

PREPARATION OF ALLOPHANIC ESTER,  
ITS REACTIONS WITH AROMATIC AMINES.

A THESIS SUBMITTED TO THE FACULTY OF THE GRADUATE  
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BY

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### ABBREVIATIONS .

The customary well known abbreviations have been used for the journals. In the case of reagents, the usage of Chemical Abstracts has been adopted, thus EtOH = Alcohol, Et<sub>2</sub>O = Ether, etc. For solubilities, the initials i. s., v. s., and etc have been used to show the relative solubility.

PREPARATION OF ALLOPHANIC ESTER.

ITS REACTIONS WITH AROMATIC AMINES.

THEORETICAL PART.

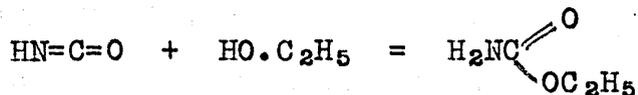
Allophanic Ester, the Ethyl ester of Allophanic acid, was first prepared by Liebig and Wöhler, and subsequently has been made by many investigators. Its preparation has, however, usually resulted from a research upon other topics, or has been purely accidental. Very little work has been done with the compound directly.

The present research was conducted with two ends in view, - first, to find a convenient laboratory method for the preparation of the ester with a good yield, - second, to study the reactions of the ester with various aromatic amines; determine the course of the reaction, and the resulting products.

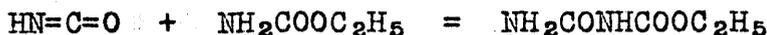
It may be mentioned that Allophanic acid finds its practical application in medicine, - its salts are all tasteless and odorless, and it decomposes in the body to inert compounds; hence it can with safety be used to neutralize medicines with a nauseating taste or odor.

## SYNTHESES OF ALLOPHANIC ESTER.

If Alcohol be treated with Cyanic acid, the first product is Urethane,--



The further introduction of Cyanic acid results in the production of Allophanic ester,--



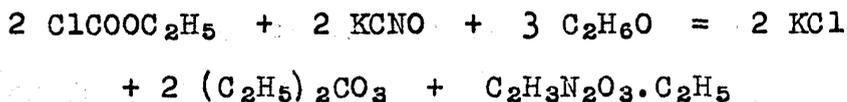
This is the method of synthesis employed by Liebig and Wöhler (P 20,396) (Original paper not read), and is the basis for several methods used by other investigators, which will be mentioned. In all probability it is not a practical method, and no mention could be found in the literature of its having been repeated. It was not tried in the course of this work, but the similar reactions mentioned above have been carried out.

Amato (J 1873,749) gives the following directions for the preparation of the ester,--dissolve 50 grams of KCNO in 300 ccs of 65% Gay-Lussac Alcohol, add HCl to acid reaction, and reflux for two days. Distill off the Alcohol, and extract the residue with Ether. This method was tried twice with negative results. A third trial

with purified KCNO gave the same results,--no ester could be isolated.

(2) Saytzeff (A,135,230) uses 90% Alcohol,with KCNO, and Chloroacetic acid,with directions for 15 hours refluxing. This is virtually the same as the method of Amato.

(3) Wilm (A,192,2~~3~~<sup>4</sup>) similarly uses KCNO,Alcohol,and Chloroformic ester. Presumably these are heated for some time,though no directions are given. The reaction mixture is treated with water,which salts out the ester,and the remaining portion is extracted with Ether. The following empirical equation is given for the reaction,--



The equation for (2) would be as follows,--

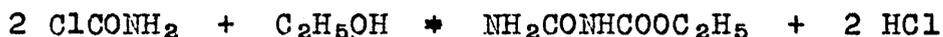


These reactions are practically similar with those given, the addition of the Chloroformic ester in (3) serving no useful purpose so far as the yield of Allophanic ester is concerned. Neither of the above two reactions was repeated in this work.

(4) In order to shorten the reaction and improve the yield,the following synthesis was attempted,--20 g of Urethane,20 g of KCNO,120 ccs of 95% Alcohol,and 20 ccs

of water, (making about 74% Alcohol), were mixed together,<sup>4</sup>  
made slightly acid with HCl, and refluxed for some hours.  
The reaction mixture was tested from time to time, but af-  
ter two days, there was still no evidence of production of  
any Allophanic ester.

Preparation of the ester from Chloroform-  
amide and Alcohol is described by Gatterman (A, 244, 38)  
Also noted by Werner (J Chem Socy II 3, 696, 1918).



The Alcohol is added slowly, as the heat of reaction is  
great. Production of HCl quantitative. It would appear  
that this is a good method of synthesis, but it did not  
appear practical in the present instance to make the  
Chloroformamide.

Somewhat similar to the above is the  
method of Folin (Am I 9, 341) which employs Chloroformyl  
Urethane and  $\text{NH}_3$ , --



This method was not repeated as it did not appear ad-  
visable to prepare the starting materials.

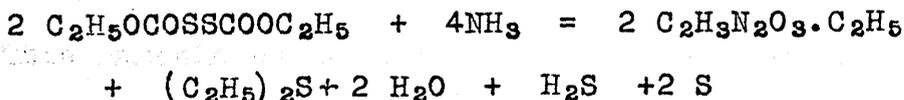
Other methods mentioned in the litera-  
ture, but not repeated in this work, are as follows, ---

(I) KCNS and Chloracetyl Urea in Alcoholic solution  
(Fredrichs, C 1899, 2, 287)

(2) Nitrogen Tricarboxylic Ester and 25% NH<sub>3</sub> (Diels, B,36,743). A fair yield is claimed, and directions given for the preparation of the starting product. It seemed, however, to be too involved a process, and too time consuming to be practical.

(3) Evaporation of C<sub>6</sub>H<sub>5</sub>CH(OH)CON<sub>3</sub> with Alcohol (Curtius and Muller, B,34,2798) No directions or data are given. Several equations are presented by the authors, but evidently no work was done by them to clear up the course of the reaction or to make it practical.

(4) Introduction of Ammonia into an Ether solution of Ethyl Carbonsulphide. (Debus, A,82,<sup>2</sup>56).



