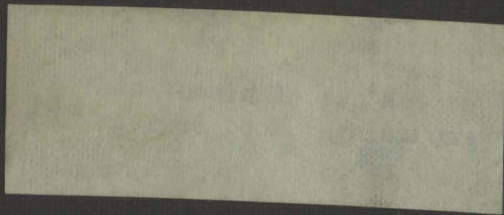


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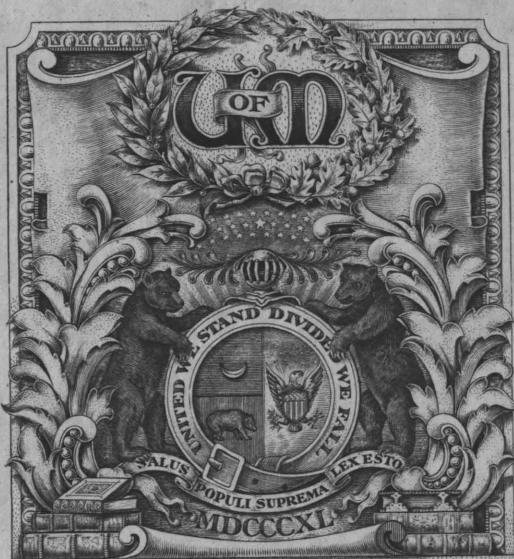


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METHYLENE CONDENSATIONS

by

WEBSTER NEWTON JONES, A. B.

SUBMITTED IN PARTIAL FULFILMENT OF THE
REQUIRMENTS FOR THE DEGREE OF
MASTER OF ARTS

in the

GRADUATE CONFERENCE
(COLLEGE OF ARTS AND SCIENCE)

of the

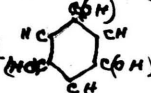
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It has long been known that such compounds as acetoacetic ester, $\text{CH}_3\text{CO}\cdot\text{CH}_2\cdot\text{COOC}_2\text{H}_5$, benzoyl acetone $\text{C}_6\text{H}_5\text{CO}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3$, acetyl acetone $\text{CH}_3\text{CO}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3$, acetone dicarboxylic ether $\text{C}_2\text{H}_5\text{CO}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{C}_2\text{H}_5$ malonic ester $\begin{matrix} \text{CO}\cdot\text{OC}_2\text{H}_5 \\ | \\ \text{CH}_2 \\ | \\ \text{CO}\cdot\text{OC}_2\text{H}_5 \end{matrix}$ or, in other words, bodies which contain the $\text{CO}\cdot\text{CH}_2\cdot\text{CO}$ group gave conflicting reactions, sometimes acting as if the group $-\text{CO}\cdot\text{CH}_2\cdot\text{CO}-$ were present and at other times as if the group $-\text{C}(\text{OH})\cdot\text{CH}\cdot\text{CO}-$ were present.

Phloroglucinol  while formerly accepted as a hydroxy compound has lately been included amongst the previous examples for reasons that will be brought out later. (1) Laar considered that there was one substance doing duty for two structural isomers and gave to this phenomenon the name tautomerism, and accounted for the peculiarity by the mobility or shifting of a hydrogen atom.

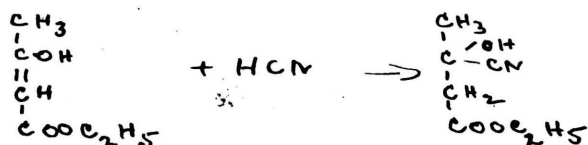
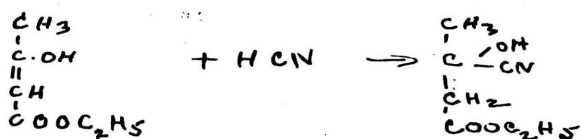
The question as to whether acetoacetic ether was of the keto or enol type was a subject of a long discussion between Geuther who upheld the enol form and Frankland who favored the keto form. From the constitution of acetoacetic ether $\text{CH}_3\text{CO}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{OC}_2\text{H}_5 \rightleftharpoons \text{CH}_3\cdot\text{C}(\text{OH})\cdot\text{CH}\cdot\text{CO}\cdot\text{OC}_2\text{H}_5$ it seems that it ought to be an easy matter to distinguish

(1) Ber. 18, 648

2.

between the carbonyl and the hydroxyl group, but on examining the addition products more closely one can see that the addition can be explained equally as well with the enolic as with the ketonic form. For an example we will consider the addition of hydrocyanic acid.

With either formula we arrive at the same product.



Thus we see that the data which is obtained may have a double interpretation which may lead to conflicting conclusions.

The enolic $-\text{C}(\text{OH})\text{:CH}\cdot\text{CO}-$ structure is strongly supported by the ease with which it forms sodium copper and iron salts. If we assume the ketone structure for the ester the sodium atom would have to add itself directly to the carbon atom. This reaction which at one time appeared startling has lost its peculiarity since similar condensations have been brought about between sodium and acetylene. Wislizenus found, however, that one and only one atom of sodium could enter the molecule.

