification of the Curtius reaction. This method employs the conversion of an acid chloride to an acid azide, thence to the isocyanate by thermal decomposition. The isocyanate, being a very reactive agent, was used as the key compound in the making of more stable alpha nitrogen derivatives. It was reacted with Grignard reagents to produce derivatives of a substituted carbamic acid; with bases to form salts of a substituted carbamic acid; and with alcohol to form an ester of the substituted carbamic acid.

The derivative of carbamic acid was the 2-furyl derivative and the nature of the ring was also noted in several instances. It was noted that the sensitized nucleus may form a peroxide, and retain the nucleus intact. An hydrazone of this peroxide was investigated.
Technique was developed for the preparation of several of these compounds and two distinct improvements were applied in the analytical work.

The following new compounds were prepared and characterized: 2-furyl isocyanate, 2-benzoyl amino furan, 2-propanoyl amino furan, 2-furyl barium carbamate and 2-furyl potassium carbamate.
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INTRODUCTION
In the study of any series of compounds it is first necessary to prepare a large variety of compounds and to investigate their properties, after which rules may be formulated that may be applicable to the whole series. In the furan series, knowledge of a variety of types of compounds is conspicuously lacking. The work described in this thesis supplies some of the missing information.

The following pages are devoted to a study of the preparation and properties of derivatives of furan containing nitrogen in the alpha position, emphasis being placed on the derivatives of alpha amino furan. As the amine itself is probably too unstable for independent existence, the behavior of closely related compounds is deserving of attention. The chemical properties to which chief attention was given were hydrolysis reactions under various conditions. The series of hydrolysis reactions begun with the most stable derivative of alpha amino furan obtainable and ended with the relatively unstable salts of 2-furyl carbamic acid. The reactions studied offer some insight into the stability and reactivity of the furan nucleus under different circumstances.

In the preparations, herein included, standard methods were adopted as much as possible in order to determine to extent these reactions may be applied to the furan series.
Failures in some cases were to be anticipated, but it was expected that new avenues for accomplishing the same ends should suggest themselves. As a matter of fact, this led to the development of a number of new methods.

Hence, the preparations and properties advanced in this paper represent a contribution to our knowledge of furan chemistry.
HISTORICAL DISCUSSION
Furan, $\text{C}_4\text{H}_4\text{O}$, was first prepared in 1870 by Limboiricht and Rhode (1) by the destructive distillation of barium pyromucate with soda lime. It was found to be a colorless liquid that boiled a little above room temperature.

Several configurations have been assigned to its structure, among which the following are the most plausible:

(2):

- Configuration I has been generally accepted as the structure of furan, and of the furan nucleus in its derivatives.

A few derivatives of furan, notably furfural and furcic acid, were well known prior to the isolation of the parent compound. 2-Furfural, the most abundant compound of the series, was discovered accidentally in 1827 (3). Its isomer, 3-furfural, was synthesized exactly one hundred years later (4). 2-Furcic acid was first observed by Scheele (5) in 1750 among the products resulting from the destructive distillation of uric acid. Böeae (5) determined its composition in 1834, and v. Baeyer (6) established its constitutional formula in 1877. Among the other furan derivatives that received early investigation
were: 2,5-methyl furfural acid; and a few of their derivatives. These products investigated were, for the most part, alpha substituted furans, and were prepared conveniently from natural products.

In spite of the long history of furan, there is an astonishing lack of information regarding reactions involving the nucleus itself. Hill and co-workers, and Marquis, made the greatest advancement of any of the early investigators. Their studies, like those of earlier workers, were confined largely to stable compounds such as furoic acid. When other well-known compounds, even as stable as 2-furfural or 2-furfuryl alcohol, were investigated, tarry substances were often obtained as part or all of their products. This caused discouragements, that were destined to limit our present-day knowledge of that part of furan chemistry that depends on substitution reactions chiefly to the work of the past decade.

This recent work consisted largely of an accumulation of data concerning new compounds synthesized from the easily accessible natural products, or their immediate derivatives. It included careful observation of their stabilities, and of the reactions that they underwent.

Examination of the structure of furan itself revealed two distinct types of possible reactions, namely: addition reactions and substitution reactions. The latter were by far the most important, because after addition to
the nucleus had taken place, its characteristic properties were destroyed, and the derivative behaved as an ordinary aliphatic compound. In rare instances, such compounds have been prepared by ring closure reactions, but these methods shed no light upon the stability of the furan nucleus, and they had a limited application. Substitution reactions, retaining the furan nucleus, furnished the main source of new types of compounds.

Knowledge of the chemistry of these compounds has been markedly circumscribed by limitations in methods for the introduction of nuclear substituents and by the uncertainty regarding the positions occupied by these substituents, together with an inadequate understanding and formulation of rules of orientation. Within recent years the number of substitution products has been greatly extended. However, most of these derivatives have been found incapable of conversion to other furan compounds.

Such rules of orientation as have been formulated do not enjoy the accurate general application of similar rules in the benzene series. In view of our present knowledge, Gilman and Wright (7) have advanced generalizations which, in essence, are as follows: "Substitution takes place in the alpha positions, exclusively, if they are not both occupied by some group other than hydrogen. If both alpha positions are occupied, further substitution takes place
in the beta position or positions, provided that neither of the groups held in the alpha positions is meta direction according to the Crumm-Brown-Gibson rule. If both groups are meta directing, no substitution takes place. If one group held in the alpha position is meta directing, substitution takes place on the carbon atom adjacent to the ortho-para directing group. If both groups in the alpha positions are ortho-para directing and unlike, a mixture of isomers results."

Since the hydrogen atoms in the alpha positions happen to be the most reactive, compounds synthesized by substitution in the alpha positions were easiest to obtain, most abundant, and most useful. However, the beta positions have also received attention. Hydrocarbon radicals have been placed in both beta positions; the aldehyde group in one beta position; and the halogens, notably iodine, in both beta positions; and of recent importance, Reichstein (8) has prepared all of the possible carboxylic acids. The alpha substituted derivatives have received the greater part of attention due to the readiness with which they may be formed by direct or nearly direct means. Puran and its derivatives have been subjected to all of the reactions characteristic to the benzene series, with more or less favorable results. The nucleus has been found to undergo metalation, halogenation, and nitration; and its halides
have participated in the Grignard reaction, and the Friedel-Crafts reaction. But, it did not undergo sulfonation directly, furan sulfonic acid being prepared only by indirect means. (7)

Brewer (9) prepared alpha sodium furan by the action of sodium ethylate on furan. This compound was of value in the establishment of the configurations of some furan derivatives.

Gilman, Mallory and Wright (10) prepared 2-iodo furan by direct action of iodine on furan, and subsequently 2-iodo magnesium furan which was found to be a very active Grignard reagent.

Chloro and bromo furans have also been prepared, but with difficulty, and failed to be of much value in further syntheses.

In the course of synthesizing various types of furan derivatives, it was found that the nucleus was quite unstable towards oxidation, by oxygen or halogens. It was found to be quite sensitive towards mineral acids, particularly hydrochloric and nitric, sulfuric acid having a much slighter influence towards ring rupture. In most cases, the furan nucleus has been found to be comparatively stable in moderately concentrated alkaline solutions. Tenth normal solutions of alkaline earth hydroxides have been used as ring closure agents. The carboxylic acids have been made to undergo the Cannizzaro reaction in 30
to 40 percent solutions of alkali without appreciable decomposition.

Throughout the entire study of furan substitution, especially when attempts have been made to place our knowledge on a systematic basis, stability of the nucleus has been of the greatest concern. Two groups were observed to be decidedly stabilizing, namely: carbonyl and nitro. The other groups that have been attached directly to the nucleus have been found to possess varying stabilizing influences. The two groups, amino and hydroxyl, have been found to possess such slight stabilizing influence that they have been classed as sensitizing groups.

The nitro group was found to be incapable of undergoing change without destroying or sensitizing extremely the furan nucleus. This indicated a peculiar influence perhaps exerted upon the nucleus by the nitrogen atom. Extensive work on the nitro compounds was delayed until recently.