(5) Heating of Allophanic acid azide with Alcohol (Thiele, Uhlfelder, A 303,103)



An interesting synthesis is mentioned by Loeb (B 19,2344). After heating Phosgene with Urethane in Benzene solution in a sealed tube for some time, he noted on opening the tube a large production of HCl, and also found some Allophanic ester among the products. He suggests

that this could have been formed as here shown by the condensation of the Urethane,--



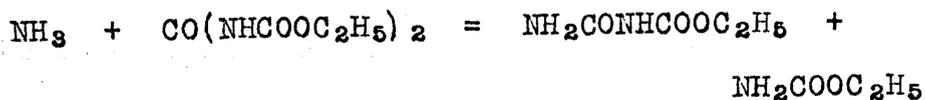
or perhaps that Carbonyl Diurethane was produced, which broke down during the crystallization. Unfortunately he does not state that he isolated any of the latter among the products, but this is to be inferred from the production of HCl,--



It is suggested that the following equations might show how the Allophanic ester was produced,--



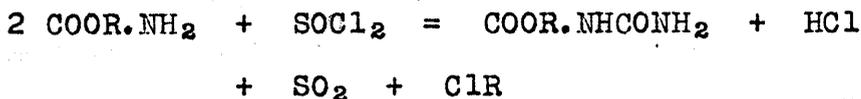
This Ammonia would then react with the Carbonyl Diurethane as shown below, to give Allophanic ester.



The latter reaction has been used by Dr. F.B. Dains as a practical method of making the ester, and gives a yield of about 80%. As the yield in making the Carbonyl Diurethane runs from 70-80%, the final yield is thus in the neighborhood of 60%, and the method would be practical in lack of a better one.

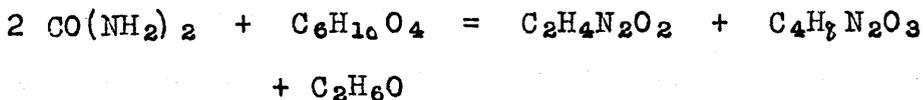
Lack of a supply of Phosgene prevented

carrying out this reaction, which would have been interesting to follow through; however, another synthesis, practically similar, was carried through, unfortunately with negative results. This is the method of Schroeter and Lewinski (B 26, 2172), in which Urethane is heated with Thionylchloride in Benzene solution. The directions were carefully followed, and several modifications afterwards introduced into the process, but no ester could be isolated. S and L offer the following equation to explain the reaction,--



A synthesis of the same type was attempted with Urethane and  $\text{S}_2\text{Cl}_2$  in Benzene solution. The results were negative.

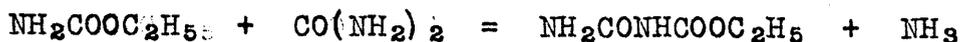
Hlasiwetz (A, 134, 116) describes a synthesis using Ethyl Oxalate and Urea, which produced Allophanic ester with a number of other products. This was tried several times, but no ester could be isolated. The main product in each case was Oxamide. The equation given by H, as follows,--



is only partial as  $\text{CO}_2$  is given off, also Ammonium Oxa-

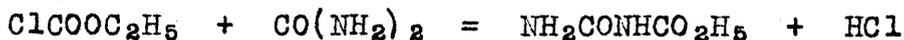
late is a product.

It was thought that the synthesis might be carried out by heating Urea with Urethane, according to the following equation,--



This reaction was carried out in several ways, the largest yield being 4.5%; therefore this method was dropped as being impracticable.

The greater portion of the Allophanic ester used in this work was made by the action of Chloroformic ester on Urea, a method probably used first by Wilm (A, I47, I55). The reaction was assumed to take place in this manner,--



and for this reason the first experiments were carried out with the use of Pyrridine, and Quinoline to absorb the HCl. The Urea and Pyrridine were placed in a flask under reflux, in an ice bath, and the ester poured down the tube. After some time heat was applied, and the reaction carried to completion. It was necessary in each case to recrystallize the product, especially with the use of Quinoline, which gave a very impure yield. The percentage of yield varied from 9.5% to 23%. The use of Acetone as a solvent did not improve the yield.

It was soon noted that the first heat of reaction was due to a side reaction between the Pyrridine and the Chloroformic ester, therefore the reaction was tried under the hood without the use of any Pyrridine. It was not necessary to use the ice bath in starting the reaction, and although the same went smoothly to completion, no HCl fumes were given off.

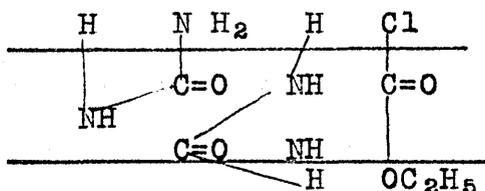
Review of the literature shows that this fact was observed by Schiff (A, 291, 372) but his conclusions regarding the reaction have been shown to be erroneous. He states that by the use of equal moles of Urea and Chloroformic ester he succeeded in producing 3.5 g of Cyanuric acid, some Ethyl Carbonate, and Ammonium Chloride, and Biuret, but no Allophanic ester. His directions are not specific, but he evidently heated for several hours, and states that he finally boiled the ester.

In a repetition of his work, 10 g of Urea, 20 g of Chloroformic ester were heated under reflux, one hour at about 80°, and one hour at the boiling point of the ester. An examination of the products showed Cyanuric acid present, some Cyanic acid, Ammonium Chloride, but no Ethyl Carbonate; moreover, 1 g of Allophanic ester of melting point 189°-190 was isolated from the lot.

Schiff reports an experiment using 2 moles of Urea to 1 of Ester, the end products being in this case, Cyanuric acid, Biuret, Ammonium Chloride. Also a small yield of Allophanic ester, 1 g from 6 g of Urea.

He states that it was very impure, hard to purify, and that this is a poor method for its preparation. The scheme which he gives for the production of the products he observed, and which is here copied, is ingenious but probably not correct. The production of Biuret, and Cyanic acid is easy to understand when we take into consideration the high temperature to which he heated a mixture containing Urea. At temperatures over  $90^{\circ}$ , the breaking down of Urea into  $\text{NH}_3$  and Cyanic acid is quite rapid (Werner, J Chem Socy 1916 -17)

Considerable polymerization of the Cyanic acid to Cyanuric acid would also occur at water bath temperature. It is highly probable that some of the Urea does react with the Chloroformic ester as previously set forth, with the production of  $\text{HCl}$ ; this with the  $\text{NH}_3$  from the breaking down of the Urea would account for the  $\text{NH}_4\text{Cl}$ . However the complete course of the reaction has still to be determined. The scheme mentioned is shown below,--

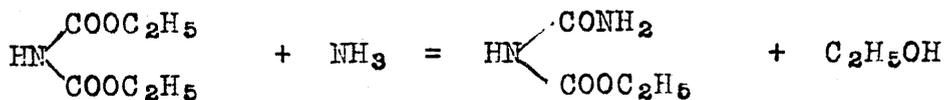


By varying the amounts of Urea taken with one mole of Chloroformic ester, it was shown that a proportion of 2.1 moles of the former to 1 of the latter would give the best yield, and at present this runs from

62-68% . Proceeding by the directions given in the experimental part of this paper, the Allophanic ester is produced with a melting point of 191°-2, and needs no further purification before use. The entire synthesis takes from 3 to 4 hours and is both simple and convenient.

