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USE OF FORMAMIDINES IN THE
DETERMINATION OF STRUCTURE

by

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SUBMITTED IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF
MASTER OF ARTS

in the

GRADUATE DEPARTMENT
(COLLEGE OF ARTS AND SCIENCE)

of the

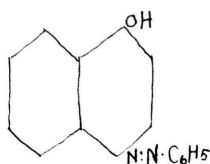
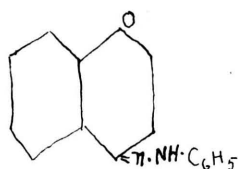
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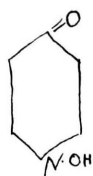
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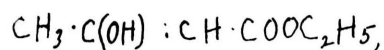
In a paper in 1885 Laar¹ discussed the phenomenon of one substance doing duty for two structural isomers and called this particular phenomenon "tautomerism". He illustrated this phenomenon by discussing several substances; Isatin occurred first. He represented the two isomers thus:



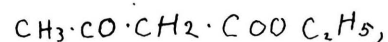
The first one is formed by the interaction of diazobenzene chloride and a-naphthol and the second by phenylhydrazine and a-naphthaquinone. He mentions the twofold character of nitrosophenol or quinoneozime, which on the one hand, behaves like a phenol and, on the other, like a dioxime.



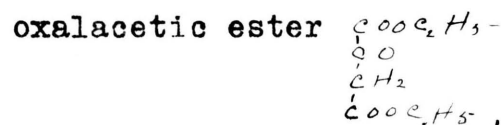
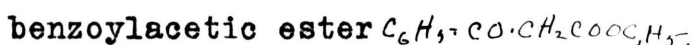
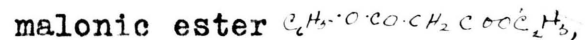
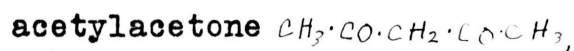
The classical tautomeric compound, acetoacetic ester which permits of a problem between the following two structures:



AND



came under his attention. Since then numerous other compounds with similar migratory hydrogen atoms have been observed by chemists among which can readily be mentioned the following:



1. Ber., 1885, 18, 648.

and other bodies containing $-CO-CH_2-CO-$ group. These bodies sometimes act as if the ketone group were present and at other times as if the enol group $-CO-CH:CO-$ were present, the hydrogen seeming to shift to form the hydroxyl group.

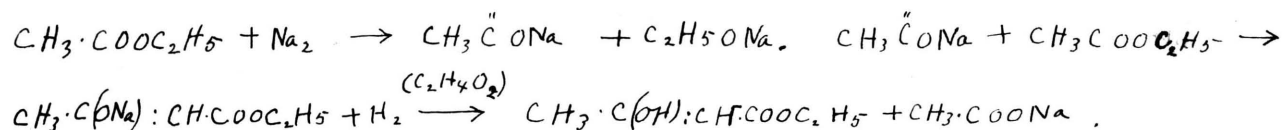
Laar's theory (tautomerism) of having one substance do duty for two structural isomers is analagous to Kekule's theory of the oscillation of hydrogen atoms in the benzene molecules, and does not permit of a formula which could represent either structure. The theory would have the molecules to exist in a constant state of oscillatory change from the one grouping to the other. This is not generally accepted according to Lowry¹ for most chemists hold that the known forms of such compounds are to be represented by a definite grouping of atoms which under certain conditions pass over into the isomeric grouping by a rearrangement of the bonds made necessary by the displacement of a hydrogen atom.² Lowry takes as evidence against Laar's theory the fact that labile isomerides in well defined crystalline form occur in so many cases which would not be possible with the oscillation theory. Also as evidence are the facts that these bodies pass from the one into the other with great slowness, a catalyst usually being necessary to establish equilibrium between the two.

Reverting to the structure of the classic acetoacetic ester, it will be well to review its two phase activities.

1. Lowry, Science Progress 1908, 634.
2. Lowry, Science Progress 1909, 636.

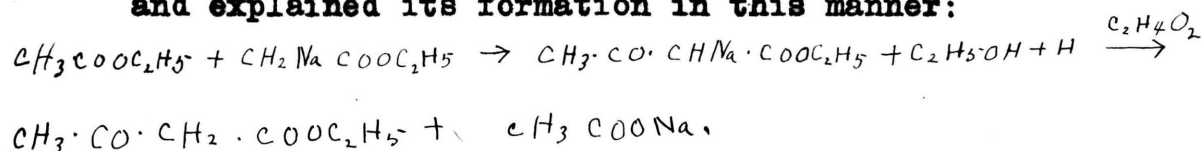


Geuther¹ believed that acetoacetic ester contained the hydroxyl, or the enolic structure, $-C(OH):CH \cdot CO-$ and explained its formation by the following reactions:



Frankland and Duppa² assigned the keto structure,

and explained its formation in this manner:

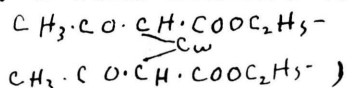


Experiments and results supporting each structure are numerous and often very conflicting.