After replacing the sodium by an alkyl radical the resulting acetoacetic ether was again able to take up an atom of sodium. He was thus indirectly able to replace the two hydrogen atoms by metals. Although it is true that the sodium salt is possible it is highly improbable that it would attach itself to the carbon direct when the strongly electro negative oxygen atom is available. This result favors the enol structure for the sodium salt $\text{CH}_3 \cdot \text{C}(\text{ONa}) : \text{CH} \cdot \text{COOC}_2\text{H}_5$.

It has been found further that with chloroformic ester $\alpha \cdot \text{COOC}_2\text{H}_5$ a derivative of the enol form (1) was obtained. $\text{CH}_3 \cdot \text{C}(\text{O} \cdot \text{COOC}_2\text{H}_5) : \text{CH} \cdot \text{COOC}_2\text{H}_5$ and with ammonia and amines crotonic esters of the general formula $\text{CH}_3 \cdot \text{C}(\text{NR}_2) : \text{CH} \cdot \text{COOC}_2\text{H}_5$ resulted. With Acetyl chloride the sodium compound gives diacetoacetic ether $\begin{matrix} \text{CH}_3 \cdot \text{CO} \\ \text{CH}_3 \cdot \text{CO} \end{matrix} > \text{CH} \cdot \text{COOC}_2\text{H}_5$ which is evidence for the keto structure. If, however, the reaction is brought about in pyridine (2) the acetyl derivative of hydroxycrotonic ester $\text{CH}_3 \cdot \text{CO}(\text{COCH}_3) : \text{CH} \cdot \text{COOC}_2\text{H}_5$ is formed. The results seem to show that the constitution of the substance cannot be deduced from the nature of the derivatives as the solvent or the reagent itself

(1) J. Prakt. Chem. 37, 473

(2) Ber. 21, 3307.

may have an influence on one or the other of the isomers.

The result of the decomposition of acetoacetic ether with dilute and strong alkalis favors the keto structure. With dilute alcoholic potash the ether is converted into a ketone.

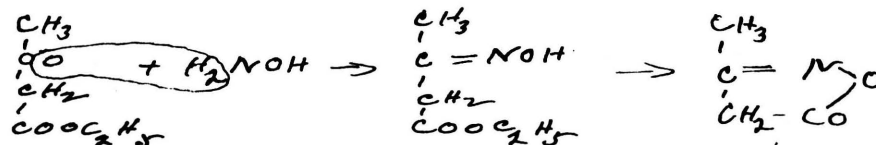
$$\begin{array}{c} \text{CH}_3 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{COOC}_2\text{H}_5 \\ | \quad | \quad | \\ \text{H} \quad \text{O} \quad \text{H} \end{array} \rightarrow \text{CH}_3 \cdot \text{CO} \cdot \text{CH}_3 + \text{CO}_2 + \text{C}_2\text{H}_5\text{OH}$$

With concentrated alcoholic potash it decomposes into an acid.

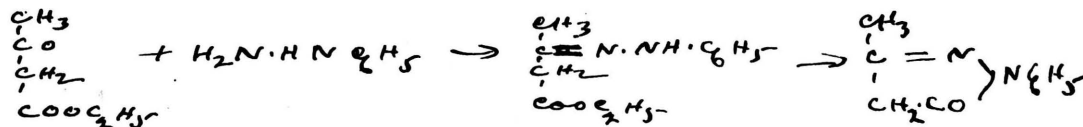
$$\begin{array}{c} \text{CH}_3 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{COOC}_2\text{H}_5 \\ | \quad | \quad | \\ \text{HO} \quad \text{H} \quad \text{HO} \quad \text{H} \end{array} \rightarrow 2 \text{CH}_3 \cdot \text{COOH} + \text{C}_2\text{H}_5\text{OH}$$

On reduction it gives hydroxy butyric acid $\text{CH}_3 \cdot \text{CHOH} \cdot \text{CH}_2 \cdot \text{COOH}$.

It combines with hydroxylamine to form oximino-butyric ester which loses alcohol and passes into methyl oxazolone.



It unites with phenylhydrazine $\text{C}_6\text{H}_5 \cdot \text{NH} \cdot \text{NH}_2$ to form a hydrazone which loses alcohol and passes into Phenyl methyl pyrazolone.



The sodium compound with Iodine gives diaceto-succinic ether.

