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Form 26
MORE EVIDENCE UPON THE STRUCTURE OF PHLOROGLUCINOL
AND SOME NEW DERIVATIVES

by

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HISTORICAL.

In 1876 Butlarow (1) suggested that in the case of certain bodies a kind of intramolecular vibration was continually taking place, which may explain why some substances react at one time in one way and again in another according to the kind of reagents with which they were treated. Some years later Laar (2) (1885) collected a number of cases of substances acting as if they had two constituents which could be explained by the oscillation of the hydrogen atom from one carbon atom to another. Laar called this particular phenomenon, of one substance doing duty for two structural isomers, "tautom erism". Isatin occurred among the number collected and he represented the two isomers thus:

\[
\text{I} \quad \text{II}
\]

He accounts for the second form by the wandering of the hydrogen atom from the nitrogen to the more stable position beside the oxygen atom. By him a - naphtha - quinone phenylhydrzone and its isomer are represented thus:

\[
\text{I} \quad \text{II}
\]

(1) Annalen 1876, 189, 76;
(2) Ber. 1885, 18, 648; 1886, 19, 730.
The first is formed by the interaction of a - naphtha quinone and phenyl hydrazine and the second by a - naphthol and diazo-benzene chloride. He also mentioned the two fold character of nitrosophenol which at one time reacts like a dioxime and the other like a phenol:

![Chemical Structure Image]

The tautomeric compound, aceto acetic ester was the subject of discussion between Geuther and Frankland. Geuther, (1) who upheld the enolic structure, \( \text{C}_3\text{H}_2\text{OH}:\text{CH}_3\text{COO}_2\text{H}_5 \)

offered the following equation to explain its formation:

\[
\begin{align*}
\text{CH}_3\text{COO}_2\text{H}_5 + \text{Na}_2 \rightarrow & \text{CH}_3\text{CO}_2\text{Na} + \text{C}_2\text{H}_5\text{Na} \\
\text{C}_3\text{H}_2\text{CO}_2\text{Na} + \text{CH}_3\text{COO}_2\text{H}_5 \rightarrow & \text{C}_3\text{H}_2\text{CO}_2\text{Na} \cdot \text{CH}_3\text{COO}_2\text{H}_5 + \text{H}_2 \\
\text{C}_3\text{H}_2\text{CO}_2\text{Na} \cdot \text{CH}_3\text{COO}_2\text{H}_5 + \text{CH}_3\text{CO}_2\text{H} \rightarrow & \text{CH}_3\text{CO}_2\text{Na} \cdot \text{CH}_3\text{CO}<\text{O}_2\text{H}_5 + \text{C}_2\text{H}_5\text{CO}_2\text{Na}.
\end{align*}
\]

Frankland, (2) who favored the keto structure \( \text{CH}_3\text{CO},\text{CH}_3\text{COO}_2\text{H}_5 \)

explained its formation in this manner:

\[
\begin{align*}
\text{CH}_3\text{COO}_2\text{H}_5 + \text{Na}_2 \rightarrow & \text{CH}_3\text{NaCOO}_2\text{H}_5 + \text{H} \\
\text{CH}_3\text{NaCOO}_2\text{H}_5 + \text{CH}_3\text{COO}_2\text{H}_5 \rightarrow & \text{CH}_3\text{HCN} \cdot \text{COO}_2\text{H}_5 + \text{C}_2\text{H}_5\text{OH} + \text{H} \\
\text{CH}_3\text{HCN} \cdot \text{COO}_2\text{H}_5 + \text{CH}_3\text{COO}_2\text{H}_5 \rightarrow & \text{CH}_3\text{HCN} \cdot \text{COO}_2\text{H}_5 + \text{C}_2\text{H}_5\text{CO}_2\text{Na}.
\end{align*}
\]

To distinguish between the hydroxyl and the carbonyl groups in aceto acetic ester and similar bodies seems at first sight an easy matter, but on further examination of the addition products one can see that the addition can be explained equally well with the enolic or ketoic structure.