Geuther's formula, $CH_3 \cdot C(OH):CH \cdot COOC_2H_5$ is supported by the facts:

(1) the ester has an acidic character which enables it to form (a) a sodium salt $CH_3 \cdot CO \cdot CHNa \cdot COOC_2H_5$;

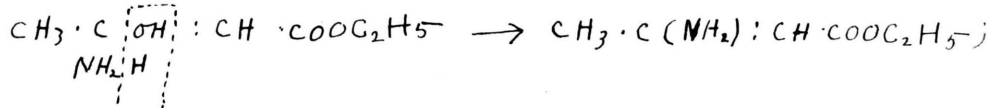
(b) a well defined and crystalline copper salt



(c) a violet colored ferric salt $(C_6H_5O_3)_3 Fe$

corresponding to the sodium and copper salts;

(2) with ammonia the ester gives B-amino-crotonic ester,



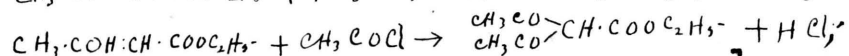
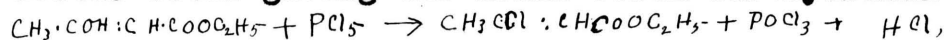
(3) with amines the esters of the formula $CH_3 \cdot C(NR_2)CH \cdot COOC_2H_5$;

(4) phosphorous pentachloride and acetyl chloride, the common tests for hydroxyls, both interact with the aceto-

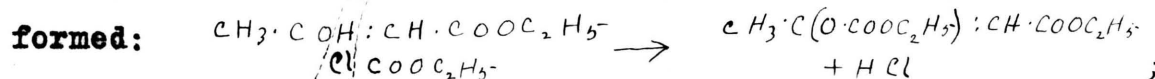
1. Annalin, 1883, 219, 123.

2. Phil. Trans., 1866, 156, 37; Annalin 1886, 138, 204, 328.

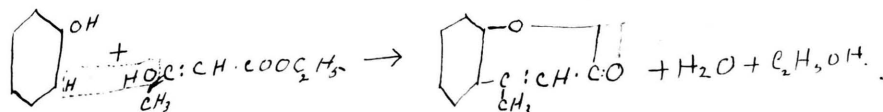
acetic ester giving the usual tests for hydroxal groups;



(5) with chloroformic ester¹ a carbonic ester is



(6) the interaction between acetoacetic ester and other compounds where a molecule of water is eliminated is most easily explained by the enol rather than the ketone formula, as, for example, the formation of methyl-coumarin from phenol:²



Now, on the other hand, the evidence for the ketone formula is equally as strong:

(1) the ester reacts with sodic-hydric sulphite as do the ketones;



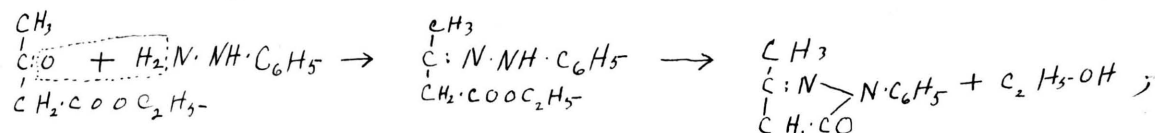
(2) it combines with hydrogen cyanide



(3) with hydroxylamine;



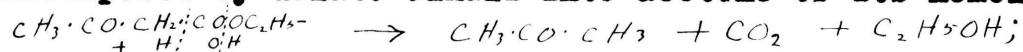
(4) it combines with phenyl hydrazine to form a hydrazone which passes into phenyl methyl-pyrazolene on losing alcohol;



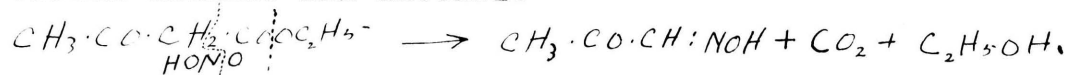
1. Michael, J. Prakt.Chem., 1883, (2) 37, 473; 1891, 45, 580; 1892, 46, 189.

2. V. Peckmann and Duisburg, Ber. 1883, 16, 2119.

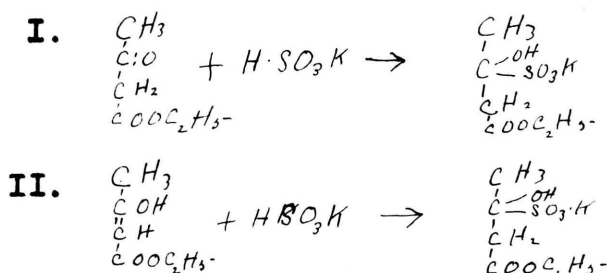
(5) acetoacetic ester with its alkyl derivatives is decomposed by dilute alkali into acetone or its homologues



(6) nitrous acid converts it into isonitroso acetone, carbon dioxide and alcohol:



The marshalling of such evidence, however, does not lead us to any definite proof, for in the addition products either the ketonic or enolic formula would explain the reactions;- The addition of potassium bisulphite illustrates this:



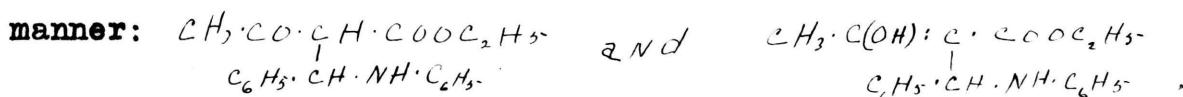
The addition of a metal to the ester is not sufficient proof. If we presuppose the keto form the sodium atom may replace the hydrogen atom which is attached direct to the carbon and not to the oxygen atom as has occurred in other compounds, e.g. a sodium addition product of acetylene. Moreover, it is generally believed that almost all of the previously mentioned reagents cause isomeric change, or the shifting within the molecule from the ketonic to the enolic form or vice versa, and that the compounds under discussion change with temperature, pressure, solvent and strength of solution. This phenomena of change excludes the bases¹ and acids, and the derivatives which are obtained by the acid of the bases and acids. The sodium compounds have been shown to be principally enolic; but no inference can be made

1. Cohen, Organic Chemistry, 194.

that the derivative obtained by the use of the sodium compound is a guide to the structure of the original substance. Acetic anhydride can not be used for a similar reason. Both forms of formal phenylacetic esters yield the same acetyl derivative. Phenyl carbimide when it is dissolved in a non-ionizing solvent is a reagent which appears to have no, or but little, effect upon the isomers. It reacts in cold solutions with hydroxy- and amino- compounds forming carbanic esters and carbamido compounds:



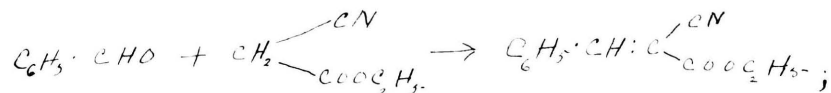
Phenyl carbimide in this manner combines with phloroglucinol, but not with succino-succinic ester, indicating that the former is enolic and the latter ketonic. Schieff attempted to determine the presence of the two forms of acetoacetic esters by using benzalaniline. It combines with the two forms in this



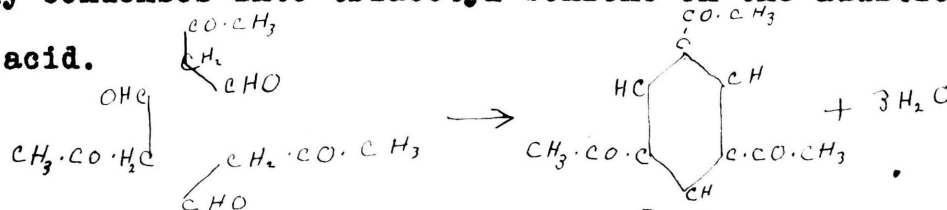
He was able to separate the two compounds and found that they melt at 78° C. and 104° C. respectively.

We have undertaken the research with different formamidines with the view that they would condense with only those molecules that are in the keto form and cause them to separate out of solution and that they would not interfere with the molecules in the enolic form. We expected this to give a qualitative test for the presence of the keto structure as well as a rough quantitative test for the percentage of the compound that was in the keto form under the conditions of the experiments.

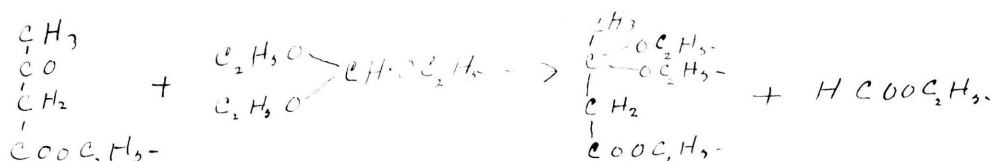
Before turning to the research I wish to give a hasty review of some condensations that are either well known or bear very closely upon the formimidine condensations. The compounds containing the group $-C(=O)CH_2CO-$, or $-C(=O)CH=CHCO-$ have many condensation products. It was early believed that these were definite indications of the keto or enol structure, but more recently they do not carry with them that belief, since many of them are thought to bring about isomeric change. The following substances occur among the condensations: (1) cyanacetic ester combines with benzaldehyde when a minute quantity of sodium has been added.



(2) Acetone and formic ester in presence of sodium ethoxide yield the sodium compound of acetaldehyde, $CH_3 \cdot CO \cdot CH_2 \cdot CHO$, which immediately condenses into triacetyl benzene on the addition of acetic acid.



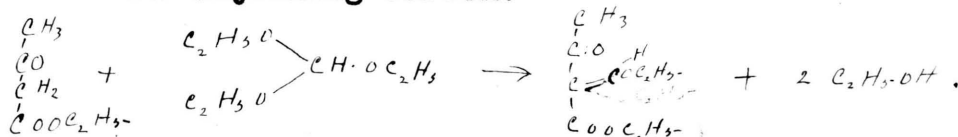
The second step shows a ketonic action. (3) ¹Ortho-formic ester condenses with acetoacetic ester in presence of acetyl chloride removing the atom of oxygen which constitutes the keto structure:



The condensation comes about in a different manner if acetic anhydride is used as the condensing agent. In this case the oxygen atom remains intact while two atoms of hydrogen are

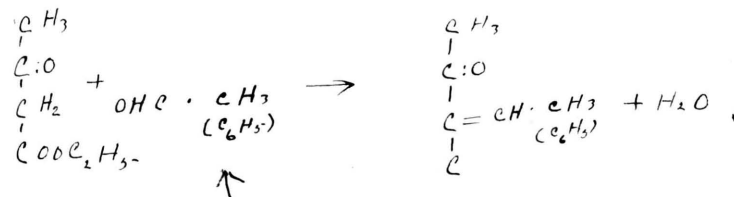
1. Cohen, Org.Chem., p.284.

removed from the adjoining carbon.

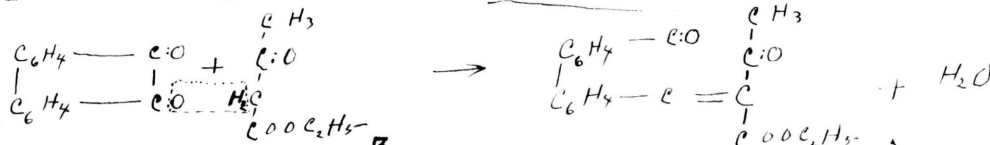


Either reaction shows the ester in the keto form but this form can be accounted for by the presence of the condensing agent which tends to change the equilibrium of the two isomeric bodies toward the keto form.

Cloisen¹ obtained condensation products with acetaldehyde, benzaldehyde and acetoacetic acid by having hydrochloric acid present:



Japp and Streatfield² used ammonia as the agent in condensing phenanthra-quinone and acetoacetoacetic ester:



In 1893 Knoevenagel³ used ammonia in his investigations and also ammonia substituted products, namely: diethylamine $(\text{C}_2\text{H}_5)_2\text{NH}$, piperidine $\begin{array}{c} \text{CH}_2 - \text{CH}_2 \\ | \quad | \\ \text{CH}_2 - \text{NH} \\ | \quad | \\ \text{CH}_2 - \text{CH}_2 \end{array}$ and aniline $\text{C}_6\text{H}_5\text{NH}_2$.