Another method of synthesizing Allophanic ester which has been used to some extent in this work, is that reported by Maguin (Ann 8,22,1911 349,358) from Potassium Oxalo Carbonic Ureide and Ammonia. This method is quite complicated and rather uncertain, but if carefully watched it can usually be depended upon. The product is very pure, the yield rather low, usually about 22%, figured from the weight of Oxamethane used. Directions are given in the experimental part.

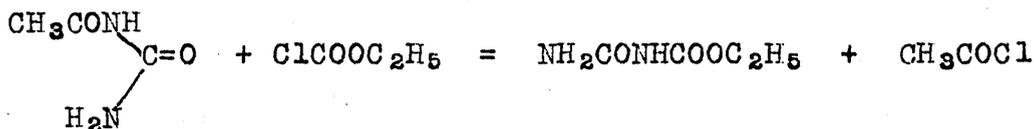
A synthesis which would probably work successfully is the reaction of Imido Dicarboxylic Ester and Ammonia, --



a method similar to the synthesis of Oxamethane later described. It is necessary to use Chloroformic ester to make the dicarboxylic ester, and the use of Urethane is called for as well, and shortage of materials prevented trying the synthesis. It would however be interesting from the theoretical standpoint.

Werner cites a method of making Acetyl

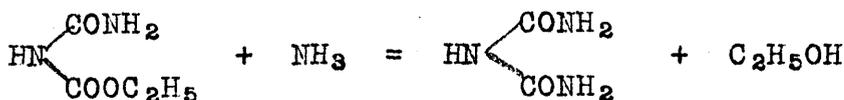
Urea by the use of  $H_2SO_4$  and Acetic Anhydride (J Chem Socy 113,622,1918) with 80% yield, and the reaction between Acetyl Urea and Chloroformic ester was tried to see if the final yield could be raised by synthesizing in this way. The yield never ran over 38%, thus this method is not as good as the direct treatment of Urea, assuming that Werner's yield of 80% could be realized.



### REACTIONS OF ALLOPHANIC ESTER WITH AMINES.

With Ammonia.

This reaction was carried out by Hoffmann (B4,265). As Allophanic ester is the monamide of Imido Dicarboxylic ester, it would be expected to react with  $NH_3$  to give the diamide (Biuret), --

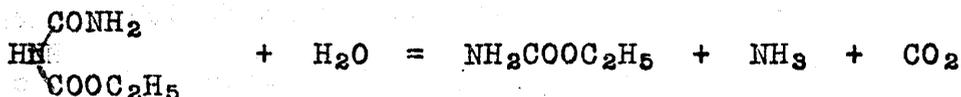


This result was realized, and it is likely that the heating in sealed tubes, as carried out by Hoffmann was entirely unnecessary; without doubt it would take place as well in Alcoholic solution, the only disadvantage here being the rather large quantity of solvent which would be required.

The reaction of Allophanic ester and Liquid  $\text{NH}_3$  was tried in this laboratory, with the assistance of Mr. Buffington. With perfectly dry materials no action was observed, and the unchanged ester was recovered after evaporation of the  $\text{NH}_3$ .

In another experiment 2 g of the ester and 2 ccs of water were used and about 100 ccs of Liquid  $\text{NH}_3$  put with the mixture. In this case also there was no action.

Hoffmann (B 4,265) found that Ethylamine would not react with Allophanic ester. Heated to  $160^\circ$ , the ester was hydrolyzed as follows,--



With Aniline.

The reaction with Aniline was studied by Hoffmann (loc. cit.) In carrying out the reaction he heated a mixture to boiling for some time, and isolated from it Diphenyl Biuret. He states that the " Monophenyl Biuret first formed, by exchange of Ammonia for Aniline had gone to the Diphenyl-". However there is a question upon this point; the Aniline may enter either group presented to it, the  $\text{NH}_2$  or the Ethoxy; Hoffmann assumed that the Ethoxy group was first displaced, and the logical thing would have

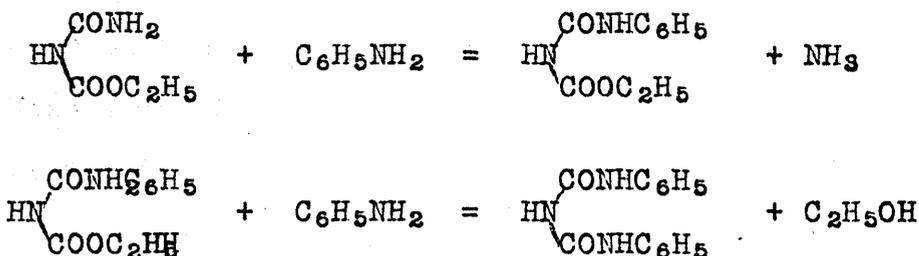
been to isolate Monophenyl Biuret from a mixture heated not quite so long or at so high a temperature.

Repeated attempts to isolate Monophenyl Biuret, or the analogous compounds in the case of Anisidin, Toluidine (ortho), or m-Nitranilin have all failed.