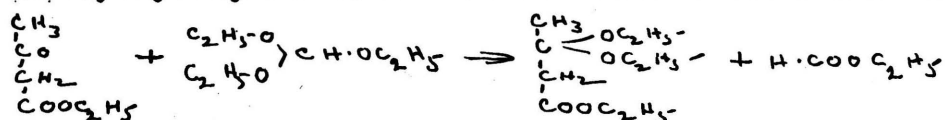
$$\begin{array}{c} \text{CH}_3 \cdot \text{CO} \cdot \text{C} \cdot \text{H} \cdot \text{COOC}_2\text{H}_5 \\ | \\ \text{CH}_3 \cdot \text{CO} \cdot \text{C} \cdot \text{H} \cdot \text{COOC}_2\text{H}_5 \end{array}$$

These are the arguments advanced in favor of both structures. Acetoacetic ether and hydroxycrotonic

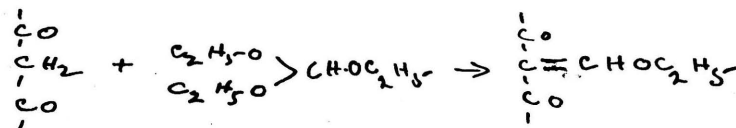
ether may be regarded as tautomeric substances. Which of the substances is the more stable depends upon the nature of the solvent and reagents used.

The condensation of acetoacetic ether with orthoformic ether in the presence of acetyl chloride is strong evidence in favor of the keto structure.

Diethoxybutyric ester was the result of the reaction.



If, instead of acetyl chloride, acetic anhydride is used the reaction which is typical of the $-\text{CO}\cdot\text{CH}_2\cdot\text{CO}-$ group takes place.

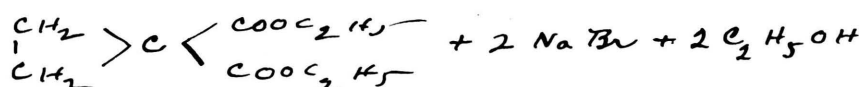
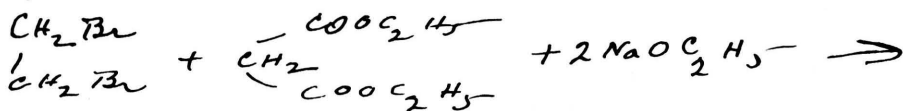


Claisen, concludes that the $-\text{CO}-\overset{\text{O}}{\text{C}}-\text{CO}-$ which is present in this substance may play the part of the =O atom in a carboxylic acid.

The action of sodium compounds of the $-\text{CO}-\text{CH}_2-\text{CO}-$ (1) is utilized by Perkin to bring about the production of cyclic compounds. When sodium malonic ester is treated with ethylene bromide, cyclopropane dicarboxylic ester results.

(1) Ber. 1902. 35, 2091.

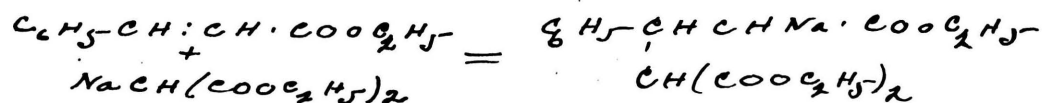
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Ethylene bromide with acetoacetic ether and sodium ethyoxide yields acetylcyclopropane carboxylic ester from the keto structure $\begin{array}{c} \text{CH}_2 \\ | \\ \text{CH}_2 \end{array} > \text{C} < \begin{array}{c} \text{COCH}_3 \\ | \\ \text{COOC}_2\text{H}_5 \end{array}$ and methyl

dehydropentane carboxylic ester from the enol structure $\begin{array}{c} \text{CH}_2 - \text{OC} \cdot \text{CH}_3 \\ | \\ \text{CH}_2 - \text{C} \cdot \text{COOC}_2\text{H}_5 \end{array}$ (1)

Michael has according to his positive and negative theory shown that the sodium salts of the group $-\text{CO} \cdot \text{CH}_2 \cdot \text{CO}-$ condense with unsaturated compounds of the general formula $\text{R} \cdot \text{CH} : \text{CHX}$ or $\text{R} \cdot \text{C} : \text{C} \cdot \text{X}$ where R is a positive or negative radical and X a strongly negative radical like a carbonyl or a cyanogen group. Michael condensed sodium malonic ester with cinnamic ester.



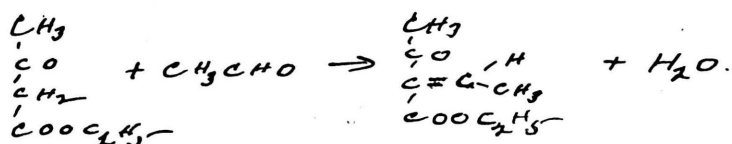
In this same way fumaric $\begin{array}{c} \text{COOC}_2\text{H}_5 \\ | \\ \text{C} \cdot \text{H} \\ | \\ \text{H} \cdot \text{C} \cdot \text{COOC}_2\text{H}_5 \end{array}$ maleic $\begin{array}{c} \text{H} \cdot \text{C} \cdot \text{COOC}_2\text{H}_5 \\ | \\ \text{H} \cdot \text{C} \cdot \text{COOC}_2\text{H}_5 \end{array}$ and citraconic $\begin{array}{c} \text{CH}_3 \cdot \text{C} \cdot \text{COOC}_2\text{H}_5 \\ | \\ \text{H} \cdot \text{C} \cdot \text{COOC}_2\text{H}_5 \end{array}$ condense with the sodium salt of malonic acid.