Benzaldehyde and aceto-acetic ester in presence of a small amount of diethylamine, at a low temperature, gave the same product that Claisen obtained in using hydrochloric acid as a reagent on the same two compounds. $\text{C}_6\text{H}_5 - \text{C} \begin{array}{l} \nearrow \text{CO} \cdot \text{CH}_3 \\ \searrow \text{COOC}_2\text{H}_5 \end{array}$

The keto and enolic compounds under discussion were found by Daines⁴ to be very reactive with the formamidines of

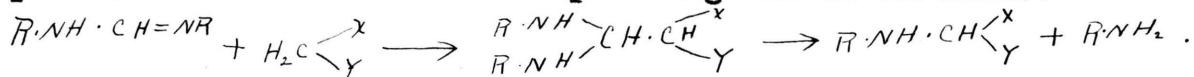
1. Annalin 1883, 218,172.

2. Trans.Chem.Soc. 1883, 43,27.

3. Annalin, 1894, 281,25; Ber., 1904, 37,4461.

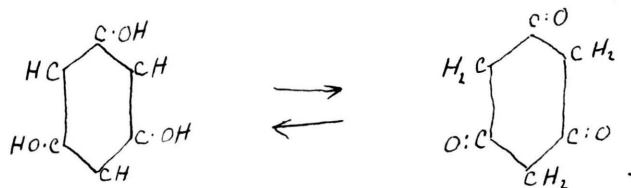
4. Ber., 35, 2496.

the type $H \cdot C \begin{smallmatrix} \nearrow N \\ \searrow N \end{smallmatrix} \begin{smallmatrix} R \\ H \end{smallmatrix}$ Daines early concluded that the groups $-CO-CH_2-CO-$ and $H \cdot C \begin{smallmatrix} \nearrow N \\ \searrow N \end{smallmatrix}$ were necessary for the condensations. He accounted for the reaction by an addition process at first and then a splitting off of an amine.



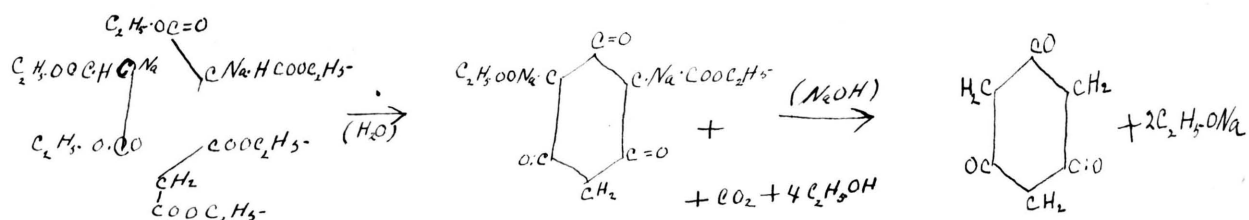
Webster Jones¹ under the guidance of Professor Sydney Calvert, did research with these compounds. Near the end of the year he tried to condense phlonglucinol with the formamidines some of which we are following out to confirm the keto structure.

Phlonglucinol behaves in the most of its reactions as a try-hydroxy phenol. However, some of its reactions point to a ketone structure as well as an isomeric change between the two.



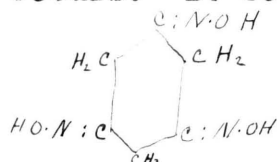
It can be synthesized by forming its dicarboxylate and fusing this with potash.

The dicarboxylate is synthesized by heating at 145°C . ethyl sodic-malonate, $\begin{smallmatrix} COOC_2H_5 \\ H \\ COONa \end{smallmatrix}$ with ethyl malonate $\begin{smallmatrix} COOC_2H_5 \\ CH_2 \\ COOC_2H_5 \end{smallmatrix}$: as represented by this equation:



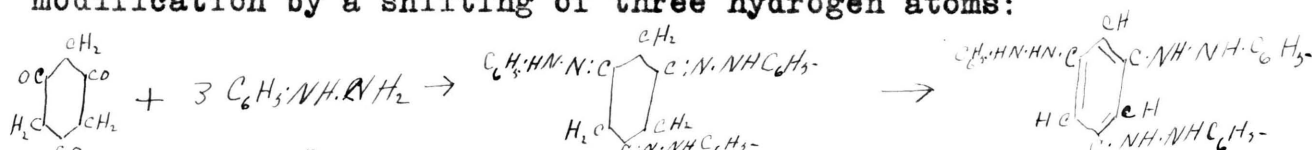
1. Methylen Condensations, Thesis 1909, University of Missouri.

this reaction gives the triketo arrangement if no isomeric change occurs. It condenses with hydroxylamine giving the tri-oxime



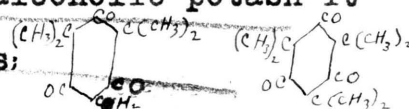
With phenyl hydrazine a similar re-

action takes place. Bayer thinks it undergoes a structural modification by a shifting of three hydrogen atoms:



When¹ alkylated in presence of alcoholic potash it

yields tetra - and hexa-alkyl derivatives;

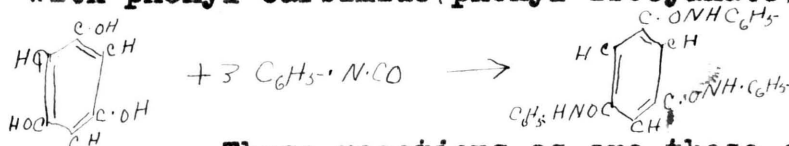


On the other hand it shows its isomeric form distinctly as

in the following cases; it forms metallic derivatives, $C_6H_3(OH)_3$;

trimethyl ethers, $C_6H_3(OC_2H_5)_3$; a tri-carbanilic derivative

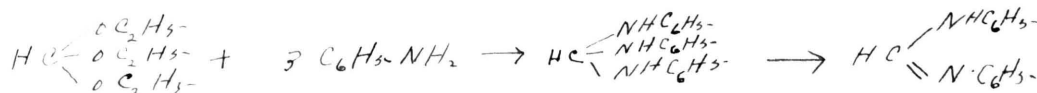
with phenyl-carbimide (phenyl isocyanate)



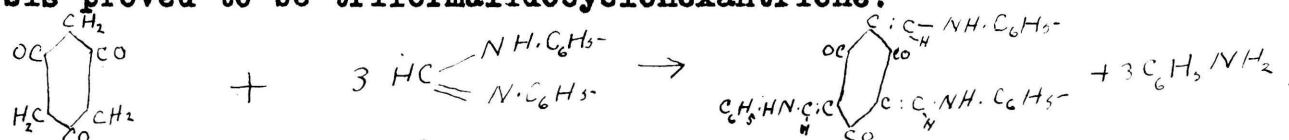
These reactions as are those of the aceto acetic

ester are conflicting, but many chemists prefer to assign the tri-hydroxy structure as the formula for phloroglucinol. However, they think that it can easily be made to pass over into the keto form by the use of different catalysts or good ionizing solutions.