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(1) Annalen, 1883, 219, 123.
(2) Annalen 1886, 204, 328; Trans. 1886, 156, 37.
Thus for example, we shall consider the addition of hydrogen:

\[
\begin{align*}
\text{CH}_3 & \quad \text{C}_2\text{H}_5 & \quad \text{CH}_3 & \quad \text{CH}_3 \\
\text{COOH} + 2\text{H} & \rightarrow \text{CH}_2\text{OH} & \quad \text{CO}_2\text{H}_5 & \quad \text{CO}_2\text{H}_5 \\
\text{N} & \quad \text{CH}_3 & \quad \text{C}_2\text{H}_5 & \quad \text{CO}_2\text{H}_5 \\
\text{COOCH}_2\text{H}_5 & \quad \text{COOCH}_2\text{H}_5 & \quad \text{COOCH}_2\text{H}_5 & \quad \text{COOCH}_2\text{H}_5
\end{align*}
\]

In either case we see the final product is the same. Experiments and results supporting each structure are numerous and often very conflicting.

Some of the arguments in favor of the enolic structure \( \text{CH}_3\text{CON}\text{CH}_2\text{CO}_2\text{H}_2 \) are as follows:

1. the ease with which it forms
   - (a) a sodium salt: \( \text{CH}_3\text{CONa} : \text{CH}_2\text{CO}_2\text{Na} \)
   - (b) a well crystalline copper salt: \( \text{Cu}_2\text{C} : \text{CH}_2\text{CO}_2\text{Na} \)
   - (c) a violet colored ferric salt: \( \text{Fe} (\text{C}_6\text{H}_5\text{O}_3)_3 \)

2. it reacts with phosphorus pentachloride giving the characteristic reaction for the hydroxyl group:

   \[
   \text{CH}_3\text{CON} : \text{CH}_2\text{CO}_2\text{Na} + \text{PCl}_3 \rightarrow \text{CH}_3\text{CON} : \text{CH}_2\text{CO}_2\text{H} + \text{HCl} + \text{PCl}_3
   \]

3. with the secondary amines it gives the ester of the formula:

   \( \text{CH}_3\text{CON} : \text{C} (\text{NH}_2) : \text{CH}_2\text{CO}_2\text{Na} \)

4. with ammonia, it gives \( \beta \)-amino-crotonic ester:

   \( \text{CH}_3\text{CON} : \text{C} (\text{NH}) : \text{CH}_2\text{CO}_2\text{H} \)

5. with chloroformic ester it gives a carbonic ester:

   \[
   \text{CH}_3\text{CON} : \text{CH}_2\text{CO}_2\text{Na} \rightarrow \text{CH}_3\text{CO} (\text{CO}_2\text{H}) : \text{CH}_2\text{CO}_2\text{H} + \text{HCl}
   \]

6. with phenol it condenses with the formation of methyl coumarin:

   \[
   \begin{array}{c}
   \text{CH}_3\text{CON} : \text{CH}_2\text{CO}_2\text{Na} + \text{C}_6\text{H}_5\text{OH} \rightarrow \text{CH}_3\text{CO} (\text{CO}_2\text{H}) : \text{CH}_2\text{CO}_2\text{H} + \text{C}_6\text{H}_5\text{ON}
   \end{array}
   \]

There are still other reactions where a molecule of water splits...
off that can be explained more readily by the enolic than the ketonic formula.