(2)

Claisen was one of the first to bring about

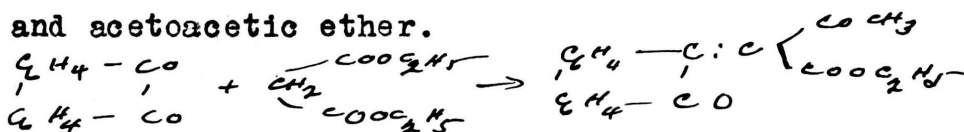
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- (1) J. Prakt. Chem. 35,351; 43,395; 45,55; 49,20;
Trans. Chem.Soc. 1898, 73, 1006.
(2) Annalen, 218,172.

condensation between the group $-CO-CH_2-CO-$ and aldehydes by the action of HCl . He succeeded in bringing about a condensation between acetoacetic ether and acetaldehyde.



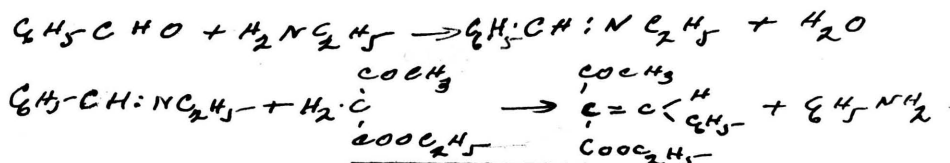
(1)

Later Japp and Streatfield by the use of ammonia were able to bring about a condensation between phenanthraquinone and acetoacetic ether.



(2)

It was Knoevenagel who first used the primary and secondary amines and he found them to be very effective. A small quantity of the amine was able to bring about a very extensive condensation. Knoevenagel explained the reaction by assuming that the amine first combined with the aldehyde with the loss of water and the setting free of an imino-compound. The imido group then reacted with the $-CO-CH_2-CO-$ bringing about the condensation and setting free the amine which is then able to react with another molecule.

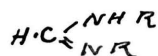


(1) Trans. Chem. Soc. 43, 27.

(2) Ber 31, 738.

(1)

Dains found that the formamidines of the type

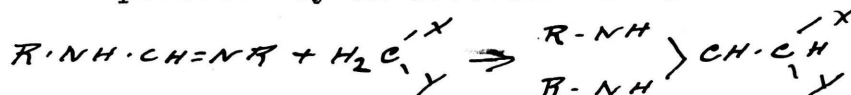


were very reactive with bodies like malonic ester, acetoacetic ester and was of the opinion that the groups $H \cdot C \begin{matrix} \swarrow N = \\ \searrow N - \end{matrix}$ and $-CO-CH_2-CO-$ were necessary for acetdiphenyl amidine $H \cdot C \begin{matrix} \swarrow N \begin{matrix} \swarrow C_6H_5 \\ \searrow OCCH_3 \end{matrix} \\ \searrow N \begin{matrix} \swarrow C_6H_5 \\ \searrow \end{matrix} \end{matrix}$ gave

no reaction with malonic ester nor did ethyl malonic

ester $H \cdot C \begin{matrix} \swarrow C(OC_2H_5) \\ \searrow C_2H_5 \\ \swarrow C(OC_2H_5) \end{matrix}$ react with diphenyl formamidine.

He was inclined to the belief that the reaction was first preceded by an addition thus:



and this subsequently eliminated the substituted amine

$R \cdot NH_2$ as follows:



He admits, however, that "the reaction has similarity with one put forth by Knoevenagel by which compounds of the type $\pi \cdot C \begin{matrix} \swarrow H \\ \searrow NR \end{matrix}$ react with acetoacetic ether etc. forming compounds of the type $\pi \cdot C \begin{matrix} \swarrow H \\ \searrow NR \end{matrix}$ with the splitting off of an amine."

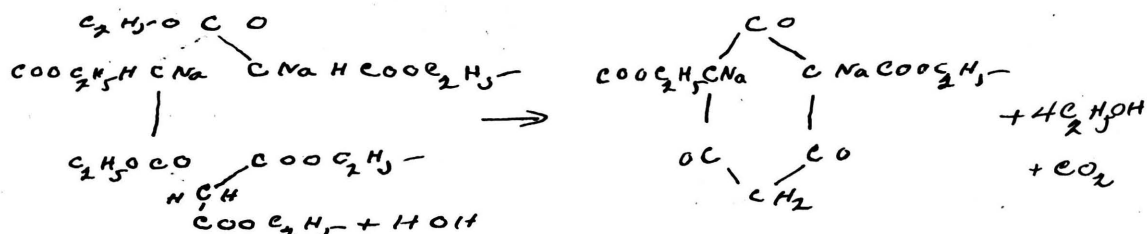
In pursuing these reactions we endeavored to determine what groups are necessarily present in order that such condensations with the group $-CO-CH_2-CO-$ shall

take place and took up principally a further study of

the types $H \cdot C \begin{matrix} \diagup NHa \\ \diagdown Na \end{matrix}$ and $\pi \cdot C \begin{matrix} \diagup H \\ \diagdown Na \end{matrix}$ We

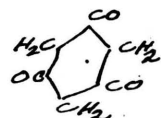
desire also to use the easy reactivity of the formamidines to determine the structure of several disputed bodies.