Jones prepared diphenyl formamidine by heating ortho-formic ester and aniline on a water bath

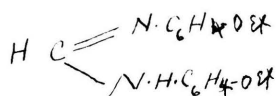


and then condensed this with phloroglucinol in an alcoholic solution. A yellow precipitate separated out which on analysis proved to be triformalidocyclohexantrione.



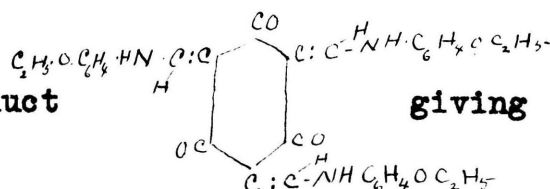
The yield was about 15% of the possible theoretical amount.

If the phloroglucinol had been originally in the enolic condition this would indicate that only a part of it had been changed into the keto form and would also be evidence that the equilibrium between the two isomers (enol and keto) is not maintained on the separation of one phase which would let all of it pass into the other isomer. He repeated the experiment using a different formamidine (methenyl-di-para phenitidine)



and obtained a similar

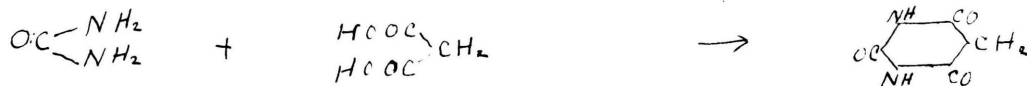
condensation yielding the product



giving

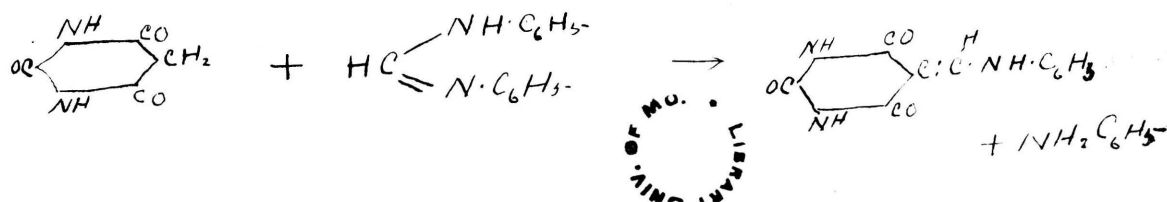
the same evidence as the previous result.

Barbituric acid is synthesized from malonic acid and urea in the presence of phosphorous oxychloride.

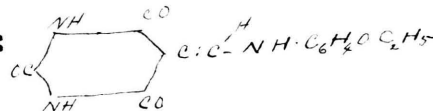


This compound has the group $-\text{CO} \cdot \text{CH}_2 \cdot \text{CO}-$ and is an acid.

Although acids as a rule, hydrolyze the formamidines, this one condensed with diphenyl formamidine in alcoholic solution yielding the derivative of the methylene group.

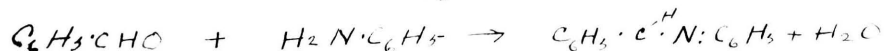


Jones attempted to confirm this reaction by means of di-para-phenitidine formamidine which on analysis indicated the following condensation product:



although he was not able to get the compound absolutely pure.

He accepted Knoevenagel's explanation of the condensations of aldehydes and ketones with 1.3 - diketones and ketonic esters in that the aldehydes or ketones first unite with a base. Benzaldehyde and aniline combine as follows:



The product then interacts with the diketone and regenerates the base. Thus it plays the part of a catalyst.



Jones isolated the intermediate products such as benzylidene

aniline $\text{C}_6\text{H}_5\cdot\overset{\text{H}}{\underset{\text{H}}{\text{C}}}\cdot\text{N}\cdot\text{C}_6\text{H}_5$, oximes $\text{C}_6\text{H}_5\cdot\overset{\text{H}}{\underset{\text{H}}{\text{C}}}\cdot\text{N}\cdot\text{OH}$, and $\text{C}_6\text{H}_5\cdot\overset{\text{H}}{\underset{\text{H}}{\text{C}}}\cdot\text{N}\cdot\text{OH}$

hydrazones $\text{C}_6\text{H}_5\cdot\overset{\text{H}}{\underset{\text{H}}{\text{C}}}\cdot\text{N}\cdot\text{NH}\cdot\text{C}_6\text{H}_5$ or those bodies that contain the

$\text{H}\overset{\text{R}}{\underset{\text{N}\cdot\text{R}}{\text{C}}}=\text{N}\cdot\text{R}$ group, and tried to condense them with phloroglucinol, taking the latter as a representative of such

bodies as malonic ester, acetoacetic ester, and barbituric

acid - all of which have the diketo group, $\text{CO}\cdot\text{CH}_2\cdot\text{CO}$ - But

no successful condensations were obtained. He was thus

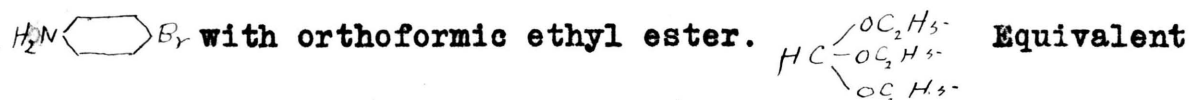
forced to the conclusion that the only group that reacts

readily with the group $\text{CO}\cdot\text{CH}_2\cdot\text{CO}$ - was $\text{H}\overset{\text{NH}_2\text{Ar}}{\underset{\text{NAr}}{\text{C}}}=\text{NAr}$