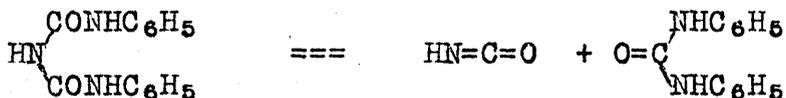
As a mixture of Aniline and Allophanic ester, equal moles, is heated,  $\text{NH}_3$  begins to come off at about  $115^\circ$ - $120^\circ$ , and if the heating is done under a reflux condenser, no alcohol will reflux at this time. This makes it evident that the  $\text{NH}_2$  group is first attacked, and by careful heating it is possible to isolate Phenyl Allophanic ester from the reaction mixture, as shown in the experimental part. Alcohol does not begin to reflux for some time even if the temperature is raised. Thus in one experiment at  $150^\circ$ ,  $\text{NH}_3$  was observed in 2 minutes, but Alcohol did not reflux until 18 minutes had passed, which will give some idea as to the manner in which the substitutions take place

The first reaction resulting in the production of Phenyl Allophanic ester is very slow, thus, in the experiment just mentioned,  $\text{NH}_3$  continued to come off for over 4 hours. In spite of this fact it is difficult to isolate more than .15 to .2 g of the Phenyl Allophanic ester from 5 g of starting material, this indicating that the second reaction, which forms Diphenyl Biuret, is fairly fast. As the first reaction takes so long for its completion, and the second follows rather closely upon it, the isolation of

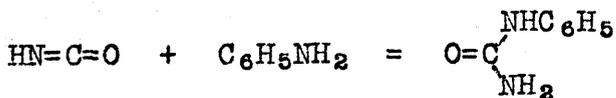
this intermediate product is rendered much harder than if the second reaction were a slow one, or requiring a higher temperature than the first. The two reactions are graphically as follows,--



In the presence of excess of Aniline, Diphenyl Biuret will, break down, giving Mono- and Diphenyl Ureas. Probably the substituted biuret breaks down as simple Biuret would, giving Diphenyl Urea and Cyanic acid,--



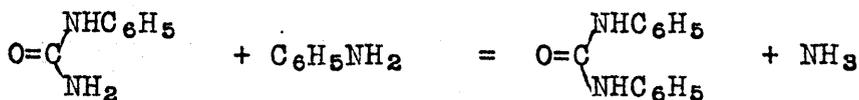
the latter uniting with Aniline to give Monophenyl Urea, as Cyanic acid and  $\text{NH}_3$  unite to form Urea,--



These reactions involving a splitting of the molecule as well as a substitution, require a higher temperature, as is shown in the experimental part.

The reaction between Monophenyl Urea and excess of Aniline to give Diphenyl Urea follows next

in order,--



and as this reaction is rather rapid, it is a matter of some difficulty to isolate any great amount of Monophenyl Urea from the reaction mixture. In no case was more than .1 to .2 g isolated, usually much less than this amount.

Theoretically there is the possibility of the formation of still other compounds by reaction of Allophanic ester and Aniline. Thus, as shown below, the first products might be Phenyl Urea and Urethane,--



As secondary products in this reaction, with excess of Aniline we would have,

- (1) Phenyl Urea + Aniline = Diphenyl Urea
- (2) Urethane (heat) = Cyanic acid + Alcohol
- (3) Cyanic Acid + Aniline = Phenyl Urea (see I)

The final products here would be Diphenyl Urea, Alcohol and Cyanic acid or its polymers.

Another possibility is the production of Urea and Phenyl Urethane,--

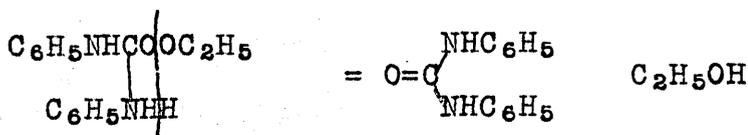


Here again the final products would result from further action of the Urea and an excess of Aniline, and also the breaking down of the Phenyl Urethane, the final products being Cyanic acid or its polymers, Diphenyl Urea, and Alcohol.

The production of Cyanic acid in the presence of excess of Aniline might also lead to the production of Phenyl Cyanuric acid in either of these cases.

Actually, none of the higher melting polymers of Cyanic acid were observed, neither were any Urethanes isolated. However it may very well be the case that the Alcohol produced in the reactions came from the breaking down of Phenyl Urethane. In this case the complete series of reactions would be,--

- (1) Allophanic ester + Aniline = Urea + Phenyl Urethane
- (2) Urea + Aniline + Phenyl Urea + NH<sub>3</sub>
- (3) Phenyl Urea + Aniline = Diphenyl Urea + NH<sub>3</sub>
- (4) Phenyl Urethane + Aniline = Alcohol + Diphenyl Urea,--



(NOTE) In the experiment previously mentioned on page 14 in which NH<sub>3</sub> was produced for 4 hours the final product was Diphenyl Biuret. Thus equation (3) above does not explain its continuous production.

With o-Anisidine.

The reactions between Allophanic ester and the following--o-Anisidine, o-Toluidine, m-Toluidine, and m-Nitranilin were precisely analogous with the reaction already taken up for Aniline. There seems therefore no logical reason why they should be taken up in detail. The conditions found necessary for the promotion of the different phases of the reactions, in order to secure appreciable yields of the intermediate products, will be found in the experimental part.

In the case of p-Bromaniline, difficulties have been encountered, which have as yet not been overcome. The reaction appears to proceed in the same way as with the Amines already studied. The products, however, have no constant melting point, and the practical insolubility of several has made purification extremely difficult of accomplishment.

From the observations made it can be said that in this case the reaction is initiated at a much lower temperature than with the other Amines studied,  $\text{NH}_3$  coming off freely at  $115^\circ$ . In general the course of the reaction appears to be more rapid. Further work will be done with this compound.

SUBSTITUTED ALLOPHANIC ESTERS.

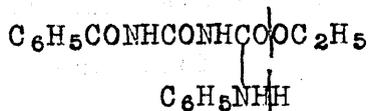
## Benzoyl Allophanic ester.

This was made by the method of Kretzschmer, (B 8,104), with a yield of 17%, also by the method of Pechman and Vanino (B 28,2833), which did not give so good a yield, but is on the whole a more convenient way to prepare the ester. As no changes were made in the original methods, they are not repeated in the experimental part.

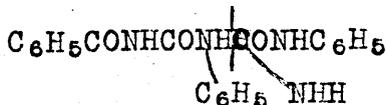
## Benzoyl Allophanic ester and Aniline.