Klinkhardt (11) in 1882 prepared a nitro furonic acid believed to be 2,5-nitro furonic acid. Hill and Palmer (12) repeated the work of Klinkhardt and advanced their belief that the compound was 2,5-nitro furonic acid, but absolute proof of orientation of nitro compounds has been inadequate.

Marquis (13) in 1902 prepared a nitro furan presumably the alpha derivative, and attempted unsuccessfully to pre-
pare 2,5-nitro furfural (14) the same year. However, the latter compound was prepared in 1930 by Gilman and Wright (15).

Among other nitro derivatives of furan which have been prepared, the following may be mentioned: 2,5-nitro ethyl furoate; 2,5-nitro furfural diacetate; 2,5-nitro furfuryl chloride; 2,5-nitro furfuryl alcohol; 2,5-nitro furfuryl methyl ether; 2,5-nitro furyl methyl ketone; and 2,5-nitro methyl furan.

In much of the work described above, the absolute determination of positions of substituent groups was impossible or incomplete owing to the lack of a sufficient number of derivatives of these compounds, or of other derivatives of furan having definitely established structures.

According to Gilman and Wright (14), "The nitro group markedly increases the stability of the furan nucleus." In the course of the nitration which they performed, strong mineral acids were used, causing ring fission. In this and similar instances, the ring has been re-formed by treatment with certain basic materials, notably: aniline, pyridine or alkaline earth hydroxides. It was sometimes found possible to close the ring by the mere application of heat, but poor yields resulted. An example of ring closure whereby the intermediate compound was isolated by Gilman and Wright (14) may be illustrated by the following scheme
for the preparation of 2,5-nitro furfural diacetate:

\[
\begin{align*}
&\text{HC} - \text{CH} \\
&\text{HC} - \text{C(OCOCH}_3)_2 \\
&\xrightarrow{\text{Pyridine}} \\
&\text{HC} - \text{CH} \\
&\text{H} - \text{C(OCOCH}_3)_2
\end{align*}
\]

Pyridine, perhaps by virtue of its solubility in water, proved to be by far the best ring closure agent. This reaction was checked by the author and entirely substantiated. In the nitration of other derivatives of furan whereby the nucleus was ruptured, ring closure accomplished by use of pyridine has been explained in a similar manner.

Gilman and co-workers (15 and 16) have reduced a number of nitro derivatives of furan by means of hydrogen and finely divided platinum as a means of preparing the corresponding amino derivatives. These amino compounds proved to be somewhat less stable than the nitro derivatives from which they were derived, but possessed a fair degree of stability. This was dependent upon the influence that the other groups present exerted upon the nucleus; a carbonyl group attached directly to the nucleus in the al-pha posi-
tion seemingly being necessary for the permanently stable existence of an amino furan derivative.

In spite of many repeated trials, it has been impossible to prepare 2-amino furan from 2-nitro furan or by any other means. According to Gilman and Wright (18), "Even if 2-amino furan should be prepared, it is altogether probable, by analogy with substituted furans, that it would not yield a product such as the diazonium compound."

Incidentally, even substituted 2-amino furans have not been diazotized. However, the same investigators (19) diazotized a beta substituted amine, namely: 4-amino-5-acetamino-2-ethyl furoate. They reported the isolation of the diazonium salt, coupled it with beta naphthol, also the successful Sandmeyer reaction between cuprous cyanide and the diazonium salt. Such favorable reports have not yet been obtained with the diazotization of an alpha amino furan.

Burtner (20) reported the preparation of 3-amino furan by the hydrolysis of 3-benzoyl amino furan in 5% sulfuric acid. He subjected this amine to diazotization and subsequent coupling with positive results.

In various efforts to prepare 2-amino furan, the early investigators attempted to attach an amino group to the furan nucleus in the alpha position by the hydrolysis
of 2-furyl urethanes. Curtius and Leimbach (21) and Marquis (22) and Freundler (23) subjected 2-furyl ethyl and methyl urethanes to hydrolysis in acid and in alkaline media, with negative results. Decomposition products resulted with elimination of ammonia being very pronounced in every case. Research on the hydrolysis of 2-furyl urethanes was soon abandoned; as well as the apparent hope of preparing alpha amino furen by this or any other means.

In connection with the identification of the hydrolysis products obtained in the various attempts to prepare alpha amino furen, very little has been definitely proven. When 2-furyl methyl or ethyl urethane was hydrolyzed, ammonia was the chief product recognized. The furan nucleus appeared to have undergone decomposition followed by polymerization. Marquis (22) hydrolyzed 2-furyl methyl urethane in an alkaline medium, and isolated a non-basic constituent that was found, by analysis, to have the following composition: C--41.08%, H--8.58%, N--15.17%, and M.P.--46°, B.P.--179-183. This appeared to be a mixture of polymerization products, rather than a single compound. Other investigators have been satisfied with reporting decomposition products of undetermined nature as a result of hydrolysis. In brief, the furan ring underwent changes not at all understood by the investigators.
Kohler, Westheimer and Tishler (24) advanced the idea that the furan nucleus may form a peroxide under the proper conditions. Their specific example was the reaction of 2,4,5-triphenyl-3-hydroxy furan with oxygen from the air according to the following scheme:

It was observed that only half of the oxygen from the peroxide was removable. This suggested the possibility of peroxide formation with other derivatives of furan in which the nucleus was highly sensitized.
THEORETICAL DISCUSSION
A critical review of the literature revealed that there are two general methods for the placing of a nitrogen atom on the furan nucleus. The first of these involves the substitution in the alpha position by direct nitration or the replacement of a sulfonic acid group by a nitro group; the second involves a series of degradation reactions in which a side chain is reduced successively by one carbon atom. As pointed out previously, the nitro group, in furan derivatives, does not lend itself to further modification; and the amino group that may be produced from it possesses a sensitizing influence upon the nucleus. For these and other reasons, the nitro furans were discarded in favor of other alpha nitrogen derivatives.

In the degradation of a side chain in the production of amines and amino derivatives, two general methods are usually employed. These are designated the Hofmann Amide Degradation, and the Curtius Reaction, in honor of the original investigators.

In the Hofmann reaction, an acid amide was used as starting material and allowed to progress through the following sequence of reactions (25)

\[
\begin{align*}
\text{I} \quad & \quad \overset{\text{FR}}{\longrightarrow} \quad \text{II} \quad & \quad \overset{\text{HBr}}{\longrightarrow} \quad \text{III} \\
\text{RC-NH}_2 \quad & \quad \overset{\text{C}}{\longrightarrow} \quad \text{RC-NH} \quad & \quad \overset{\text{C}}{\longrightarrow} \quad \text{(RC-N} \begin{cases} \begin{array}{c} \text{C} \\ \text{N-R} \end{array} \end{cases} \end{align*}
\]
In practice, II may be isolated, but need not be. IV may be detected by its odor, and III and V are never isolated, or observed directly. In fact, the existence of III has been questioned on the basis that no derivative has been prepared directly from this reactant.

In the present work, 2-furamide was subjected to the above sequence of reactions in an attempt to determine whether the furan nucleus would be stable enough to exist with an amino group placed on it in this way, and if not, what would be the nature of the decomposition products.

According to expectations, the main product of the reaction that lent itself readily to identification was ammonia. The characteristic purple color, reported by Saunders, that resulted from the action of sodium hypobromite on 2-furamide was strongly in evidence. (37)

The experimental work shed no light upon the mechanism of the Beckmann rearrangement of II to yield IV. However, an odor of IV was discernable.

No amino furan was isolated. It was observed that complete decomposition of the 2-furamide was effected when it was exposed to the action of sodium hypobromite for thirty minutes. Ammonia was the only product identified. The Hofmann method was, therefore, discarded in favor of
the modifications of the Curtius method subsequently described.