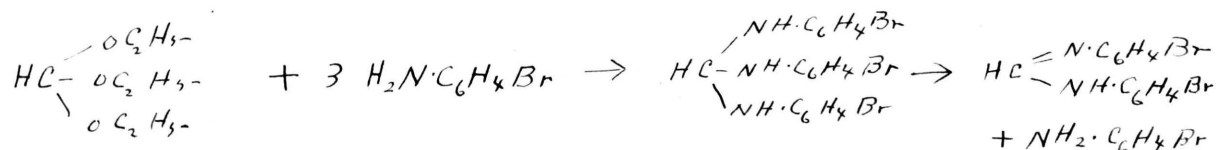
In our research we have endeavored to make a number of condensations with the formamidines with compounds containing $\text{CO}\cdot\text{CH}_2\cdot\text{CO}$ - as did Jones save that in some cases we used different bodies and also endeavored to make some entirely new formamidines and try their condensations

with the view, as mentioned above, of ascertaining (1) the possibility of condensations, (2) the presence of the keto structure, and (3) roughly the percentage of the compound that is in the keto form under the actual conditions of the experiment.

The first formamidine that we used was the dibromo-diphenyl formamidine which was made by condensing p-bromaniline

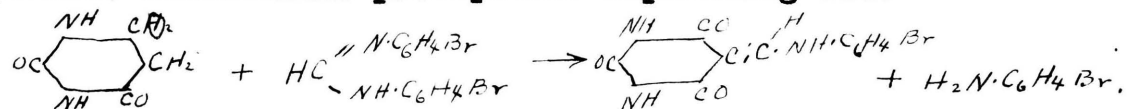


amounts were placed in a flask attached to a reflux condenser and heated on a water bath. The reaction goes without the presence of a solvent. The mixture at first goes into solution and in about twenty minutes the di-bromo-diphenyl formamidine begins to separate out, and in an hour or so the reaction is complete. The product was recrystallized several times from absolute alcohol when white needle like crystals were obtained which melted at 183°C . The yield was almost the theoretical amount. Reaction:



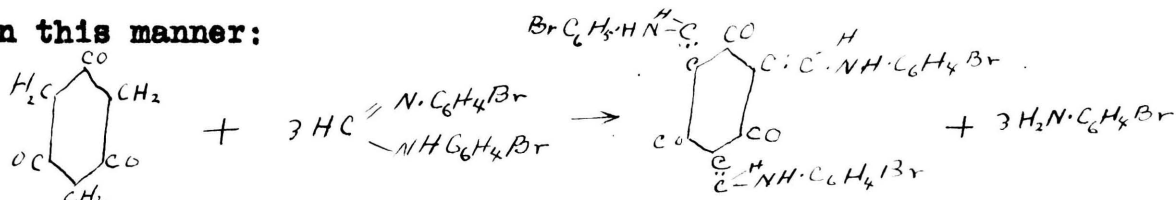
The product was analyzed for bromine by Carius' halogen determination method, that is, at a rather high temperature, $250 - 300^\circ \text{C}$, in a sealed tube with silver nitrate and fuming nitric acid. .2249 grams of the substance gave .2388 grams of silver bromide which shows the presence of 45.18% bromine in the formamidine, $\text{HC} = \begin{matrix} \text{N} \cdot \text{C}_6\text{H}_4\text{Br} \\ \text{N} \cdot \text{C}_6\text{H}_4\text{Br} \end{matrix}$ which has a

theoretical amount of 45.17%. 3.54 grams of this substance was then condensed with 1.29 grams of barbituric acid in an absolute alcoholic solution. On heating on a water bath for three quarters of an hour an almost white (slightly yellow) flocculent precipitate separating out.



The substance was recrystallized several times from alcohol and gave a yield of over 75% of the theoretical amount. It gave a melting point of 370°C. and by a halogen determination .2617 grams of the substance gave .1588 grams of silver bromide which shows 25.82% of bromine. This corresponds with the formula $\begin{array}{c} \text{NH} \quad \text{CO} \\ \diagup \quad \diagdown \\ \text{OC} \quad \text{C} \cdot \text{C} \cdot \text{NH} \cdot \text{C}_6\text{H}_4\text{Br} \\ \diagdown \quad \diagup \\ \text{NH} \quad \text{CO} \end{array}$ which has 25.79% of bromine.

A similar condensation was made with the dibromo-diphenyl formamidine with phloroglucinol using 5.30 grams of the former and .81 grams of the latter in alcoholic solution and heating on the water bath. The reaction was slow but in four or five hours a yellow amorphous solid separated out which when pure melted at 285° C. The reaction took place in this manner:

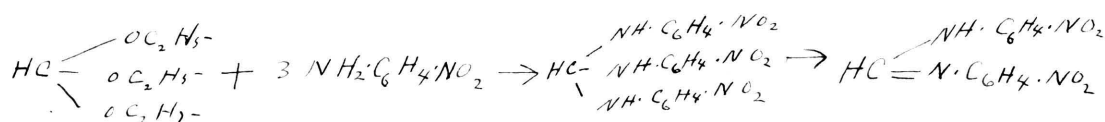


The compound was crystallized several times from absolute alcohol and then tested for the percentage of bromine by the Carius' method. .2179 grams of the compound yielded .1830 grams of silver bromide which showed the presence of 35.73% of bromine. This corresponds well with the theoretical

amount of 35.695 %. The yield was about 20% of the theoretical amount.