This experiment was undertaken to ascertain what effect would be produced by "blocking" the  $\text{NH}_2$  group of the Allophanic ester. Various interesting possibilities present themselves,--

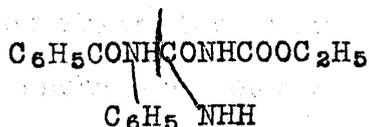
(I) The Ethoxy group might be attacked with the production of Alcohol and Phenyl Benzoyl Biuret, as indicated,--



An XS of Aniline would here work on the Biuret, with the final production of Benzoyl Phenyl Urea, and Monophenyl Urea,--

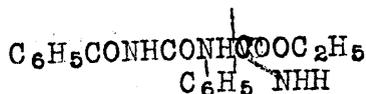


(2) If the Benzoyl group were attacked, either Benzamide or Benzanilide would be the first product. In either case, XS of Aniline would produce Benzanilide as a final product. Allophanic ester would also result which could react with the Aniline to give the series of products already taken up.



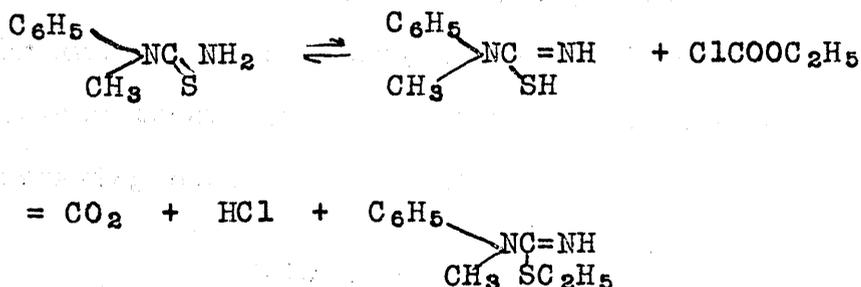
(3) If Phenyl Benzoyl Biuret were produced as in (I), it is likely that in breaking down, this compound would liberate Cyanic acid, and there would be an opportunity for the production of polymers of Cyanic acid.

The reaction between Benzoyl Allophanic ester and Aniline was found to give Benzoyl Phenyl Urea which was identified by analysis, and by mixed melting points as well. The other product of the reaction was undoubtedly Urethane, which at the heat of this reaction was broken down to Cyanic acid and Alcohol. The filtrate gave a positive Iodoform test for Alcohol, and a small amount of product melting over  $230^\circ$  was isolated, which could have been a polymer of Cyanic acid. There was not sufficient to analyze. Werner (Articles 1916-17 in J Chem Socy) has shown that Urethane slowly refluxed, will decompose to Cyanic acid and Alcohol.



## Phenyl Methyl Thioallophanic ester.

Various attempts were made to prepare this compound by reaction of unsymmetrical Phenyl Methyl Thio-urea and Chloroformic ester. When the two were heated together, without a solvent, a clear red gum resulted, from which the greater part of the Urea could be recovered unchanged. Addition of  $\text{NH}_3$  to the filtrates freed an oil with a strong odor of a Thio Ether.  $\text{HCl}$  seemed to be a product during the heating. The following equations are suggested,--



The use of Acetone as a solvent, and the employment of higher temperatures did not secure any difference in results.

In another experiment Acetyl Chloride was heated with the Urea, and a gummy product obtained, which would not clean up with water, Benzene, Ether, Gasoline, or Alcohol. It was therefore treated impure with XS of Chloroformic ester, and a lively reaction resulted after heating a short time. A reddish gum was obtained, entirely soluble in Alcohol, from which, on salting with

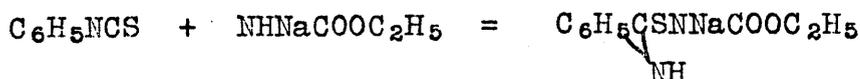
water there was obtained a very small amount of an impure brown compound melting at about 155°. The nature of this compound has not yet been determined.

#### Benzyl Phenyl Allophanic ester.

Pure unsymmetrical Benzyl Phenyl Urea was prepared from Benzylaniline and KCNO in glacial Acetic acid and treated at various temperatures, and with several modifications, with Chloroformic ester. The only product isolated was a small amount of a pinkish crystal of melting point over 270°. It seems quite evident that the Urea broke down instead of coupling with the ester. With larger amounts of starting materials it would have been possible, without doubt to isolate other products, from the breaking down of Urea and Urethane.

#### Thioallophanic ester. (Substituted)

Synthesis of this compound was attempted from reaction of Sodium Urethane and Phenyl Mustard oil in Ether solution. The reaction expected was,--



However the experiment was without success, and the chief product was Phenyl Thiourethane, which was identified by mixed melting point with a known sample.

### Acetyl Allophanic ester.

This compound is described by Seidel (J Pr Chem (2) 32,273) who made it by heating Allophanic ester and Acetyl Chloride in a sealed tube at  $80^{\circ}$ - $100^{\circ}$ . A repetition of his work, for which he gives very few directions failed to give any yield for 2 hours heating. After 4 hours heating of equal moles at  $120^{\circ}$ , a yield of .4 g of Acetyl Allophanic ester, melting at  $103^{\circ}$  was obtained. As 5 g of Allophanic ester had been used as starting material, another method of synthesis was obviously necessary for laboratory production.

Acetyl Chloride and Allophanic ester were heated under reflux, under various conditions, with and without the use of a solvent, and with the use of Pyrridine, to temperatures as high as  $175^{\circ}$ . However, no practical yield was obtained.

The same reagents were also heated to  $100^{\circ}$  in a pressure flask, both with and without the use of Pyrridine. Results were negative.

The synthesis was attempted, using Acetyl Urea and Chloroformic ester, with and without Pyrridine, at various temperatures. Results negative.

A mixture of Urethane, Pyrridine, and Acetyl Chloride was heated for 6 hours on the water bath and at the conclusion of this time appeared to contain

crystals of the Acetyl ester on cooling. Before an examination could be made the contents of the flask were lost through accident, and a repetition of the experiment gave negative results. It is believed, however, that this synthesis will give better results than those previously tried, and further work will be done to perfect it, and obtain a practical yield, after which the customary reactions with Amines will be carried out.

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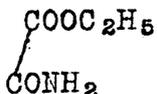
EXPERIMENTAL PART.

## Preparations.

## Allophanic Ester.

One mole of Chloroformic ester is poured onto 2.1 moles of Urea in a round bottom flask, which is at once connected with a reflux made ready, and refluxed over the water bath for at least half an hour past the time when drops cease to fall. This generally takes from 2 to 3 hours. Water is added to the hot mass, which is at once filtered with suction, and again washed with cold water. Can be air dried under the hood. Melting point runs from 189° to 192°, according to the purity of the Urea. The yield from 62% to 65%, figured from the ester.