The evidence for the ketonic structure is equally as strong:

(1) with nitrous acid it forms isonitrosos - acetone:

\[
\text{CH}_3\text{CO.C}H_2\text{C}O\text{OC}_2\text{H}_5 \\
\text{NO}_2\text{OH} \rightarrow \text{CH}_3\text{CO.C}H_2\text{NO} + \text{C}2 + \text{C}H_3\text{OH}
\]

(2) with hydroxylamine, an oxime is formed which loses alcohol and passes into methyl oxazoline:

\[
\text{CH}_3 \\
\text{C}=0 + \text{H}_2\text{NOH} \rightarrow \text{CH}_3 \\
\text{C}:\text{NOH} \rightarrow \text{H}_2\text{C} + \text{C} - \text{CN}_3
\]

(3) a hydrazone, with phenyl hydrazine which also loses alcohol:

\[
\text{CH}_3 \\
\text{C}=0 + \text{H}_2\text{NNH}_2\text{C}_6\text{H}_5 \rightarrow \text{C}=\text{NNNH}_2\text{C}_6\text{H}_5 \rightarrow \text{H}_2\text{C} + \text{C} - \text{CN}_3
\]

(4) combines with sodium bisulphite and hydrogen cyanide:

\[
\text{CH}_3 \\
\text{C}=0 + \text{NaHSO}_3 \rightarrow \text{C}=\text{NaSO}_3 \}
\text{C}=0 + \text{HCN} \rightarrow \text{C} - \text{CN}
\]

(5) by the action of iodine on the sodium compound di-aceto-
succinic ether is formed:

\[
\text{CN}_3\text{CO.C}H\text{Na.C}O\text{OC}_2\text{H}_5 - \text{CN}_3\text{CO.C}H\text{Na.C}O\text{OC}_2\text{H}_5 + 2\text{NaI}
\]

\[
\text{CN}_3\text{CO.C}H\text{Na.C}O\text{OC}_2\text{H}_5 - \text{CN}_3\text{CO.C}H\text{Na.C}O\text{OC}_2\text{H}_5
\]

This data is not conclusive proof of the enolic or ketonic structure because it is generally supposed that the reagent with which the reactions are brought about might cause isomeric change.
The stability of the two isomeric forms depends upon the temperature, pressure, solvent, and strength of solution. Acids and bases cause the shifting of the hydrogen atom within the molecule and cannot be used for determining the structure of enolic and ketonic tyrers. (1) A large number of the sodium compounds have been shown to be of the enolic type; but it would not be logical to assume that the derivatives resulting from their use is a guide as to the structure of the original substance. Both forms of formylphenyl acetic ester yield the same acetyl derivative. Phenyl carbimide is a reagent which produces little or no effect on the isomers when dissolved in a non-ionizing solvent. In the cold it reacts with hydroxy and amino-compounds in the following way to form carhamic esters and carbamido compounds:

\[ R\text{OH} + C_6H_5N\text{H:C} : O \rightarrow R\text{O.C} \text{O} \text{N} \text{H}_2 \]

When orthoformic ester, in the presence of acetyl chloride, condenses with acetoacetic ester the ketonic structure is in evidence:

\[ \begin{align*}
C\text{O} & \text{H}_3 \quad C\text{O} \text{H}_3 \\
C\text{O} & + C\text{H}_2 \text{O} \rightarrow C\text{O} \text{H}_3 \\
C\text{H}_2 & \text{O} \rightarrow C\text{CO} \text{H}_3 \\
C\text{O} & \text{O} \text{H}_3 \\
C\text{O} & + C\text{H}_2 \text{O} \rightarrow C\text{CO} \text{H}_3
\end{align*} \]

Diethyl hydroxybutyric ester is the result of the reaction. If acetic anhydride is used as the condensing agent instead of acetyl chloride the oxygen atom remains intact while two atoms of hydrogen are removed from the adjoining carbon:

---

Each reaction shows the ester in the keto form but the presence of the condensing agent tends to change the equilibrium of the two isomers toward the keto form. Condensation products with acetaldehyde, benzoaldehyde, and acetoacetic ester have been obtained in the presence of hydrochloric acid by Claisen: (1)

\[
\text{C}_3\text{H}_5\text{C}=\text{O} + \text{C}_2\text{H}_5\text{C}=\text{O} \rightarrow \text{C}_3\text{H}_5\text{C}=:\text{O} + 2\text{C}_2\text{H}_5\text{OH}.
\]