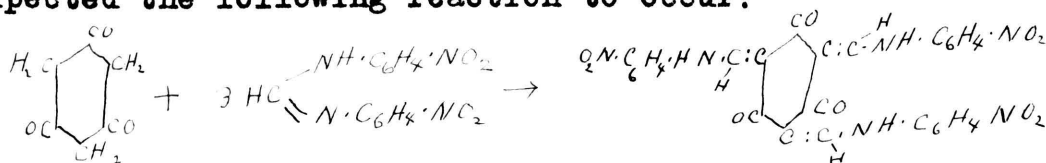
An attempt at condensation between the di-bromo-di-phenyl formamidine and oxalacetic ester $\begin{array}{c} \text{CO} \cdot \text{C}_2\text{H}_5- \\ | \\ \text{C} \\ | \\ \text{CH}_2 \\ | \\ \text{CO} \cdot \text{C}_2\text{H}_5- \end{array}$ will be discussed later.

Another formamidine was prepared by heating on a water bath for several hours ortho-formic ester and meta-nitraniline. The reaction is similar to that for the preparation of bromo-formamidine.



On crystallizing this body from alcohol it gave slender needle like crystals which melted at 195°C to -6°C .

An attempt was made to condense this with phloroglucinol. 3.26 grams of it were placed in a flask containing .62 grams of phloroglucinol and 50 cc. absolute alcohol. We expected the following reaction to occur:



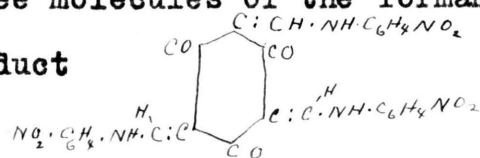
After heating for three hours the formamidine did not appear to have gone into solution. Some of it was removed and a melting point determination showed that it had remained unchanged. On heating five hours longer it went into solution giving a marked brick red color. No precipitate separated out on standing even though nearly all of the alcohol evaporated off. More alcohol was added, the solution heated to boiling and then hot distilled water was added which caused crystallization of beautiful yellow flakes. The crystallization was repeated four times. The crystals were then dried

and gave a yield of over 35% of the theoretical amount and a melting point of 106° C.

Analysis of the compound for the percentage of nitrogen by the Dumas' method followed:

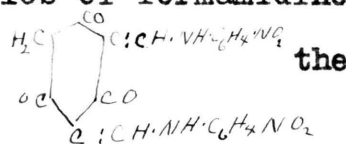
.1974 grams of the substance gave a volume of 37.02 cc. of nitrogen at 22° C. and 440 m.m. This on calculation yielded 20.66 % of nitrogen. On repeating the above .2018 grams of the substance gave 38.3 cc. of nitrogen at 25° C and 744 1/2 m.m. which calculates 20.71 % of nitrogen; the average of the two is 20.68%. This result does not correspond with any of the expected condensation products. If

three molecules of the formamidine had condensed giving this product

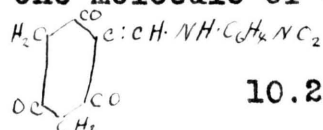


14.73% of nitrogen would

have been produced, if only two molecules of formamidine had combined to give this product,



analysis would have shown 13.27% of nitrogen, and had but one molecule of each condensed giving the product



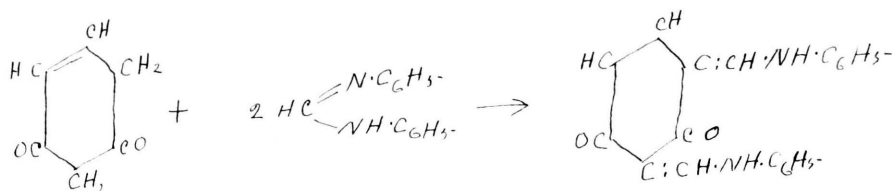
10.22% of nitrogen would have been given. The

condensation was repeated with small amounts, but the product on purification gave the same melting point 106° C and as the amount was very small no determination of the nitrogen was made. The supply of nitraniline had all been used so that no further experimenting with this body was possible.

The following three bodies had failed with Jones to condense with the formamidines and we have tried to condense

them by varying the conditions as indicated in each case.

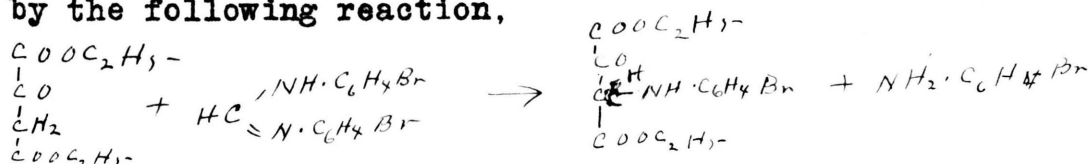
T Resorcinol was placed in pressure tubing with diphenylformamidine and a few cubic centimeters of absolute alcohol. The tube was sealed and heated four hours at 220° C. The tube was allowed to cool and the contents examined. A reaction had taken place as indicated by the melting point and the red color, but the reaction had not stopped where we had expected.



Another condensation between resorcinol and diphenyl formamidine was attempted by heating the two in alcoholic solution in the presence of small amount of pyradine with the view that the pyradine would act as a strong catalytic agent. On boiling two or three hours no precipitate had formed, but on boiling still longer and allowing to stand a precipitate came down that looked like the original formamidine and had the same melting point. The action between these two substances therefore is not an easy one, or, at least, we did not find satisfactory conditions for it.

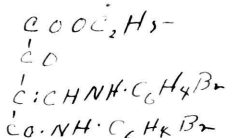
Phloroglucinol and nitrosodimethyl aniline were placed in an absolute alcohol solution and heated in a reverse condenser. After prolonged heating a black precipitate separated out which was very hard and granular and did not have the characteristics of the condensation products.