## Oxamethane.



Dissolve one mole of Ethyl Oxalate in 2 to 3 Volumes of Alcohol, keep at 0° and pour in 1 mole of Alcoholic NH<sub>3</sub> very slowly. The yield will be increased if this addition be made over a very long period, say 3 or 4 hours. The precipitate is washed with Alcohol and air dried. Reported m.p. is 114°-5, actual 114°. Yield 82%. The Alcoholic NH<sub>3</sub> should be titrated just before using. A

strength of 2 to 3.5 N is satisfactory.

#### Allophanic ester (Maguin method)

Dissolve 59 g of Acetamide in 160 g of Bromine, put in a freezing mixture, and add slowly 112 g of KOH in 500 ccs of water. Add 117 g of Oxamethane and heat on the water bath to 40°. Filter at this point if necessary. An ice bath should be at hand and the mixture kept at 40° by frequent immersion thereafter. In from 1 to 2 hours the reaction is completed, however the yield is better if the mixture be left for some hours, preferably over night. The addition of concentrated  $\text{NH}_3$  precipitates Allophanic ester, the precipitation being complete in about an hour. M.p. 190-191°. Yield, figured from the Oxamethane is usually about 22%.

#### Reaction Products.

These reactions were carried out for the most part in large test tubes, which were heated in a paraffin bath. Large amounts of material could not be used on account of shortage of starting materials to make the ester. In those cases where enough was run through to preserve a sample, the fact is noted.

Allophanic ester and Aniline.

(I) Phenyl Allophanic ester.



5 g of ester and a slight XS over 1 mole of the amine were heated to 120°-125° for one hour. The mass was well washed with cold dilute NaOH several times, the filtrates combined, and acidified with dil HCl. This precipitates the substituted ester as a white mass, which is recrystallized from EtOH in small white crystals, melting at 104°. Phenyl Allophanic ester had been prepared by Dr. Dains from the reaction of Phenyl Isocyanate and Urethane; this compound had been analyzed and found correct. Its melting point was 104°. When mixed with the compound prepared as above described, the m.p. observed was 102°.

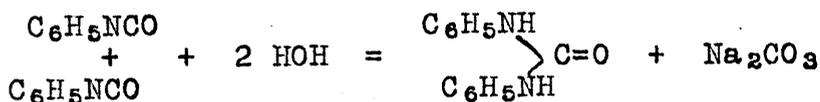
It may be mentioned here that attempted synthesis of Phenyl Allophanic ester by the following methods failed.

(a) Monophenyl Urea and Chloroformic ester. Several modifications of this reaction were tried under varying conditions, but no ester was produced.

(b) Phenyl Isocyanate was treated with dry HCl gas and a white crystalline product resulted, which was treated with Urethane. There was an evident reaction on heating on the water bath, and a compound was

isolated melting over  $250^{\circ}$ . Kjeldahl analysis gave total Nitrogen 9.47%, 9.23%. Nitrogen calculated for Phenyl Cyanuric acid, which was suspected in this case, 11.768%. The nature of this compound has not yet been determined.

(c) In another experiment Sodium Urethane was prepared in  $\text{Et}_2\text{O}$  solution and treated with 1 mole of Phenyl Isocyanate. The main product in this reaction was Diphenyl Urea melting at  $234^{\circ}-5$ , and a small amount of a substance of m.p. over  $280^{\circ}$ , evidently a polymer of Cyanic acid. As addition of HCl to a water solution of the mixture caused a free evolution of  $\text{CO}_2$ , the following reaction is suggested,--



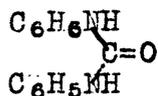
## (2) Monophenyl Urea.



3g of ester and a little XS over 2 moles of Aniline were heated for 2 1/2 hours at  $160^{\circ}-175$ . The solid mass resulting was broken up and washed several times with hot water. The filtrate deposited a white crystal of m.p.  $144^{\circ}-7$ . Monophenyl Urea had been prepared by heating Urea and Aniline. It melted at  $146^{\circ}-7$ . The reported m.p. of Monpphenyl

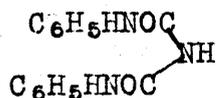
Urea is 146.5<sup>o</sup>-7. Mixture of these two compounds gave m.p. of 142<sup>o</sup>-5.

(3) Diphenyl Urea.



3 g of ester and XS over 2 moles of amine heated to 160<sup>o</sup>-175 for P 1/2 hours. The semi-solid mass was washed with boiling EtOH four or five times. A residue remained, which was quite pure and had the m.p. 233<sup>o</sup>-4. Mixed with a sample of Carbanilide of m.p. 235<sup>o</sup> the m.p. observed was 234<sup>o</sup>-5. Reported m.p. is 236<sup>o</sup>-7.

(4) Diphenyl Biuret.



5 g of ester and XS over 2 moles of Aniline heated to 125<sup>o</sup> for 1 hour. The mixture was well washed first with dil NaOH, then with dil HCl. The residue was recrystallized from EtOH several times, and came out as a felty mass of white needles with a silky lustre. The m.p. was 209<sup>o</sup>-10. Analysis for total N follows,--

Sample	NaOH	<del>HCl</del> H <sub>2</sub> SO <sub>4</sub> 卄
0.0878 g	64.17 ccs	50.16 ccs
0.1177	60.46	50.00

log conversion factor, NaOH to  $H_2SO_4 = \bar{1}.834686$

log factor, value of 1 cc of  $H_2SO_4$  in N, =  $\bar{3}.338108$

	(1)	(2)
N Found	16.63%	16.44%
N Calc	16.47	16.47

$C_{14}H_{13}O_2N_3$

SAMPLE.

Allophanic ester and o-Anisidine.

(I) o-Anisidine Allophanic ester.

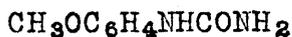


5 g of ester and a slight XS over 1 mole of o-Anisidine were heated for 2 hours at  $130^{\circ}$ - $145^{\circ}$ . The reaction mixture was semi solid. It was treated with dil NaOH and the filtrate made slightly acid with HCl. The substituted ester was thus precipitated, and was purified by crystallization from EtOH. M.p.  $125^{\circ}$ - $30$ . Anisidin Allophanic ester had been prepared from reaction of o-Anisidine and Urea (o-Anisidine Urea) and Chloroformic ester. Its m.p. was  $125^{\circ}$  (subl). M.p. of a mixture of these two compounds was  $124^{\circ}$  (subl).