Phloroglucinol behaves in most of its reactions (1) so far as is presently known as a trihydroxyphenol. Until the synthesis by Von Baeyer by heating diethyl sodium malonate (2) with diethyl malonate the only view held for the structural formula for phloroglucinol was the phenolic structure.



On fusing the diethyl phloroglucinoldicarboxylate with potassium hydroxide the ethyl carboxyl group is replaced by hydrogen, phloroglucinol resulting.

This reaction leads to the ketone structure

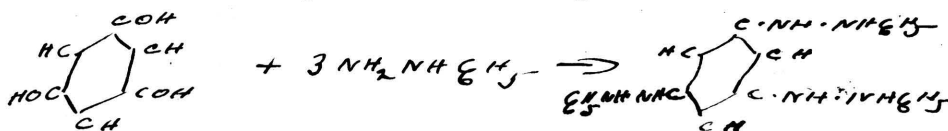


of phloroglucinol. On examination of phloroglucinol in the regular way with hydroxylamine it was found to give a trioxime.



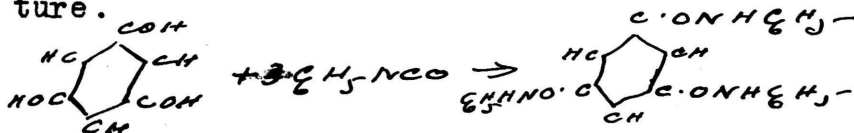
- (1) Richter Chemie de Kohlenstoff Verbindungen 1906
 (2) Ber 18, 3458.

But on the other hand, the evidence obtained by the action of phenylhydrazine $C_6H_5NH.NH_2$ is in a certain sense confusing, or at any rate, not very positive. Baeyer brings proof that the action of phenylhydrazine is not a hydrazone but a hydrazone of the enol form caused by the wandering of an H atom.



The arguments in favor of the enol structure are; its formation of a potassium salt with KOH ; its formation of the ether with potassium hydroxide and methyl iodide; its formation of a triacetyl derivative with acetyl chloride. These reactions, however, may not be a guide to the original substance as it is possible that the action of these compounds may bring about an isomeric change from the keto form to the enol form, or vice-versa. It is generally conceded that the sodium and potassium salts are in the enolic condition. For this reason sodium could not be used as a reagent to determine the structure of phloroglucinol. The carbimides are reagents which seem to have no effect on the isomeric types. With phenyl carbimide $C_6H_5N:C:O$ phloroglucinol conducts itself

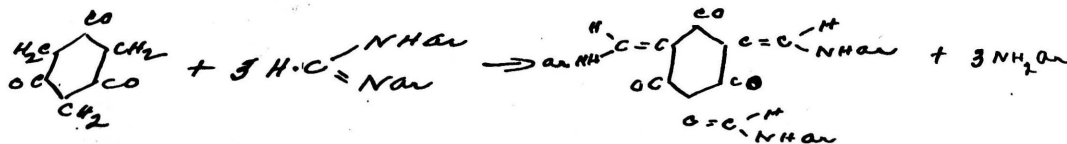
like a trihydroxyphenol yielding a tricarbonyl derivative which would go to prove that it has an enolic structure.



(1)

Michael and Smith in a recent paper with the use of the tertiary amines as reagents for the differentiation between stable enol and ketone derivatives come to the conclusion that phloroglucinol is on one hand a phenol; on the other a ketone and that its properties are in harmony with the conception that it is a ~~hydroxy~~ ~~diketotrihydro-~~ benzol. This is based on the fact that it formed compounds with trialkylamines in apparently the same manner that other compounds reacted which were believed to be enolic. The particular compound isolated and analyzed corresponds however only in a very rough way to the following formula, $(\text{C}_6\text{H}_3\text{O}_3)_2 \text{N}(\text{C}_2\text{H}_5)_3$ which upon analysis yielded 30.4%; 30.2% instead of 28.6% as required by the formula.

Our work goes to show that phloroglucinol reacts with the formamidines in the following manner.



which is strong evidence in favor of the keto structure.