He (2) concludes that the \(\text{C}=\text{O} \rightarrow \text{C}=\text{O}\) group which is present in these substances may play the same part as the \(\text{O}\) oxygen atom in a carboxylic acid, a view which is readily understood by a comparison of the two atomic groupings:

\[
\text{C}_3\text{H}_5\text{C}=\text{O} \quad \text{C}_3\text{H}_5\text{OH}
\]

Hydroxymethylene diketone, Formic acid

By the aid of Michael's (3) positive and negative theory, Michael has shown that the sodium salts of the \(\text{C}=\text{O} \rightarrow \text{C}=\text{O}\) group condenses with unsaturated compounds of the general formula \(R\text{C}=:\text{C}H\chi\) or \(R\text{C}=:\text{C}\chi\) where \(R\) is a positive or negative radical and \(\chi\) a strong negative radical like carbonyl.

(1) Annalen 1883, 218, 172.
(2) Annalen 1897, 272, 1.
(3) J. Prakt. Chem. 37, 473; 43, 395; 45, 55; 49, 20.
or cyanogen group. A condensation between sodium malonic ester and cinnamic ester takes place according to Michael as follows:

\[
\text{C}_6\text{H}_5\cdot \text{CH} \cdot \text{CH} \cdot \text{CO}_2\text{H}_5 + \text{C}_6\text{H}_5\cdot \text{CH} \cdot \text{CH}_2\cdot \text{CO}_2\text{H}_5 - \text{N} \cdot \text{CH} \cdot \text{CO}_2\text{H}_2 \rightarrow \text{C}_6\text{H}_5\cdot \text{CH} \cdot \text{CH}_2\cdot \text{CO}_2\text{H}_5 - \text{N} \cdot \text{CH} \cdot \text{CO}_2\text{H}_2
\]

In a like manner maleic \(\text{H} \cdot \text{C} \cdot \text{CO}_2\text{H}_5\) fumaric \(\text{H} \cdot \text{C} \cdot \text{CO}_2\text{H}_5\) esters condense with the sodium salt of malonic acid.

Japp and Streatfield \(^{11}\) used ammonia to bring about a condensation between phenanthraquinone and acetoacetic ester,

\[
\begin{align*}
\text{C}_6\text{H}_4\cdot \text{C} + \text{CO}_2\text{H}_5 & \rightarrow \text{C}_6\text{H}_4\cdot \text{C} \cdot \text{CO}_2\text{H}_5 + \text{H}_2\text{O}, \\
\text{C}_6\text{H}_4\cdot \text{C} \cdot \text{CO}_2\text{H}_5 & \rightarrow \text{C}_6\text{H}_4\cdot \text{C} \cdot \text{CO}_2\text{H}_5 + \text{H}_2\text{O}.
\end{align*}
\]

Knoevenegel carried out a much more complete investigation, using primary and secondary amines as well as ammonia to combine with the group \(-\text{C} \cdot \text{C} - \text{C} \cdot \text{O} -\) and assumed that there was first an addition of the aldehyde with the base and then a splitting off of the amine.

Formaldines of the type \(\text{H} \cdot \text{C} \cdot \text{C} \cdot \text{N} \cdot \text{R}\) were found, by Daines, \(^{3}\) to be very reactive with substances containing the \(-\text{C} \cdot \text{O} \cdot \text{C} - \text{H} - \text{C} \cdot \text{O} -\) group. Ethyl malonic ester \(\text{C}_2\text{H}_5\cdot \text{C} \cdot \text{CO}_2\text{H}_5\) did not react with diphenyl formamidine, nor did acetodiphenyl-formamidine, \(\text{H} \cdot \text{C} \cdot \text{N} \cdot \text{C}_6\text{H}_5\). Therefore, he concludes that the group \(\text{C} \cdot \text{O} \cdot \text{C} - \text{C} \cdot \text{O} -\) and \(\text{H} \cdot \text{C} \cdot \text{C} \cdot \text{N} \cdot \text{R}\) are necessary for condensation and accounted for the reaction thus:

\(\text{(1)}\) Trans. Chem. Soc., 1883, 55, 27; Ber. 1898, 31, 738.