Solubility.

$R_2CO$ ....v.s.  
 $Et_2O$ ....v.s.  
 $H_2O$ .....i.s.  
 $EtOH$ ....s.s.  
 $C_6H_6$ ....v.s.

## (2) o-Anisidin Urea.

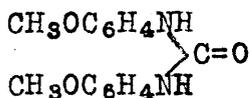


This compound was not isolated, though repeated attempts were made to obtain the right conditions. For the benefit of future work, the various heats tried are here listed,--

I15 <sup>o</sup> -I20	4 hours
I60	I I/2
I60-I75	I/2
	2
I70	2
	3
I70-I75	2
I7 <del>5</del> -I90	I
I80-I90	2
I90	2
I60-I75	2 I/2 then
I75-I90	I/2

Several of these lots were mixed with additional amine after being tested, and again heated for varying times at various temperatures. All trials were alike without success. The supply of Anisidine was exhausted and no further work could be done.

## (3) Di-o-Anisidin Urea



One mole of ester and two moles of o-Anisidin were heated to 170°-175 for 2 hours. Treatment with hot EtOH gives a filtrate which deposits long white needles of m.p. 182°. Di-o-Anisidin Urea of m.p. 177°-8 had been prepared by reaction between Urea and o-Anisidin. When the two were mixed the m.p. observed was 175°. Analysis gave the following results for total N,--

Sample	NaOH	HCl
0.2869 g	15.85 ccs	26.91 ccs

log conversion factor, NaOH to HCl =  $\bar{1}.878766$

log factor, value of  $I_{cc}$  of HCl in N, =  $\bar{3}.294028$

N Found - 10.24%

N Calc - 10.29 (SAMPLE)

$C_{15}H_{16}O_3N_2$

#### Solubility.

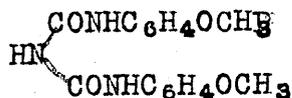
H<sub>2</sub>O.....i.s.

EtOH.....s.s.

Et<sub>2</sub>O....v.s.s.

R<sub>2</sub>CO....v.v.s. (Can throw down pure from EtOH with water with m.p. of 179°-181)

#### (4) Di-o-Anisidin Biuret.



5 g of ester and slight XS over 2 moles of Anisidin

were heated 2 hours to 130°-145°. Treatment with hot EtOH gave a residue which was crystallized from R<sub>2</sub>CO, or boiling EtOH as a felty mass of white needles. The m.p. was 211°-12, with partial sublimation. Kjeldahl analysis for total N gave the following,--

Sample	NaOH	HCl
0.2523 g	46.05 ccs	51.70 ccs

log conversion factor, NaOH to HCl =  $\bar{1}.878766$

log factor, value of 1 cc HCl in N<sub>2</sub> =  $\bar{3}.294028$

N Found	13.159%	(SAMPLE)
N Calc	13.33	
C <sub>16</sub> H <sub>17</sub> O <sub>4</sub> N <sub>3</sub>		

#### Solubility.

H<sub>2</sub>O, hot or cold....i.s.  
 EtOH .....s.s.  
 Et<sub>2</sub>O .....v.s.s.  
 R<sub>2</sub>CO.....s.s.

Allophanic ester and o-Toluidine.

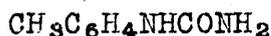
(I) o-Tolyl Allophanic ester.



2 g of ester and one mole of Toluidine were heated to 115°-120 for 4 hours, and then well washed with cold dil NaOH. HCl was added to acid reaction, which precipitated the

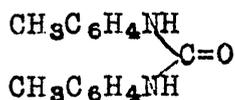
compound as a mass of flakes, which was purified by crystallization from EtOH. M.p.  $130^{\circ}$  with sublimation. Mixed with o-Tolyl Allophanic, ester, prepared by Dr. Dains, of m.p.  $132-3^{\circ}$ . the m.p. of the mixture was  $131^{\circ}$ , (subl).

(2) o-Tolyl Urea.



2 g Allophanic ester, and XS over 2 moles of Toluidine were heated for 2 hours to  $160^{\circ}$ , then for an additional hour to  $190^{\circ}$ . Washed with boiling water which deposited the Mono Urea as a pinkish crystal, which was again taken from hot water and was then quite pure. o-Tolyl Urea was made by reaction between Urea and o-Toluidine, of m.p.  $188-9^{\circ}$ . A mixture of these two compounds gave m.p.  $188^{\circ}$ . Reported m.p. in the literature is  $190-1^{\circ}$ . (SAMPLE) /

(3) Di-o-Tolyl Urea.



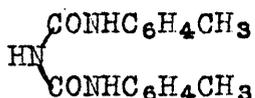
3 g ester and 6 g of amine were heated to  $170^{\circ}$  for 2 hours. The mass was well washed with boiling EtOH, which left the Di Urea as a white residue, which was crystallized out of a large amount of hot EtOH. M.p.  $245-7^{\circ}$ . Melted with Di-Tolyl Urea made from Urea and Toluidine, of m.p.  $246-7^{\circ}$ , the observed m.p. was  $246-7^{\circ}$ . Reported m.p.  $250^{\circ}, 243, 256$ .

Solubility.

## Solubility.

$H_2O$ , hot or cold, = . . . . i. s.  
 EtOH. . . . . s. s. (can be thrown  
      $Et_2O$ . . . . . v. v. s. s. with water).  
      $R_2CO$ . . . . . s. s. (can be thrown  
      $C_6H_6$ . . . . . v. s. s. with water).  
 $HCCl_3$ . . . . . v. s. s.  
 Gas. . . . . i. s. (SAMPLE)

## (4) Di-o-Tolyl Biuret.



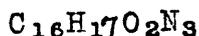
3 g ester and XS over 2 moles of amine were heated to  $170^\circ$  for 2 hours, then washed many times with hot EtOH. The filtrates were combined, and deposited on standing a mass of white needles, which was again crystallized from EtOH. The m. p. is  $204^\circ-5$ . Small portions of the Di-Urea also separate out, and the partition of these two is a difficult procedure. Kjeldahl analysis as follows, --

Sample	NaOH	HCl
0.2744 g	10.92 ccs	28.28 ccs

log conversion factor, NaOH to HCl =  $\overline{1.878766}$

log factor, value of 1 cc HCl in N, =  $\overline{3.294028}$

N Found	14.36%	
N Calc	14.84	(SAMPLE).