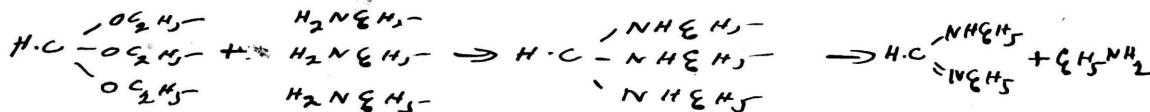
(1) Annalen 363; 36 (1908)

In order to study the action of the formamidines on Phloroglucinol we decided to use diphenyl formamidine (1)

$\text{H}\cdot\text{C} \begin{matrix} \text{NH}\text{C}_6\text{H}_5 \\ \text{N}\text{C}_6\text{H}_5 \end{matrix}$ This was prepared according to Walther by the action of aniline $\text{C}_6\text{H}_5\text{NH}_2$ on ortho formic ether.

The reaction goes with great ease. All that is necessary is to place equivalent amounts of the substances in a flask attached to a reflux condenser and heat for $\frac{1}{2}$ hour. The crude product which separates out on cooling is recrystallized several times from absolute alcohol. M.P. 137°

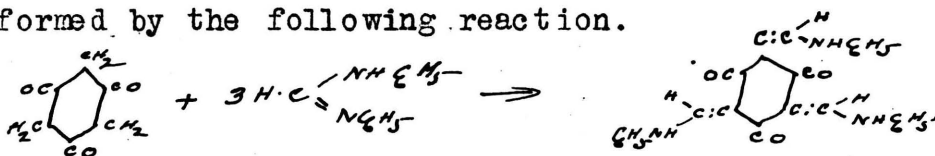
The reaction takes place in the following manner:



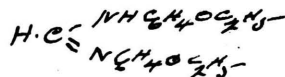
After purifying the formamidine 2.73 gr. of it was placed with .63 gr. of phloroglucinol in a flask attached to a reflux condenser and 50 cc. of absolute alcohol added. After heating for 15 minutes a yellow precipitate began to separate out which gradually increased in bulk as the heating continued. After 3 hours boiling the reaction was interrupted, and the yellowish silky precipitate filtered off. The compound was almost insoluble in alcohol, benzene, carbon disulphide, ligroin ether but soluble in chloroform. Recrystallized from

(1) J. Prakt. Chem. 55, 41 (1891)

chloroform several times and dried on a porous plate it gave a M.P. 303°. On analysis, .3070 gr. of substance gave 52.4 cc. of N. at 23 C. and 736 M.M. pressure which calculates 9.70 % N. The percentage composition corresponds to the percentage nitrogen (calculated 9.65%) in the compound formed by the following reaction.



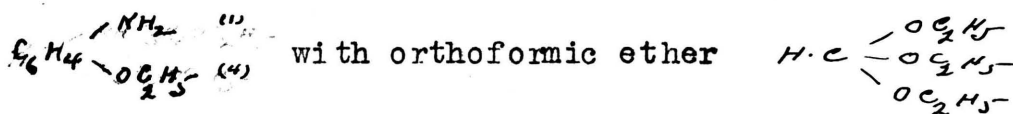
The yield of 1:3:5 triformanilido cyclohexanetrione amounted to about 15%. It appears therefore that in alcohol a considerable amount of phloroglucinol is ketonized. The marked yellow color of the compound also points to a quinoid construction. Our result is a further proof of the presence of 3 keto groups and not one as Michael maintains, and affords another neat proof of the structure of phloroglucinol as determined by the action of hydroxylamine. To confirm our result we decided to take up the action of another formanidine, namely methenyl di-para phenitidine or diethyl ether of 4 oxyphenylamido 4 oxyphenylimido methane



(1)

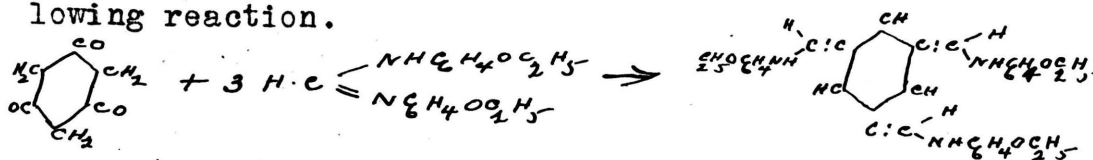
This substance was prepared according to Walther by heating for $\frac{1}{2}$ hour equivalent amounts of phenitidine

(1) J. Prakt. Chem. 55:41.



in a flask attached to a reflux condenser. The crude product is recrystallized several times from absolute alcohol until the proper melting point 114° was obtained. 4.22 gr. was placed with .63 gr. of phloroglucinol in a flask attached to a reflux condenser and 50 cc. absolute alcohol added.

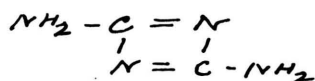
After 15 minutes heating a yellow silky, precipitate began to separate. After heating for 3 hours the reaction was discontinued. This substance was much more soluble in alcohol than the previous derivative and was able to recrystallize from absolute alcohol M.P. 110° . The compound on analysis gave the following result .2018 gr. of substance gave 13.4 cc. of N. at 22°C 448 MM. This on calculation yields 7.40% of N. The percentage composition corresponds to the percentage (calculated 7.41% N) in the compound formed by the following reaction.