In the original Curtius method, the following sequence of reactions was employed (26):

\[ \begin{align*}
\text{R-O-OR} & \xrightarrow{\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}} \text{II} \\
& \xrightarrow{\text{HONO}} \text{III} \\
\text{R-CH} & \xrightarrow{\text{heat}} \text{R-N-C-OR} \\
& \xrightarrow{\text{H}_2\text{O}} \text{IV} \\
& \xrightarrow{\text{R-NH}_2 + \text{R-OH} + \text{CO}_2} \text{V}
\end{align*} \]

This reaction is very satisfactory in the preparation of stable amines, and the earliest attempt to prepare 2-amino furan was by this method. The ester of the substituted carbonic acid, IV, is a urethane. Curtius and Leimbach (21), Marquis (22), and Freundler (23) attempted to hydrolyze 2-furyl ethyl and methyl urethanes. The usual procedure was to heat the urethane with concentrated hydrochloric acid in a sealed tube for several hours at 120-180 °C. Their results were unsatisfactory, and in general agreement. Ammonia was one of the products, together with decomposition products from ring cleavage. Their attempts to hydrolyze the same urethanes by digesting with alkaline hydroxides produced, in general, similar negative results.

This suggested to the present author that, the urethanes might be entirely too stable to be hydrolyzed and still re-
tain the furan nucleus intact. A new path of investigation then suggested itself. Other derivatives that should be more easily hydrolyzed than a urethane were sought. Since the literature contained no account of the preparations of such derivatives of furan, new methods of synthesis were made necessary.

The preparation of 2-benzoyl amino furan was suggested by the work of Burtner (20) in which the preparation of 3-benzoyl amino furan was reported. The 3-aminofuran prepared by the hydrolysis of 2-benzoyl amino furan was reported to be stable enough for diazotization and subsequent coupling. From these results, it seemed possible that 2-aminofuran might be prepared by a similar method. The following sequence of reactions, related to the Curtius reaction, was carried out:

\[
\begin{align*}
\text{I} & \xrightarrow{\text{NaBH}_4} \text{II} & \xrightarrow{-N} \text{III} \\
\text{III} & \xrightarrow{} \text{IV} & \xrightarrow{} \text{V}
\end{align*}
\]
This method differed from the Curtius reaction in two important respects: (a) the acid azide was prepared from an acid chloride and sodium azide instead of by the oxidation of the corresponding hydrazide by nitrous acid, and (b) the 2-furyl isocyanate was added to an alcohol to form a urethane in the Curtius method, whereas the isocyanate was added to a Grignard reagent in this method.

It will be observed that in both, the Hofmann and Curtius reactions, a common intermediate product was formed, namely: the isocyanate. This was arrived at presumably through a Beckmann rearrangement (27) in the course of the reaction. This necessitated an intermediate compound formation prior to the formation of the isocyanate. According to the theory advanced by Stieglitz (28) a univalent nitrogen compound existed momentarily; but this theory has never been substantiated despite numerous attempts to isolate a derivative to prove its existence. (29)

Hurtner (20) reportedly prepared 3-benzoyl amino furan by a method employing the decomposition of 3-furoyl azide in boiling benzene. The cooled solution was added to phenyl
magnesium bromide, then subsequently hydrolyzed with ammonium chloride solution. The 3-benzoyl amino furan prepared in this way was easily hydrolyzed by 5% sulfuric acid to yield a product volatile with steam and capable of undergoing diazotization with subsequent coupling with beta naphthol and with dimethyl aniline to yield characteristically colored condensation products. No products were isolated in the entire preparation except 3-furoyl azide and 3-benzoyl amino furan.

The present author paralleled Furtner's work with the alpha derivatives. It was found necessary to increase the boiling point of benzene by the addition of about 20% of its volume of toluene. An analogous compound, 2-benzoyl amino furan, was obtained. It hydrolyzed easily with 5% sulfuric acid, and the hydrolysis products yielded the same color reactions as the hydrolysis products of 3-benzoyl amino furan after diazotization. This merely represented a qualitative test for a primary amine. The colors produced were due to decomposition of the furan nucleus, but typical of the diazo linkage.

The hydrolysis products from 2-benzoyl amino furan was converted to the hydrochloride, and subsequently displaced by liquid ammonia. Aniline appeared in yields of 3-10 percent of theoretical as the only constituent less basic than ammonia. This revealed that 3-10 percent of
the original 2-benzoyl amino furan, though possessing the
correct analysis and molecular weight, was the isomeric
2-furoyl anilide. This seems to be adequate proof of the
existence of a univalent nitrogen free radical. Its
presence may be explained on the assumption that the benz­
enene solution contained a small amount of undecomposed
2-furoyl azide. In the presence of phenyl magnesium brom­
ide, the free radical produced from 2-furoyl azide may
react according to the following scheme:

\[
\begin{align*}
R-\overset{\circ}{C}-N + \text{C}_6\text{H}_5\text{MgBr} &\rightarrow R-\overset{\circ}{C}-N-\text{C}_6\text{H}_5 \text{MgBr} + \text{H}_2\text{O} \\
&\rightarrow R-\overset{\circ}{C}-N-\text{C}_6\text{H}_5
\end{align*}
\]

(When \( R^- \) was 2-furyl radical)

It was impossible to determine the physical properties
of 2-benzoyl amino furan in the presence of 2-furoyl anilide.
After repeated recrystallizations from benzene, the mixture
appeared to form isomorphous crystals, making separation
impossible by this means. Thus, it was necessary to pre­
vent the formation of the 2-furoyl anilide by isolating
2-furyl isocyanate uncontaminated with 2-furoyl azide before
adding to the phenyl magnesium bromide solution.

2-Furyl isocyanate was isolated for the first time
by the thermal decomposition of 2-furyl azide in a medium of
phenyl ether, followed by distillation of the 2-furyl iso­
cyanate, 111-112 , made subsequent separation of this
product very difficult.

2-Benzoyl amino furan produced from the reaction of 2-furyl isocyanate and phenyl magnesium bromide showed the same composition upon analysis as that prepared by Method I (contaminated 2-furoyl anilide) but its melting point was considerably different from the mixture. Whereas the hydrolysis products of 2-benzoyl amino furan (Method I) included furoic acid, benzoic acid, aniline, ammonia and decomposition products resulting from changes of the furan ring, the hydrolysis products of that prepared by Method II gave no aniline and no furoic acid. The salt obtained proved to be ammonium chloride, and consequently no diazotization of hydrolysis products was possible.

These results may be explained on the assumption that in method I there evidently existed a small amount of an univalent nitrogen compound, R-CO-N\textsuperscript{-}, having a transitory existence, but capable of adding to phenyl magnesium bromide to form 2-furoyl anilide. This, upon hydrolysis, yielded aniline; and, subsequently, produced characteristic reactions of a primary amine. In method II, the univalent nitrogen compound had undergone the Beckmann rearrangement to form 2-furyl isocyanate completely before the addition of the 2-furyl isocyanate solution to phenyl magnesium bromide, and no 2-furoyl anilide was formed.
Since Burtner (20) employed a method similar to method I, it seems very probable, by analogy, that he prepared 3-benzoyl amino furan contaminated with 3-furoyl anilide. The latter, upon hydrolysis, would yield aniline and might lead to an erroneous conclusion that he had prepared a primary furyl amine. The diazotization, and subsequent color reactions which he offered as sole proof of the preparation of 3-amino furan would therefore seem to be inadequate for that purpose. They merely prove that some primary aromatic amine was isolated; it might have been nothing but aniline. The preparation and isolation of 3-amino furan cannot be considered an accomplished and established fact until further evidence is offered.

Acid hydrolysis and alkaline hydrolysis of 2-benzoyl amino furan (Method II) gave essentially the same products, namely: ammonia, benzoic acid, and decomposition products that were either resinous or a water suspension of colloidal particles. These colloidal suspensions did not contain any matter volatile with steam or soluble in ether. Long standing, continued in some instances over a period of six months, resulted in the settling out of a tarry residue. A sample of this residue, dried, glowed without rapid burning when heated in air.