\(\text{(2)}\) Annalen 1894, 284, 25; Ber. 1904, 77, 4461.

\(\text{(3)}\) Ber. 1902, 35, 2496.
Calvert and Jones (1) worked with bodies of the type 
$\text{NC}_3H_7\text{Nar}$ and $\text{R}_2\text{e}_2\text{Nar}$ in order to determine what groups are necessary for the condensation with the methylene group $-\text{CO-CH}_2-\text{CO-}$.

They succeeded in condensing phloroglucinol with the formamidines, some of which we are studying in order to confirm the keto structure providing no shifting takes place with the reagents and solvent.

Phloroglucinol, in most of its reactions behaves like a trihydroxyphenol and was considered as such for a long time, until Von Baeyer (2) synthesized it by heating at 145°C sodium malonic ester with $\text{Na}_2\text{CO}_3$ and $\text{CH}_3\text{OH}$. This gave ethyl phloroglucinol tri-carboxylate which on heating with potassium hydroxide gave phloroglucinol:

---

(1) methylene condensation, Thesis 1909, University of Missouri.

(2) Ber. 1885, 18, 3458.
This reaction gives the triketo structure. Phloroglucinol will condense with hydroxylamine giving the trioxime:

\[ \text{H}_2\text{C} = \text{N} - \text{H} \text{N} - \text{H}_2 \rightarrow \text{H}_2\text{C} - \text{N} - \text{H} - \text{N} - \text{H}_2 \]

also condenses with phenylhydrazine but Baeyer(1) thinks it is a hydrazide caused by the wandering of a hydrogen atom from the benzene nucleus to that of hydrazone radical and not a hydrazone of the keto form.

When chlorine \(^{(2)}\) acts on phloroglucinol in chloroform solution, a hexachlorophloroglucinol results. Also yields a tetra- and hexa- alkyl derivative when alkylated in the presence of alcoholic potash. The arguments in favor of the enolic structure are: it forms metallic derivatives \(\text{C}_6\text{H}_3(\text{ONa})_3\); triacetyl derivative with acetyl chloride; a trimethyl ether: \(\text{C}_6\text{H}_3(\text{OCH}_3)_3\); a tricarbanilic derivative with phenylisocyanate:

Thus we see that reactions of this kind are almost as conflicting as those of acetoacetic ester, and may not be used as a guide.

(1) Ber. 1891, 24, 2688.

(2) Ber. 1889, 22, 1476; Ber. 1890, 22, 230.
to the original structure of the substance for the reagents may cause isomeric change from the enolic to the ketonic form, or vice-versa.

The diphenyl formamidine prepared according to Walther (1) was condensed with phloroglucinol in alcoholic solution by Calvert and Jones. The yellow precipitate which separated out, on analysis proved to be 1; 3; 5 triformanilido cyclohexantrione. The yield of this body was about 15% which is good evidence that the equilibrium between the two isomers is not maintained on the separation of one phase which would let all of it pass into the other form. The experiment was repeated using ethyl dipara phenetidine which gave a similar condensation product.

\[
\begin{align*}
\text{H}_2\text{C} & \text{=CH} \text{N} \text{-C:O} \\
\text{C:O} & \text{C:O} \text{C:O} \text{C:O} \text{C:O}
\end{align*}
\]

With barbituric acid, a compound containing the methylene grouping \(-\text{O}\text{C} - \text{C}_2\text{H}_4\text{C} - \text{O}\), a condensation was obtained with both diphenyl formamidine and ethyl depara phenetidine. The nitrogen content of the latter was little high, probably due to some ocluded barbituric acid which was difficult to extract.