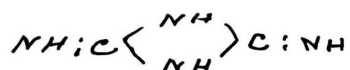
This result confirms along with hydroxylamine the ketone structure for phloroglucinol. We are unable to study the condensations of phloroglucinol with the

many substituted amidines as our supply of orthoformic ether was exhausted and we were unable to procure any in the United States market.

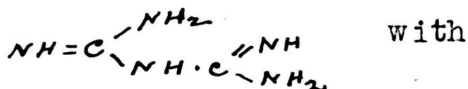
Dicyandiamide or cyanguanidin is formed by the polymerisation of cyanamide $NH_2 \cdot CN$ or an evaporation of the same especially in the presence of some ammonia. Haus gave it the following constitutional formula



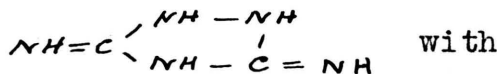
while Baumann thought it should have the following structure



On the other hand, since it gives a derivative of bi-guanide (1) or guanylguanidine



piperidine and guanazole



hydrazine hydrochloride, the following structure has

lately been accepted $NH = C \begin{array}{l} \diagup NH_2 \\ \diagdown NH \cdot CN \end{array}$ If it possessed

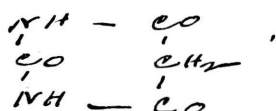
amino groups it should give condensation products with the carboxyethyl groups of such esters as oxalic ester $\begin{array}{c} COOC_2H_5 \\ COOC_2H_5 \end{array}$

cyanacetic ester $CN \cdot CH_2 \cdot COOC_2H_5$ orthoformic ester

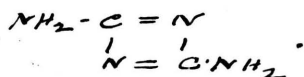
$\begin{array}{c} OC_2H_5 \\ | \\ H \cdot C - OC_2H_5 \\ | \\ OC_2H_5 \end{array}$ On the other hand if the latter formula were

(1) Ber. 24, 899; Ber. 25, 525.

correct one would expect that it would lose the imide group $=NH$ with the methylene group $-CO-CH_2-CO-$ of such compounds as acetoacetic ester $CH_3 \cdot CO \cdot CH_2 \cdot COO C_2H_5$, malonic ester $C_2H_5 \cdot O \cdot CO \cdot CH_2 \cdot CO \cdot O C_2H_5$ or barbituric acid



Heated 2.4 gr. of dicyandiamide with 5.4 gr. of ortho-formic ester in a flask attached to a reflux condenser. If the $-NH_2$ group were present we would expect from the previous experiments that a formamidine would form with ease. In this case, however, the formamidine did not form, which rather condemns the formula

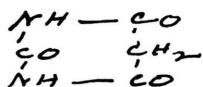


Placed .8 gr. dicyandiamide, 1.2 gr. barbituric acid and 50 cc alcohol in a flask attached to a reflux condenser and heated. If the $=NH$ group were present we would expect it to react with the methylene group $-CO-CH_2-CO-$ and give us a condensation product. No compound separated. On evaporating the liquid and ^{determination} drying, a melting point, seemed to show that no reaction had taken place.

These experiments tend to show that the first formula is almost certainly incorrect, and to throw

doubt on the others unless it should be that the unsubstituted imid-group does not react with the methylene group. The conditions affecting the removal of the imide group are, as our results tend to show, not yet completely ascertained.

Barbituric acid has the following structure

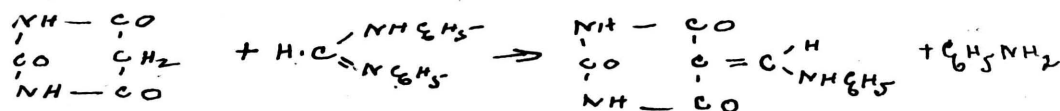


In this substance while the compound contains the group $-\text{CO}-\text{CH}_2-\text{CO}-$ it is not a neutral ester such as malonic ester, or acetoacetic ester, but an acid. Acids as a rule readily hydrolyze the formamides giving the acid amides. Nevertheless we hoped that it would be possible to bring about reactions with it and the imino group.

1.28 gr. of barbituric acid was heated with 1.96 gr. of diphenyl formamide $\text{H} \cdot \text{C} \begin{array}{l} \text{NH} \text{C}_6\text{H}_5 \\ \text{=N} \text{C}_6\text{H}_5 \end{array}$ in an absolute alcoholic solution for $\frac{1}{2}$ hour. At the end of this time a white crystalline solid had separated. The alcoholic solution was tested with bleaching powder and with bromine giving good tests for aniline. The substance was practically insoluble in the ordinary solvents and hence could only be purified by a tedious method of extraction. After repeated treatment with absolute alcohol ^{the compound was} filtered and dried on a porous plate. A melting point determination



showed that the body was neither barbituric nor the original formamidine. An analysis of the substance gives the following results: .3032 gr. of substance gave 51.8 cc of nitrogen at 26.2° C and 746 m. m. pressure. On calculation this gives 18.61 % nitrogen which corresponds with the nitrogen calculated (18.61% nitrogen) in the compound formed in the following reaction.