The removal of the benzoyl radical by hydrolysis, there-
fore, proved unsatisfactory. This suggested the introduction of a group more adaptable to hydrolysis, viz., an acyl group.

2-Propionyl amino furan was prepared by a similar series of reactions using ethyl magnesium bromide and 2-furyl isocyanate. It was found to hydrolyze more easily than 2-benzoyl amino furan, but the results were similar. The furan nucleus decomposed with the liberation of ammonia and the production of propionic acid, and unidentified residues similar to those described above. This was found to take place even when the hydrolyzing agent employed was a 3% solution of barium hydroxide, a ring stabilizing base in some cases.

In hydrolysis reactions of the urethanes, other investigators employed concentrated hydrochloric acid, a ring sensitizing agent. In these experiments with the hydrolysis of a 2-benzoyl and 2-propionyl amino furans, 5% sulfuric acid was used. This acid is the only mineral one that does not exert a marked sensitizing influence on the ring. The 2-benzoyl and 2-propionyl amino furans were hydrolysed, but decomposition products were obtained instead of any primary amine. These results proved that acid hydrolysis of these compounds was impossible.

2-Furyl isocyanate was used as a starting material in many of the reactions. It was added to an alcohol with the
production of a urethane in an excellent yield, whereas the decomposition of 2-furoyl azide in an alcoholic medium to produce the same compound gave a poor yield (30). 2-Furyl isocyanate was added to water to produce 2,2-difuryl urea. It was added to concentrated solutions of potassium hydroxide and barium hydroxide to produce the corresponding salts of 2-furyl carbamic acid. The usual procedure for making analogous potassium carbamates is to subject a suspension of small pieces of potassium in an amine to an atmosphere of carbon dioxide (31).

2-Furyl barium carbamate was destructively distilled in an attempt to form 2-furyl amine by a reaction similar to the production of aniline from phenyl barium carbamate (31). This furan compound was found to decompose completely when heated to 250-300° even under 10 mm. pressure. On standing at room temperature, 2-furyl barium carbamate decomposed slowly with liberation of ammonia. When dissolved in warm water, a similar decomposition preceded very rapidly.

2-Furyl potassium carbamate proved to be more serviceable in its reactions. It was prepared in greater yield than the barium compound. The crystalline product was more easily purified and analyzed. It was very soluble in water. The aqueous solution gradually turned to a dark red color with evolution of ammonia on standing.

2-Furyl potassium carbamate was transformed to
2-furyl methyl urethane by dimethyl sulfate as follows:

\[
\begin{align*}
\text{HC} & \quad \text{CH} \\
\text{HC} & \quad \text{O} \quad \text{C-N-C-C} \quad \text{CH}_3
\end{align*}
\]

\[
\overset{(\text{CH}_3)_2\text{SO}_4}{\rightarrow}
\begin{align*}
\text{HC} & \quad \text{CH} \\
\text{HC} & \quad \text{O} \quad \text{C-N-C-C} \quad \text{CH}_3
\end{align*}
\]

The product prepared was identical with that prepared by the action of 2-furoyl azide on methyl alcohol. This established the structure of 2-furyl potassium carbamate.

However, when ethyl iodide was used as an alkylating agent, carbon dioxide was produced. In such a case, ethyl amino furan was also expected, but decomposition of the compound ensued. The products identified were: potassium iodide, carbon dioxide, ammonia and a small amount of ethyl amine.

Examination of the structure of 2-furyl potassium carbamate shows that it is related to a urethane, except that an alkyl radical has been replaced by potassium. On neutralization with a mineral acid, the 2-furyl carbamic acid was probably produced; it immediately losing carbon dioxide and producing the mineral acid salt of the amine. Concentrated acid was necessary in order to insure the complete removal of carbon dioxide; otherwise a contamination with 2,2-difuryl urea, mentioned above, resulted. This was evidently formed in numerous instances by the liberation of only a portion of carbon dioxide from 2-furyl carbamic acid.
Hydrochloric and sulfuric acids were employed in the preparation of 2-furyl amine hydrochloride and sulfate, respectively. These salts were not purified sufficiently for analysis. In the course of their attempted isolation, decomposition products were formed which were extremely difficult to remove. However, a hygroscopic solid was obtained in each case that responded similarly to subsequent treatments.

When neutralized with sodium carbonate, the amine salt yielded ammonia, and an ether-soluble constituent that decomposed when subjected to distillation. On exposure to air for several hours, the ether solution yielded a flocculent, white precipitate. This precipitate was soluble in alkali; and quite soluble in water, with an evolution of small bubbles of oxygen. An alkaline solution turned red on heating. When a portion of the aqueous solution of this material was made slightly acidic with acetic acid, then condensed with phenyl hydrazine, a phenyl hydrazone was formed in the form of colorless plates. A suggested mechanism for the formation of this hydrazone is as follows:
Either the cyclic structure of the peroxide \( V(a) \) or the open formula \( V(b) \) may be used to explain the position of the oxygen. The steps following the formation of \( IV(a) \) are entirely paralleled by a similar peroxide formation reported by Kohler and co-workers (24).

The fact that only one carbonyl group was available for phenyl hydrazone formation (as shown by the molecular weight, 174.5, of the phenyl hydrazone formed) led to the conclusion that the furan ring remained intact in the above series of reactions. If the ring had have been broken on either side of the nuclear oxygen, either tarry materials would have resulted from the polymerization of the unsaturated compounds resulting, or a second carbonyl group would
have been formed. No tarry materials were observed. A phenyl hydrazone with a molecular weight of 279.1 would have resulted from the reaction of two carbonyl groups with phenyl hydrazine; this, as previously stated, was not the case.

The modification of the Curtius method with which most of this work deals (the degradation of an acid chloride to form amines or derivatives of amines) represents an innovation when viewed as a comprehensive scheme, although parts of it have been used for a long time. As a check on the method, it was used for the preparation of the vastly more stable aniline. Benzoyl chloride was used as starting material and successively converted into the azide, phenyl isocyanate, phenyl potassium carbamate, aniline hydrochloride, then aniline, fair yields being obtained at all steps.
EXPERIMENTAL
2-Furoyl Chloride

A procedure analogous to that employed by Gilman and Selby (32) for the preparation of 3-furoyl chloride was adopted.

A solution of 26 g. (0.22 mole) 2-furoic acid and 50.4 g. (0.4 mole) thionyl chloride in 240 cc. of anhydrous benzene was refluxed four and a half hours, until sulfur dioxide and hydrogen chloride ceased to escape. After the benzene and excess thionyl chloride were removed by distillation at atmospheric pressure, the residual liquid was distilled under reduced pressure. A colorless liquid with a powerful lachrymatory effect was obtained. E.P.—67-0°/7mm. Yield—21.9%.

2-Furamide

A solution of 130.5 g. (1 mole) 2-furoyl chloride, dissolved in 200 cc. benzene, and contained in a 500 cc. two-neck flask, fitted with a mechanical stirrer and a inlet tube, was cooled to the temperature of an ice-salt freezing mixture. Gaseous ammonia was admitted with stirring and continued cooling. As soon as the lachrymatory effect of 2-furoyl chloride became noticeably weak, the solid mass was covered with a small amount of liquid ammonia in order to complete the reaction. The white,
crystalline mass was pressed into a Buchner funnel and the benzene removed by suction. The mass was then washed with cold water to remove ammonium chloride, and dried. It was sufficiently pure for further use. A small amount was re-crystallized from 95% ethyl alcohol. M.P. --141-2°. Yield --- quantitative.

The Hofmann Degradation of 2-Furamide

A mixture of 44.4 g. (4 mole) 2-Furamide, 50 cc. water, and 64 g. (20.8 cc.) bromine was cooled to room temperature in a 500 cc. Erlenmeyer flask. To this mixture was added a solution of 35.5 g. sodium hydroxide dissolved in 350 cc. water, until the maximum brown color was developed. This required most of the alkali. This solution was admitted, with stirring, through a dropping funnel into a liter three-neck balloon flask, containing 56.8 g. sodium hydroxide in 150 cc. water. The temperature was maintained at 70-75° by means of an oil bath. The reaction was allowed to proceed, with rapid stirring, for fifteen minutes.