Calvert and Jones accepted Knoevenagel's theory of condensation of primary amines with aldehydes and ketones in that the aldehyde or ketone unites with the amine to form an intermediate compound, \(\text{C}_6\text{H}_5\text{C} = \text{C} - \text{H} + \text{H}_2\text{N} \text{C}_2\text{H}_4 \rightarrow \text{C}_6\text{H}_5\text{C} = \text{N} \text{C}_2\text{H}_4\text{H}_2\text{O} + \text{H}_2\text{O}\). The imide group then condenses with the diketone and regenerates the primary amine, playing the part of a catalyst.

(1) J. Prakt. Chem. 55, 41.
Calvert and Jones used a number of these compounds containing the imide or substituted imide groups such as benzylidine aniline, \( \text{C}_6\text{H}_5 - \text{C}^-' = \text{N} \cdot \text{C}_6\text{H}_5 \), benzaldehyde phenylhydrazone, \( \text{C}_6\text{H}_5 - \text{C} = \text{N} \cdot \text{NH} \cdot \text{C}_6\text{H}_5 \), and acetophenone oxime \( \text{C}_6\text{H}_5 - \text{C} = \text{N} \cdot \text{O} \) and tried to condense these with phloroglucinol as a representative of the diketo structure. Their results were all negative. Thus they concluded that the only group that condenses readily with the \(-\text{CO}-\text{C}_6\text{H}_5-\text{CO}-\) group is \( \text{H} \cdot \text{C} = \text{N} \cdot \text{H} \cdot \text{Ar} \).

Later Calvert and Stagner did research with formamidines on substances containing the methylene grouping with the view of ascertaining the percentage of the compound in the keto form. Calvert and Stagner prepared dibromdiphenyl-formamidine by heating equivalent amounts of parabromaniline with orthoformic ester, without the presence of a solvent, on a water bath.

\[
\text{H} \cdot \text{C} = \text{O} \cdot \text{C}_6\text{H}_5 + 3 \text{H}_2 \text{N} \cdot \text{C}_6\text{H}_5 \cdot \text{Br} \rightarrow \text{N} \cdot \text{C}_6\text{H}_5 \cdot \text{Br} \rightarrow \text{H} \cdot \text{C} = \text{N} \cdot \text{C}_6\text{H}_5 \cdot \text{Br} + \text{H}_2 \cdot \text{N} \cdot \text{C}_6\text{H}_5 \cdot \text{Br}
\]

and condensed this formamidine with barbituric acid in absolute alcohol solution. A white flocculent precipitate separated which on analysis of bromine content corresponds to the body formed by the equation:
This yield was over 75% of the theoretical amount. They also condensed this formamidine with phloroglucinol, obtaining a yield of about 20% of the theoretical amount.

They next prepared a formamidine of the formula \( \text{HC} = \text{NCH}_2\text{ON}_2 \) by the action of metanitraniline on orthoformic ester and attempted to condense it with phloroglucinol. On analysis of the nitrogen by Dumas' method, it gave 20.58% N. This result did not correspond to any of the expected condensation products. As the supply of nitroaniline had been used, it was impossible to make further experiments with this body.