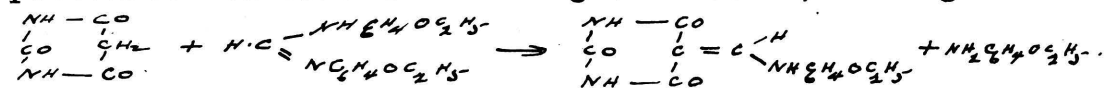


From this we conclude that barbituric acid condenses with the formamidines, giving us the derivative of methylene 5 barbituric acid or phenyl formamido barbituric acid.

To confirm our results we decided to take up another formamidine, namely di para phenitidine $\text{H} \cdot \text{C} \begin{array}{l} \text{NH}_2 \\ \text{NH}_2 \end{array}$ formamidine $\text{NH}_2\text{C}_6\text{H}_4\text{CO}_2\text{H}$

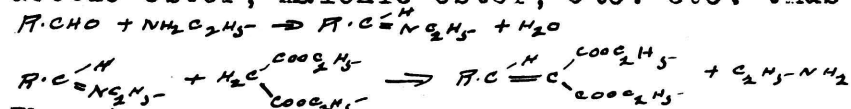
2.84 gr. of di para phenitidine was heated with 1.28 gr. of barbituric acid in an alcoholic solution for $\frac{1}{2}$ hour. At the end of this time a white crystalline solid separated. The alcoholic solution gave a good test for phenitidine. The substance was practically insoluble in all the common solvents and hence could only be purified by extraction. After repeated treatment with alcohol it was filtered and dried on a porous plate. An analysis

of the compound gave the following results: .2858 gr. of substance gave 40.4 cc of nitrogen at 21 C at 750 m.m. pressure. On calculation it gives 15.87 % nitrogen.

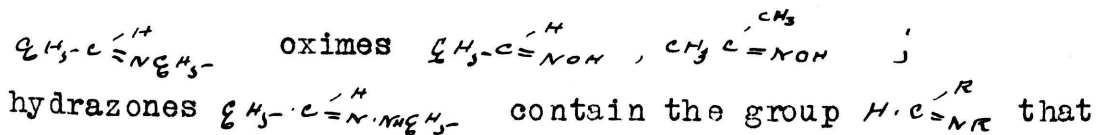


The % nitrogen is too high for the above compound which has 15.27 % nitrogen. This we concluded was due to some occluded barbituric acid which is extracted only with great difficulty.

Reverting to Knoevenagel's reactions, the theory of the mechanism of this reaction is that the primary amine forms an intermediate compound containing an imide group which condenses with the methylene group of acetoacetic ester, malonic ester, etc. etc. thus



Thus the primary amine is set free and can bring about further condensations. Now, if this theory be correct, then the intermediate compound if isolated ought to condense with such bodies as acetoacetic ester, malonic ester, barbituric acid, phloroglucinol and other compounds containing the $-\text{CO}-\text{CH}_2-\text{CO}-$ group. Benzylidene aniline



that is to say they contain the imide or substituted imide group which is supposed to be formed in the intermediate compounds

which give rise to Japp's and Knoevenagel's reactions. Accordingly we hoped that phloroglucinol would give reactions with these bodies, the substituted imide group breaking off with the hydrogen of the $-CO-CH_2-CO-$ group. The following experiments were made without successful results; phloroglucinol with benzylidene aniline $\text{C}_6\text{H}_5\text{C}=\text{N}^{\text{H}}\text{C}_6\text{H}_5$; phloroglucinol with acetophenone oxime $\text{CH}_3\text{C}(\text{CH}_3)=\text{NOH}$; phloroglucinol with benzophenone oxime $\text{C}_6\text{H}_5\text{C}(\text{C}_6\text{H}_5)=\text{NOH}$; phloroglucinol with benzaldehyde phenylhydrazone $\text{C}_6\text{H}_5\text{C}(\text{H})=\text{N}^{\text{H}}\text{NH}_2$ phloroglucinol with glucose phenylhydrazone. From these results we conclude that the only group that reacts readily with the group $-CO-CH_2-CO-$ is $\text{H}\cdot\text{C}(\text{N}^{\text{H}}\text{OH})$.

This work was undertaken at the suggestion of Professor Sidney Calvert, Professor of Organic Chemistry, at the University of Missouri. I here wish to express my thanks for his kindly interest and the assistance he has shown me in my work.

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Approved
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Prof. of Organic Chemistry.