The resultant material was steam distilled, with distillate being received in 200 cc., 4N hydrochloric acid. The latter was then evaporated to dryness on a steam bath. About two liters of distillate was collected, and the yield of salt was 19.5 grams.
The salt, thus obtained, was dried to constant weight in a dessicator, and dissolved in liquid ammonia. The ammonia was allowed to evaporate, and the solid residue was extracted with dry, alcohol-free ether. The ether was carefully removed by distillation, and a basic residue was obtained that was contaminated with ether and ammonia. It was too minute in quantity for purification by fractionation. It gave a crystalline precipitate with hydrogen chloride, and a reaction with benzoyl chloride. The benzoyl derivative, after purification for removal of the benzamide formed, was not identical with the 2-benzoyl amino furan produced by a later synthesis.

In another experiment, in which the initial reaction was allowed to proceed for thirty minutes instead of fifteen, all other details being identical with those described above, the yield of basic material was entirely ammonia. This indicates that any amine produced in the first experiment was formed during steam distillation. The instability of the furan nucleus to oxidation as well as to the action of hydrobromic acid was manifested by this result.

2-Ethyl Furoate (33)

A mixture of 150 g. (1.54 moles) 2-furoic acid and 200 g. (6.52 moles) ethyl alcohol, saturated with hydrogen
chloride, was gently boiled in a liter balloon flask under reflux for four hours.

After about 150 cc. of alcohol had been removed by distillation, the residual liquid was allowed to stand in an ice bath until crystals ceased to precipitate. The crystalline mass was filtered with suction, washed with cold water, then distilled under reduced pressure. B.P.—80-5°/1mm. M.P.—34°. Yield ----58.9%.

2-Furoyl Azide (Method I)

A solution of 50.6 g. (.401 mole) 2-furoyl hydrazide, dissolved in 300 cc. water to which was added 225 cc. of a solution of .5N sulfuric acid, was cooled to 0°. To this was added, drop-wise and with stirring, 30 g. sodium nitrite, dissolved in 75 cc. of water.

A white precipitate was immediately formed. Stirring of the solution was continued until a filtered sample of the solution no longer showed a turbidity with a few drops of a solution of sodium nitrite. The crystals were removed by suction filtration, then dried in a desiccator over phosphorous pentoxide. The filtrate was extracted with three 50 cc. portions of ether, and an additional small amount of 2-furoyl azide was obtained from these by evaporation of the ether.

Note: The preparation of 2-furoyl hydrazide is on page 56.
Characteristics: Colorless, monoclinic plates from ether. Slight lachrymatory effect similar to 2-furoyl chloride, but much more mild. Decomposes with violence about 100°, in capillary at 110°, (34) but measurably slow in solution, 75-90°. Explodes in contact with sulfuric acid. Slightly soluble in water, moderately soluble in alcohol, and very soluble in ether, benzene, phenyl ether and other typical organic solvents. Recrystallized from benzene. M.P. ---61-2°; B.P. ---75°/9 mm.; Yield ---31.9%.

2-Furcyl Azide (Method II)

A solution of 26 g. (.2 mole) 2-furoyl chloride in 75 cc. of ether was cooled to 0°. To this was added, drop-wise, and with stirring, a solution of 13 g. (.2 mole) sodium azide dissolved in 50 cc. of water. Stirring was continued at this temperature for about fifteen minutes; then the temperature of the reaction mixture was allowed to rise to room temperature. Stirring was continued for an hour in order to complete the reaction. The ether was removed by a current of air, then the crystalline mass of 2-furoyl azide was removed by suction filtration. It was sufficiently pure for subsequent use after washing with cold water, and drying in a desiccator over phosphorous pentoxide. Yield --- 91.6%.
The thermal decomposition of 2-furoyl azide was carried out in a medium of phenyl ether. A 125 cc. Claissen flask, fitted with a short side-arm condenser, and a Y-tube was employed. One branch of the delivery tube, turned downward, terminating in a 30 cc. separatory funnel used as a receiver; the other branch, turned upward, was connected to a scrubber filled with benzene, then to the atmosphere. Ice water was circulated in the condenser. See figure I.

Thirteen and seven tenths grams (0.1 mole) 2-furoyl azide was admitted into the previously dried Claissen flask, and 25 cc. phenyl ether was added. Air was displaced from the system by a stream of dry carbon dioxide. The flask was cautiously warmed in a water bath until the azide dissolved and bubbles of nitrogen were quite abundant. The temperature was not allowed to exceed 75-80° at first, because heat was liberated and when allowed to proceed too rapidly an explosion resulted. The temperature was increased to 90° as the reaction proceeded; the rate of increase being governed by the rate of nitrogen evolution. In the course of about two hours, the evolution of gas ceased. The 2-furoyl isocyanate was distilled undecomposed at atmospheric pressure.
Characteristics: Colorless liquid with a powerful lachrymatory effect. Its odor is very repulsive, and causes a dull headache (especially at the base of the brain) that lingers for hours. B.P. --- 54°/40 mm.; 111-2° (atmospheric). Yield --- 73.4%.

Analysis for C₅H₅O₂N:

<table>
<thead>
<tr>
<th></th>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>55.05%</td>
<td>54.27%</td>
</tr>
<tr>
<td>H</td>
<td>2.77%</td>
<td>2.85%</td>
</tr>
<tr>
<td>N</td>
<td>12.84%</td>
<td>12.99%</td>
</tr>
</tbody>
</table>

2-Benzoyl amino Furin (Method 1)

A method employed by Purtner for the preparation of 3-benzoyl amino furin was used. (20)

A solution of 27.4 g. (.2 mole) 2-furoyl azide in a mixture of 200 cc. of benzene and 100 cc. of toluene was dried over calcium chloride. After removal of the calcium chloride, the solution was cautiously refluxed until evolution of nitrogen had ceased, the outlet being protected from the atmosphere by a calcium chloride tube.

After the evolution of gas, the solution was dark red, and contained many black suspended particles. It was cooled to 0 °, and added, drop-wise, with stirring, to an ether suspension of .2 mole of phenyl magnesium bromide, also previously cooled to 0 °. The resultant product was hydrolyzed with
an excess of 15% ammonium chloride solution, then extracted with ether. The combined ethereal solutions were dried over calcium sulfate, then condensed to about 50 cc. by distillation. Crystals of 2-benzoyl amino furan separated and were collected by suction filtration. After repeated recrystallization from benzene, almost colorless crystals with a light yellow tinge were obtained. The molecular weight was determined by the Rast method employing the depression of freezing point of camphor. *M.P. --89-92°.* Yield -- 16.7 g. or 50.0%.

Analysis for C₁₁H₉C₂N:

<table>
<thead>
<tr>
<th></th>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>70.56%</td>
<td>70.26%</td>
</tr>
<tr>
<td>H</td>
<td>4.05%</td>
<td>4.90%</td>
</tr>
<tr>
<td>N</td>
<td>7.48%</td>
<td>7.29%</td>
</tr>
<tr>
<td>G.M.W.</td>
<td>187.07</td>
<td>G.M.W. - 190.4</td>
</tr>
</tbody>
</table>

From a study of the hydrolysis products see page , it was observed that the product obtained in this way was a mixture of two isomers -- 2-benzoyl amino furan with 3-10% of 2-furoyl anilide.

2-Benzoyl Amino Furan (Method II)

To a solution of .1 mole of phenyl magnesium bromide in 75 cc. ether, cooled to 0°, 8.9 g. (.082 mole) 2-furyl
isocyanate was added drop-wise and with stirring. After
allowing the reaction to proceed at 0° or below, the result-
ant product was hydrolyzed with 15% ammonium chloride, and
the aqueous layer extracted with ether. The combined ether
extracts were dried over calcium sulfate, after which the
solution was decanted, the ether removed by distillation,
and the product allowed to crystallize. A portion was re-
crystallized from benzene. M.P. --124.5°: Yield -- 80.0%.