Allophanic ester and m-Toluidine.

## (1) m-Tolyl Allophanic ester.

This compound has not yet been isolated from the reaction being studied. In order to prevent duplication of work in further research, the temperatures used in the different trials are here listed,--

125°	2 hours
130	2 "
140	2 "
150	2 "
125	3 "
135-148	2 "

## (2) m-Tolyl Urea.

2 g ester and about 2.5 moles of amine were heated for 2 hours to 160°, then for 1 hour to 190°. Treatment with boiling water gave an oily filtrate which deposited a white crystal, m.p. 140°-143. Mixed with m-Tolyl Urea, made from Urea and m-Toluidine, of m.p. 143°-4, the observed m.p. was 140°-1. The reported m.p. is 142°. (SAMPLE)

## (3) Di-m-Tolyl Urea.

3 g of Allophanic ester and 6 g of m-Toluidine were heated to 170° for 3 hours, then well washed with boiling EtOH, which left a residue of m.p. 217°-18. Melted with Di-

m.Tolyl Urea made by reaction of m.Toluidine and Urea, which had m.p. of 214°-15, the m.p. of the mixture was 216°-18. The reported m.p. is 215°

(SAMPLE)

## (4) Di-m-Tolyl Biuret.

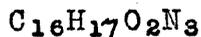
4 g ester and XS over 2 moles of amine heated for 1 1/2 hours at 170°, then the residue was crystallized several times from warm EtOH. Fine, cottony mass of white needles, m.p. 197°-99. Kjeldahl analysis as follows,--

Sample	NaOH	HCl
0.3905 g	30.22 ccs	51.94 cc

log conversion factor, NaOH to HCl =  $\bar{1}.878766$

log factor, value of 1 cc HCl in N, =  $\bar{3}.294028$

N Found	14.655%	(SAMPLE)
N Calc	14.84	



Allophanic ester and m-Nitranilin.

## (1) m.Nitro-phenyl Allophanic ester.

4 g of m.Nitranilin and 4 g of Allophanic ester were well mixed in a mortar, then carefully heated to 125° for 2 hours in Kerosene. The top liquor was then poured off,

cold dil NaOH was added to the residue, and well shaken for some time. The filtrate was made acid with dil HCl which precipitated the substituted ester. The m.p. was 140°. After several crystallizations from EtOH it attained the m.p. of 189°-90. Kjeldahl analysis as follows,--

Sample	NaOH	HCl
0.1347 g	18.25 ccs	25.25 ccs

log conversion factor, NaOH to HCl =  $\bar{1}.878766$

log factor, value of 1 cc HCl in N, =  $\bar{3}.294028$

N Found	16.714%
N Calc	16.60



(2) m-Nitro-Phenyl Urea.

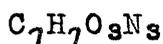
3 g Allophanic ester and 6 g m-Nitranilin were well mixed and heated for 2 hours at 170°. Treatment with hot water gave a clear filtrate which deposited a yellow crystal of m.p. about 165°. The compound in question had been made with m.p. of about 150° by treatment of Urea with m-Nitranilin, as described in the literature. A mixed melting point determination would have been useless, so the two compounds were put together and analyzed for total N, with result as follows,--

Sample	NaOH	HCl
0.1624 g	11.66 ccs	27.75 ccs

log conversion factor, NaOH to HCl, =  $\bar{1}.878766$

log factor, value of 1 cc HCl in N, =  $\bar{3}.294028$

N Found	22.94%	(SAMPLE)
N Calc	23.20	



### (3) Di-m-Nitro-Phenyl Urea.

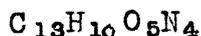
This product was isolated from the same reaction mixture (2) which produced the Mono Urea. After treatment with NaOH, the residue was crystallized from a large quantity of EtOH, and came down in greenish-yellow leaflets, m.p.  $233^{\circ}-4$ . These were analyzed as follows,--

Sample	NaOH	HCl
0.2826 g	32.36 ccs	50.76 ccs

log factor, NaOH to HCl, =  $\bar{1}.878766$

log factor, value of 1 cc HCl in N, =  $\bar{3}.294028$

N Found	18.30%
N Calc	18.54



### (4) Di-m-Nitro-Phenyl Biuret.

3 g ester and 6 g amine mixed and heated to  $145^{\circ}$  for 2 hours. Treatment with warm EtOH gave a yellow crystal m.p.  $211^{\circ}$ . The crystals were dissolved in EtOH, and thrown

by the addition of water and salt. After another crystallization from EtOH, the m.p. was 215°-16. An analysis for total N gave result as follows,--

Sample	NaOH	HCl
0.1425 g	13.96 ccs	25.33 ccs

log conversion factor, NaOH to HCl, =  $\bar{1}.878766$

log factor, value of 1 cc HCl in N, =  $\bar{3}.294028$

N Found            20.398%

N Calc             20.30



#### Benzoyl ester and Aniline.

3 g of Benzoyl <sup>1</sup>Aliphatic ester and 2.36 g Aniline were heated to 150° for 4 1/2 hours. Treatment with hot water and dilute NaOH finally left a residue which was dissolved in boiling R<sub>2</sub>CO, salted out with water, and again crystallized from R<sub>2</sub>CO. The m.p. was 209°. Reported melting points for Benzoyl Phenyl Urea run from 199° to 210°. This compound was mixed with a sample of Benzoyl Phenyl Urea, made from Benzoyl Chloride and Mono-Phenyl Urea, melting at 200°-1, and the m.p. observed for the mixture was 202.3. Kjeldahl analysis as follows,--

Sample	NaOH	HCl
0.2645 g	45.65 ccs	50.07 ccs

log conversion factor, NaOH to HCl, =  $\bar{1}.878766$

log factor, value of 1 cc HCl in N, =  $\bar{3}.294028$

N Found            II.562%

N Calc             II.65

(SAMPLE)

$C_{14}H_{12}O_2N_2$

Solubility.

H<sub>2</sub>O.....i.s.  
 EtOH.....v.s.s.  
 Et<sub>2</sub>O.....v.v.s.s.  
 R<sub>2</sub>CO.....s.s. (can  
                   be thrown with H<sub>2</sub>O

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In concluding this paper, the writer wishes to express his thanks to Dr. F.B. Dains for his interest in this work, and for the many valuable suggestions received from him.

University of Kansas,

May 15, 1919.

E. Wertheim.