Condensation products of oxalacetic ester
 with dibromo-diphenyl formamidine $\text{HC} \begin{smallmatrix} \text{NC}_6\text{H}_4\text{Br} \\ \text{NH}\cdot\text{C}_6\text{H}_4\text{Br} \end{smallmatrix}$ and diphenyl
 formamidine $\text{HC} \begin{smallmatrix} \text{N}\cdot\text{C}_6\text{H}_5 \\ \text{NH}\text{C}_6\text{H}_5 \end{smallmatrix}$ were examined. 2.20 grams of
 the ester and 4 grams of diphenyl dibromo formamidine were placed
 in a flask with reverse condenser. When the two were added the
 temperature of the mixture rose slightly and on standing a few
 minutes the color became dark. On heating an hour on a water
 bath without a solvent the mixture became a dark thick syrupy
 substance with a trace of granules in it. This was cooled and
 ether added. The ether slowly caused crystals, pale yellow
 in color, to separate out. The separation seemed to be com-
 plete in a day's time. The solid was dissolved in absolute
 alcohol with some difficulty, but later refused to crystallize
 out. The alcohol seemed to bring about some change in the com-
 pound to make it act in this manner. The alcohol was evapo-
 rated off and the compound purified by extraction several
 times with ether. The yield was small - not more than 10% of
 the calculated amount. The compound was analyzed for the
 percentage of bromine. .2038 grams of substance gave .1532
 grams of silver bromide which shows that the compound contained
 31.99% bromine. This percent does not correspond with that of
 any expected formula. If one molecule of each had combined
 by the following reaction,

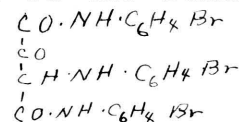


the analysis should have given 22.98% bromine. If the ester
 had combined with two molecules of the formamidine giving a

condensation product of the formula



the analysis should have given 34.16% of bromine. If one molecule of the ester had combined with three of the formamidine giving the product of this formula:

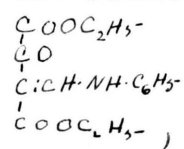


41.36% of bromine would have been present. As mentioned before, the supply of bromonitraniline was exhausted so that the experiment did not permit of repetitions under varied conditions. The data at hand could well be interpreted to mean that a mixture of products had been obtained.

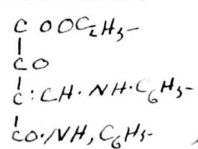
The same ester (oxalacetic) and diphenyl-formamidine were experimented with. 12 grams of the ester were added to 13 grams of diphenyl formamidine. When added the temperature of the mixture rose about twenty-five degrees and the color became dark green, but soon changed into blue. This was allowed to stand until the next day so as to ascertain whether a spontaneous reaction had occurred. The blue color had disappeared in the meantime and the formamidine seemed to have separated and gone to the bottom of the flask. A small amount of this substance was removed, purified, and its melting point $135^{\circ}\text{C}.$, showed it to be the original formamidine. 50 cc. of absolute alcohol was then added to the mixture and the whole with reverse condenser attached, was heated on a water bath for an hour. The formamidine went into solution but no precipitate separated out while heating or after the solution had cooled. The alcohol was evaporated and a thick

reddish brown syrup with scarcely more than a trace of pale yellow crystals was left. From an analogy of the action of the bromo compound and the ester we expected that the crystals of this would separate out faster on the addition of ether, but the ether seemed to be without effect. The compound was allowed to stand in the laboratory where we could observe it. At the end of the second day we could see that the amount of crystals was growing. The growth gradually continued until at the end of eight or ten days the crystals were removed by filtration in etherial solution, in which the syrupy substance was quite soluble. The solid substance and the original diphenyl formamidine were about equally soluble in all the common solvents, save benzol. It was extracted with benzol several times. The yield was two grams and the melting point was 145°C . An analysis for nitrogen was made. .3800 grams of substance gave 34.25 cc of nitrogen at 26°C . and 745 mm. pressure. This data gives 12.21% of nitrogen. As in the previous condensation between dibromo formamidine and the ester there seems to be a possibility of a combination of one molecule of the ester with one, two, three, or even four molecules of formamidine with products of

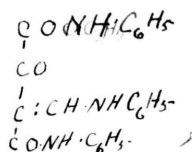
the following formula:



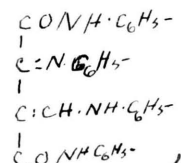
I.



II.



III.



IV.

These have 6.03%, 8.26%, 10.91%, and 12.18% of nitrogen respectively. The percent of nitrogen for the fourth formula corresponds well with the results of the analysis, 12.21%.

Accepting this as the correct reaction it will be seen from the data that the yield of two grams is about 30% of the theoretical amount of product.

No doubt the reaction in the former case with the bromo compound was analogous to this and might have been shown so had the necessary supply of material been present.

All of the attempts at condensations gave some kind of reaction except resorcinol, and the most of them gave the expected bodies. The di-nitro compound with phloroglucinol gave an abnormal reaction. It should have gone smoothly as did the bromo-derivative of phloroglucinol. The real product of the reaction will probably be found only by determining the carbon, hydrogen, oxygen, and nitrogen and securing the molecular formula.

The work seems to indicate that all the attempted condensations could be perfected if the proper conditions were selected for it. The groups essential for the condensations are $-CO-CH_2-CO-$ and $HC \begin{matrix} \nearrow NR \\ \searrow NHR \end{matrix}$ The radical R permits of a wide variation. In no case except that of barbituric acid, did the quantitative result indicate that the whole compound was in the keto condition and consequently this questions the theory of equilibrium which would have the whole to pass into the keto form on the precipitation or separation of the molecules of that structure as fast as they are formed.

In conclusion I desire to say that this work was undertaken on the recommendation of Professor Sydney Calvert, Professor of Organic Chemistry. My best thanks are due him for the interest he has taken and the help he has given in carrying it out.

Chemistry Laboratory,
University of Missouri.



University of Missouri - Columbia



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