Analysis for C_{11}H_{9}O_{2}N:

<table>
<thead>
<tr>
<th></th>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>70.56%</td>
<td>70.30%</td>
</tr>
<tr>
<td>H</td>
<td>4.85%</td>
<td>4.91%</td>
</tr>
<tr>
<td>N</td>
<td>7.48%</td>
<td>7.35%</td>
</tr>
</tbody>
</table>

This method gave a product that was free from the
isomeric 2-furcyl anilide. See basic hydrolysis of 2-benzoyl
amino furan, page 41.

**Hydrolysis of 2-Benzoyl Amino Furan (acidic)**

Forty five grams (.24 mole) 2-benzoyl amino furan
(Method I), in a liter balloon flask, was digested under
reflux for fifteen minutes with 300 cc. of 5% sulfuric
acid. From the cooled solution, a considerable quantity
of benzoic acid precipitated; this was removed by filtration.
The solution was made just alkaline with solid sodium
carbonate, then steam distilled, with the distillate being
received in an excess of 6 N. hydrochloric acid. A crystalline residue was obtained on evaporation of the distillate. Yield 22.9 g.

The salt obtained above was dissolved in liquid ammonia, and the ammonia allowed to evaporate at room temperature. The residue was extracted with dry ether, after which the ether was removed from the extract by distillation. A yield of 3.1 g (based on amino furan) of a liquid boiling at 178° was obtained. The benzoyl derivative of this compound had a melting point of 159.5-160.5°, identical with benzanilide. A mixed melting point with benzanilide gave the same melting point. Therefore, the only constituent less basic than ammonia produced in the original reaction was aniline. The residual salt from the ammonia displacement was covered with ethyl amine; and the latter was subsequently removed by distillation. This amine, being more basic than ammonia, should displace any amine having a basicity between ammonia and ethyl amine. The only evidence of a reaction was the appearance of ammonia along with the ethyl amine. This resulted from the displacement of the former from ammonium chloride.

Other products of hydrolysis were: ammonia, benzoic acid, a small amount of furfural, and a non-basic constituent that was not identified, but possessed the following constants: V.P. --115-25°/mm. M.P. --68.5-69°. Crystals
in the form of colorless plates. Analysis:
C -- 82.26%, H -- 6.42%, N -- 0.00%.

The main portion of the furan nucleus was lost in
decomposition products that were, with the exception of a
tarry residue, water soluble; and that imparted a dark red
coloration to the solution. When a solution of the decompo-
sition products was treated with ammoniacal silver oxide,
a silver mirror was produced, but no silver acetylide was
isolated from the reaction products. The aqueous solution
failed to produce a phenyl hydrazone with phenyl hydrazine.
These results prove that the decomposition products contained
no acetylenic linkage nor carbonyl oxygen.

When 2-benzoyl amino furan (Method II) was hydrolyzed
and products of hydrolysis subjected to the same treatment
as above, only benzoic acid, ammonia, and the characteristic
red-colored decomposition products were discernable. No
trace of aniline could be discovered.

Analysis of the hydrochloride from steam distillation
gave the following:

<table>
<thead>
<tr>
<th></th>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>11.76%</td>
<td>24.75%</td>
</tr>
</tbody>
</table>

Calculated on basis of 2-amino furan hydrochloride, but
results proved it to be almost pure ammonium chloride.

The significance of these results, from the preparation
of 2-benzoyl amino furan by two methods, and the hydrolysis
of the products of these methods, is discussed on page 22.

Hydrolysis of 2-Benzoyl Amino Furan
(Basic)

Ten grams of 2-benzoyl amino furan (Method II) was dissolved in 100 cc. of 5% potassium hydroxide solution, by heating under reflux almost to the boiling point for 8-10 minutes. Immediately after solution was accomplished, the material was transferred to a steam distillation apparatus, and distilled, with distillate being received in an excess of 6 N. hydrochloric acid. The acidic distillate was evaporated to dryness and two grams of a crystalline precipitate were obtained. Analysis for nitrogen: calculated --11.75% (based on amino furan hydrochloride) found --24.93%. This corresponds almost exactly to the nitrogen content of a onium chloride.

The residual liquor from steam distillation was moderately deep red in color. It was made acidic with excess phthalic anhydride, then steam distilled. The distillate was acidic to litmus, and the following Nucleus constants were obtained for successive ten cubic centimeter portions from the redistillation of 100 cc. of distillate; 4.62, 4.25, 4.04, 4.04.

According to accepted values for Nucleus constants (35) this was formic acid. By titration, the total steam
distillate contained 36.6 mg. calculated on basis of total acidity as formic acid.

Other products of basic hydrolysis were identical with those found from the acidic hydrolysis of 2-benzoyl amino furan.

A sample of steam distillate was received before it reached the hydrochloric acid, and reacted with benzoyl chloride made alkaline with sodium hydroxide. The product formed was benzamide; proving that the ammonia was not liberated after reaching the hydrochloric acid.

2-Propionyl amino furan

Nine and six tenths grams (.088 mole) 2-furyl isocyanate was added drop-wise, with stirring, to an ethereal solution of .2 mole of ethyl magnesium bromide, cooled to 0°. The resultant product was hydrolyzed with 15% ammonium chloride, and the aqueous layer extracted with ether. The combined ethereal extracts were dried over calcium sulfate, and the ether was then removed by distillation. The residual liquid was distilled under reduced pressure, and the light yellow oil that later turned to a solid mass was recrystallized from dilute ethyl alcohol. B.P. --- 154°/12 mm.; M.P. --- 90.5-91°; Yield --- 10.8 g. or 88.5%
Analysis for $C_7H_9O_2N$:

<table>
<thead>
<tr>
<th></th>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>60.45%</td>
<td>59.98%</td>
</tr>
<tr>
<td>H</td>
<td>6.52%</td>
<td>6.61%</td>
</tr>
<tr>
<td>N</td>
<td>10.07%</td>
<td>9.93%</td>
</tr>
</tbody>
</table>

Hydrolysis of 2-Propionyl Amino Furan (Acidic)

Five grams of 2-propionyl amino furan was added to 100 cc. of 5% sulfuric acid, and gently heated under reflux until solution was complete. This required only a few minutes. The orange solution was made slightly alkaline with solid sodium carbonate, then steam distilled. The distillate was received in an excess of 6N hydrochloric acid, which was subsequently evaporated to dryness. A crystalline residue with 24.75% nitrogen was obtained. It failed to char with hot sulfuric acid and proved to be almost pure ammonium chloride.

The residual liquid from steam distillation formed no phenyl hydrazone. The furan nucleus appeared to have suffered the same fate as in the acidic hydrolysis of 2-benzoyl amino furan; namely, propionic acid, ammonia and decomposition products were formed.
Hydrolysis of 2-Propionyl Amino Furan
(Basic)

Eight grams of 2-propionyl amino furan in a suspension of 100 cc. of 3% barium hydroxide was heated for two hours on a water bath under reflux, until solution was complete. A small amount of amorphous material remained as a residue which was removed by filtration.

A strong odor of ammonia was in evidence. The solution was subjected to steam distillation with distillate being received in an excess of 6N hydrochloric acid. One and a half grams of a salt was obtained on evaporation to dryness of the acidified distillate. This salt proved to be ammonium chloride.

The residual liquid from steam distillation was made acidic by adding an excess of phthalic anhydride, then steam distilled. From the distillation of a 100 cc. sample of the distillate and examining successive 10 cc. portions, the following Duclaux constants (33) were obtained, based on percent of total acidity in each 10 cc. portion: 12.46, 11.86, 11.45 and 10.58. These are in close agreement with accepted values for propionic acid.

The same decomposition of the furan nucleus as was observed with acidic hydrolysis of 2-propionyl amino furan was in evidence.
2,2 Difuryl Urea (Sym.)

Four and six tenths grams of 2-furyl isocyanate was added slowly with rapid stirring to 50 cc. water previously cooled to 5°. The oily liquid readily gave place to colorless crystals of 2-furyl carbamic acid. This crystalline substance was extremely unstable, and decomposed spontaneously at room temperature with evolution of carbon dioxide and liberation of heat. The residue remaining consisted of small, light yellow crystals which were separated by suction filtration, then recrystallized from dilute ethyl alcohol. Yield: 70%; M.P. ---190° (decomp.)

Analysis for C₉H₇O₇N₂:

<table>
<thead>
<tr>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C - 48.20%</td>
<td>C - 49.04%</td>
</tr>
<tr>
<td>H - 3.57%</td>
<td>H - 3.85%</td>
</tr>
<tr>
<td>N - 14.58%</td>
<td>N - 14.28%</td>
</tr>
</tbody>
</table>

This material was obtained whenever 2-furyl isocyanate was exposed to the moisture of the atmosphere. It required only one molecule of water to decompose two molecules of 2-furyl isocyanate.

2-Furyl Barium Carbamate

To 300 cc. of 3.5% solution of barium hydroxide cooled to 0°, 9.4 g. (.0272 mole) 2-furyl isocyanate was added
drop-wise with vigorous stirring. A mass of rhombic plates was obtained which was separated by suction filtration, washed with cold water, then dried over barium oxide. The crystals, interspersed with more amorphous solid, turned brown on standing a few hours, presumably due to decomposition. In spite of numerous attempts to separate the 2-furyl barium carbamate from barium hydroxide completely, a small amount of the latter was retained. The barium salt decomposed in warm water, preventing purification by recrystallization. In analysis, the small amount of barium hydroxide was corrected for on basis of water resulting from the combustion. A correction was also made for the carbon remaining as barium carbonate.

After making the above corrections, the following analysis was obtained (C<sub>10</sub>H<sub>6</sub>F<sub>6</sub>NaN<sub>2</sub>Ba):

<table>
<thead>
<tr>
<th></th>
<th>Calculated</th>
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<tbody>
<tr>
<td>C</td>
<td>36.84%</td>
<td>30.10%</td>
</tr>
<tr>
<td>H</td>
<td>2.07%</td>
<td>2.65%</td>
</tr>
<tr>
<td>N</td>
<td>35.21%</td>
<td>35.30%</td>
</tr>
<tr>
<td>Ba</td>
<td>7.20%</td>
<td>6.91%</td>
</tr>
</tbody>
</table>

Barium was determined as the sulfate, and nitrogen by the Kjehldahl method. Yield --- 13.5 g. or 39.9%.

**Thermal Decomposition of 2-Furyl Barium Carbamate**

Twenty four and nine tenths grams of 2-furyl barium
carbamate, dry and pulverized, was placed in a 200 cc.
balloon flask fitted with a delivery tube that terminated in
a 125 cc. distillation flask used as a receiver. The dis-
tillation flask was cooled in an ice bath, and the system
was maintained at 10 mm. pressure. The temperature of the
reaction flask was gradually increased by means of an oil
bath. At 275-300°, noticeable decomposition was evidenced
by considerable charring in the reaction flask. A few drops
of a viscous oil came over that reacted with benzoyl chloride
to form a chocolate brown product that in no way resembled
2-benzoyl amino furan. The greater portion of the starting
material remained in the reaction flask, with a polymerized
material being condensed in the soda lime tube.

2-Furyl Potassium Carbamate

To 75 cc. of 35% potassium hydroxide, heated to 50°
and maintained in an atmosphere of nitrogen, 8.7 g. (.08
mole) 2-furyl isocyanate was added slowly, in small drops,
and with vigorous stirring. Stirring was continued for
fifteen minutes after the addition of the last of the 2-furyl
isocyanate. Then the mixture was cooled in an ice bath and
the crystals separated by suction filtration. Although the
solution was somewhat red in color, the needle shaped crys-
tals were colorless. The material was pure enough for sub-
sequent use, but turned brown on standing a few hours. A sample for analysis was washed with cold methyl alcohol. Yield — 10.8 g. or 81.8%. Analysis for $\text{C}_5\text{H}_6\text{O}_3\text{N}_K$:

<table>
<thead>
<tr>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C - 36.34%</td>
<td>C - 36.03%</td>
</tr>
<tr>
<td>H - 2.44%</td>
<td>H - 2.90%</td>
</tr>
<tr>
<td>N - 8.48%</td>
<td>N - 8.60%</td>
</tr>
<tr>
<td>K - 23.68%</td>
<td>K - 23.49%</td>
</tr>
</tbody>
</table>

A correction was made for the carbon that remained as potassium carbonate.

2-Furyl Methyl Urethane

That the furan nucleus remained intact during the preceding preparation was shown by the conversion of 2-furyl potassium carbamate into 2-furyl methyl urethane by means of dimethyl sulfate.

To a solution of 4 g. 2-furyl potassium carbamate in 100 cc. water, containing 5 cc. 10% sodium hydroxide, dimethyl sulfate, 3.5 g., was added with stirring. The solution was agitated for thirty minutes at room temperature, then for thirty minutes at temperature of the steam bath. The solution was extracted with ether; ether extract dried over solid sodium hydroxide, then distilled under reduced pressure after the removal of ether at atmospheric. Yield -- 21.0% Analysis for nitrogen—calculated—9.93%.
Found --9.47%. The methyl urethane prepared in this way was identical with that prepared by the method of Curtius and Leimbach (21) by the refluxing of 2-furyl azide with absolute methyl alcohol.

**Ethylation of 2-Furyl Potassium Carbamate**

A solution of 20 g. (.121 mole) 2-furyl potassium carbamate in 50 cc. of water was cooled to 10°. To this solution was added, with stirring, 28 g. (.175 mole) ethyl iodide. Stirring was continued for two hours with no evidence of a reaction. The flask was carefully heated under reflux to 50-60°. An evolution of carbon dioxide and ammonia was effected with a deposition of ammonium carbonate in the condenser. The solution turned red; the color becoming more intense as the reaction proceeded. After the decomposition of the last of the ethyl iodide, the solution was steam distilled into hydrochloric acid. Ammonia and a small amount of ethyl amine were found to be the only volatile products of the reaction. There was no ethyl amino furan, nor any basic material in the reaction products that would form an insoluble picrate.

**2-Furyl Amine Hydrochloride**

Eight and three tenths grams (.05 mole) 2-furyl
potassium carbamate was dissolved in the least amount of water at room temperature. Two grams of animal charcoal were added then rapidly removed by filtration. This operation removed phenyl ether that contaminated the 2-furyl isocyanate, also 2,2 furyl urea formed by the action of aqueous potassium hydroxide.

The clear solution, cooled to 0°, was cautiously made acidic with 6N hydrochloric acid. A vigorous evolution of carbon dioxide ensued which soon ceased, then the clear solution was evaporated to dryness under reduced pressure. The crystalline residue was dried to constant weight. Although, the weight was within 1 g. of the theoretical weight, based on equivalent molecular quantities of potassium chloride and 2-furyl amine hydrochloride, crystals were somewhat red in color, indicating ring-rupture to some extent at least.

2-Furyl Amine Sulfate

Sixteen and five tenths grams (.1 mole) 2-furyl potassium carbamate were dissolved in the least amount of water at room temperature, and two grams of animal charcoal were added. The mixture was filtered and filtrate cooled to 0°.

The clear slightly red colored solution was cautiously
made acidic with 6N sulfuric acid that had been previously cooled to 0°. A vigorous evolution of carbon dioxide ensued, and a crystalline precipitate settled out. This was filtered and proved to be almost pure potassium sulfate. The filtrate was reduced to half its volume under reduced pressure and another crop of crystals was obtained. The mass of crystals was filtered, dried over phosphorous pentoxide, then extracted with absolute methyl alcohol. The crystals obtained in this way were highly hygroscopic, still impure, and difficult to analyze.

Ten grams of the dry crystalline mass from the second crop of crystals was treated with 25-30 cc. of liquid ammonia. After evaporation of the ammonia at room temperature, the residue was extracted with dry ether. On evaporation of the ether, nothing was obtained as a residue or in the distilled ether, showing there was nothing less basic than ammonia in the mixed salts.

The residue left after the ether extraction was dissolved in cold concentrated sodium hydroxide. An evolution of ammonia resulted that caused considerable foaming. An ether extract of this solution gave a floculent precipitate on standing in contact with the air. This precipitate was only slightly soluble in ether, very soluble in water, soluble in alkali with evolution of a gas which proved to be oxygen. The precipitate was presumably a
peroxide.

An alkaline solution of this precipitate made slightly acidic with acetic acid, and then condensed with phenyl hydrazine, gave a phenyl hydrazone in the form of colorless leafy crystals that were recrystallized from ethyl alcohol. M.P. —227° (decomp.). Molecular weight was determined by Fast method. The nitrogen was determined by a modification of the Kjehldahl by Phelps and Pandit (36) adapted to semi-micro work.

Analysis \( \text{C}_{10}\text{H}_{10}\text{ON}_2 \):

<table>
<thead>
<tr>
<th></th>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>14.73%</td>
<td>14.73%</td>
</tr>
<tr>
<td>G.M.H.</td>
<td>190.0</td>
<td>174.5%</td>
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</table>

When either the amine sulfate or the amine hydrochloride was neutralized with sodium hydroxide, in very dilute solutions, in an attempt to prepare 2-amino furan, the result was the same; ammonia was liberated and a

Note: The modification of the Kjehldahl method for nitrogen determination was so great that its insertion here is warranted.

Fifty milligram samples were employed and subjected to the following treatment: dissolved in 5 cc. ethyl alcohol to which was added 5 cc. formaldehyde, 2 g. zinc dust, and 10 cc. concentrated hydrochloric acid, then digested under reflux for fifteen minutes. An equal volume of water was added, and a chip of clay plate. The solution was evaporated until dense fumes of sulfur trioxide appeared. Potassium sulfate and copper sulfate were added as catalysts, then the procedure for an ordinary Kjehldahl determination was followed.
ketone was produced. When a portion of this solution was treated with ammoniacal silver oxide, a silver mirror was produced, but no precipitate of silver acetylide was obtained in the phenyl hydrazone (by molecular weight determination).

In the formation of the phenyl hydrazone, a solution that was too basic tended to decompose the furan nucleus completely. Hence, a greater yield of the phenyl hydrazone was obtained when the base used was sodium carbonate instead of sodium hydroxide. The latter was found to decompose aqueous solutions of the hydrazone. After a solution of the amine salt and phenyl hydrazine, made acidic with acetic acid, was made slightly basic with sodium carbonate, ammonia was removed by passing in steam. However, it was ascertained that no volatile constituent except ammonia was obtained by first receiving a portion of steam distillate in hydrochloric acid, then evaporating it to dryness. In every case, ammonium chloride was the product.

The residual liquid from the above steam distillation was made slightly acidic with acetic acid, then condensed with phenyl hydrazine. After recrystallization from ethyl alcohol, this phenyl hydrazone was found to possess the following characteristics: crystals in the form of colorless plates, moderately soluble in alcohol, very soluble in ether, unstable in the presence of tenth normal sodium
hydroxide, decomposed easily when subjected to oxidation with neutral sodium dichromate with liberation of nitrogen and deposition of a black precipitate. Then subjected to combustion in a stream of oxygen, a residual plastic was obtained in every case. This residue failed to yield to oxidation when mixed, thoroughly with each of the following compounds, then heated to redness in a stream of oxygen: cupric oxide, lead peroxide, and potassium chlorate. Potassium chlorate caused an explosion when heated with the original compound, but had little effect when fused with the residue formed by heating the hydrazone in a stream of oxygen. This made analysis of the hydrazone for hydrogen and carbon impossible.

The following parallel reactions in the benzene series were performed to bear out the correctness of the method of degrading an acid chloride to an amine.

**Benzoyl azide**

28.1 g. (.2 mole) benzoyl chloride in an ether suspension was cooled in an ice bath. To this was added with stirring 13 g. (.2 mole) sodium azide dissolved in water. After 4 hours stirring, no condensation was observed. One tenth of a gram of SnCl₂ caused complete condensation within one hour, aided by chilling the reaction mixture.
The white, crystalline precipitate was separated by suction filtration, washed with cold water, then dried in a vacuum desiccator over $\text{P}_2\text{O}_5$. Yield --- 30.1 g. or 68.3%.

Phenyl Isocyanate

Twenty and one tenth grams of benzoyl azide, in a solution of 25 cc. of phenyl ether, was cautiously heated until the evolution of nitrogen ceased, then distilled. B.P. --- 164°. Yield --- 15.1 g. or 92.6%.

Phenyl Potassium Carbamate

Fifteen and one tenth grams (.136 mole) phenyl isocyanate was added drop-wise, and with vigorous stirring to 75 cc. of 35% potassium hydroxide solution, maintained at 50°. When the odor of phenyl isocyanate was no longer in evidence stirring was discontinued, and the solution cooled. A voluminous precipitate of colorless plates was obtained. These were collected by suction filtration then dried. Yield --- 14.9 g. or 62.6%.

A small amount of aniline was found in the mother liquor.

Aniline

Ten grams (.057 mole) phenyl potassium carbamate was
dissolved in 75 cc. of water. The solution was cooled to 0°, and concentrated sulfuric acid was added drop-wise with shaking until decidedly acidic. A vigorous evolution of carbon dioxide ensued. The cold solution was extracted with ether to remove any phenyl ether that may have contaminated the potassium carbamate. A 30% solution of sodium hydroxide was added until the solution was decidedly basic, then steam distilled. The aniline was recovered from the distillate by extraction with ether, after which the ethereal solution was dried over potassium hydroxide, then fractionally distilled. B.P. --- 180-1°; Yield--3.8 g. or 71.7%.

2-Ethyl Furazide

A mixture of 112 g. (.80 mole) 2-ethyl furate and 100 g., 49°, (.57 mole) hydrazine hydrate was refluxed in a half liter balloon flask on steam bath for seven and a half hours.

After about 50 cc. of solution had been removed by distillation, the residual liquid was cooled in an ice bath, and the solid, crystalline mass was subsequently obtained by suction filtration. This material was sufficiently pure for use. However, a small portion was recrystallized from methyl alcohol-benzene. Colorless needles were obtained. M.P.---76-7°. M.P. ---145-8°/8mm.; Yield--96.02%.
CONCLUSION
1. The following new compounds were prepared and characterized: 2-furyl isocyanate, 2-benzoyl amino furan, 2-propionyl amino furan, 2-furyl barium carbamate and 2-furyl potassium carbamate.

2. Partial evidence was developed indicating the preparation of the following new compounds: 2-amino furan sulfate, 2-amino furan hydrochloride, alpha oxydihydro furan, alpha hydroxy furan, alpha hydroxy furan peroxide, alpha oxy beta hydroxy dihydro furan and beta hydroxy alpha dihydro phenyl hydrazone.

New or modified methods have been described for the preparation of the following: 2-furoyl azide, 2,2-difuryl urea, 2-furyl methyl urethane and aniline.

Additional information has been secured concerning the stability of the furan nucleus in the absence of stabilizing groups, the mechanism of the decomposition of an acid azide and the hydrolysis of substituted alpha amino furans.

3. Evidence has been developed indicating that the isolation and retention of free alpha amino furan is unlikely, and perhaps impossible.
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Major Field: ORGANIC CHEMISTRY


APPROVED:

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Major Professor and Chairman

Dean of the Graduate School

EXAMINING COMMITTEE:

[Signatures]

Date: March 20, 1937