Dibrom-diphenyl formamidine \( \text{H} \text{C} = \text{NCH}_2\text{Br} \) and diphenyl formamidine \( \text{H} \text{C} = \text{NCH}_2 \text{H} \) were condensed with oxalacetic ester \( \text{OOCCH}_2 \text{H} \) when the former was mixed with the ester there was a slight rise of temperature and the solution turned dark color; on heating it became thick and syrupy with a trace of crystals in it. The addition of ether caused pale yellow crystals to separate. Analysis of the crystals gave results which lead them to believe it was a mixture of one and two molecules of the formamidine with the ester. The supply of nitroaniline being exhausted prevented repetition under varied condition. With the diphenyl-formamidine the ester gave results for the following equation:
All attempts at condensation gave some kind of reaction except resorcinol and in most cases the expected bodies. So they concluded that condensation could be brought about if the proper conditions were selected, and the essential groups are \( \text{C}=\text{N} - \text{C}=\text{O} \) and \( \text{N} \cdots \text{N} \cdots \text{R} \) where the radical R will permit of wide variation.
EXPERIMENTAL PARTS.

Part A.

In order to study the structure of phloroglucinol we decided to use the diphenyl formamidine derivative of phloroglucinol:

\[
\text{H}_\text{c} = \text{N} = \text{C}_\text{6} \text{H}_\text{5}.
\]

This was prepared first according to Calvert and Jones by the action of diphenylformamidine on phloroglucinol. The reaction goes with great ease. All that is necessary is to place one part of phloroglucinol and three parts of diphenyl formamidine in a flask attached to a reflux condenser and add about 100 parts of absolute alcohol. After heating on a water bath for 15 or 20 minutes a yellow silky precipitate begins to form which increased in bulk as the heating continued. After heating for four hours the heating was discontinued and the yellow precipitate removed by filtering. The compound was almost insoluble in the common organic solvents such as alcohol, benzene, carbon bisulphide, acetone, and ligroin but soluble in chloroform and glacial acetic acid. Recrystallized the compound several times from glacial acetic acid and dried it on a porous plate, it gave a melting point of 703° (corr.) The reaction takes place according to the following equation:

\[
\text{H}_\text{c} = \text{C}_\text{6} \text{H}_\text{5} + 3 \text{H}_\text{c} = \text{N} = \text{C}_\text{6} \text{H}_\text{5} \rightarrow \text{H}_\text{c} = \text{C}_\text{6} \text{H}_\text{5} = \text{N} = \text{C}_\text{6} \text{H}_\text{5}.
\]

The yield of this 1: 3: 5 triformanilido cyclohexametrione is about 17%.
Later we endeavored to bring about this same condensation in the absence of a solvent by simply fusing one part of phloroglucinol with a little excess of three parts of diphenyl formamidine. The mixture was heated in a H₂SO₄ bath to 220°-225°C. for thirty minutes. The brown liquid solidified on cooling and was dissolved in hot glacial acetic acid from which it crystallized in yellow crystals. A melting point showed it to be the same substance as that produced with alcohol as a solvent. The yield was much better by this method, giving about 50%. This is good evidence that the alcohol solution changed part of phloroglucinol from the ketonic to the enolic structure.

3.35 grams of the diphenyl formamidine derivative was placed in a small flask with 30 cc. of phenyl hydrazine and heated gently for a half an hour. On cooling a yellow precipitate separated. The substance was soluble in hot alcohol from which it was recrystallized several times and finally dried on a porous plate. A nitrogen analysis gave the following results:

0.2880 grams substance gave 48.3 cc. N. at 737 mm. and 26°C.

\[ \text{calculated for } C_{45}H_{39}N_7 \]

\[ \text{Found} \]

N. \[ 17.88 \% \] \[ 18.02 \% \]

corresponding to the equation:

\[ \text{H}_2\text{CNC:C:} + 3\text{HNNH}_2\text{C:C:} \rightarrow \text{H}_2\text{CNC:C:} \]
This result confirms along with the oxime of phloroglucinol and the 1: 3: 5 triformamidio cyclohexamtrione the keto structure of phloroglucinol.

In order to get a further proof as to the structure of phloroglucinol we decided to make the oxime of the diphenyl formamidine of phloroglucinol. 4.35 grams of the diphenyl formamidine derivative were dissolved in 60 cc. of aniline and in a separate flask 3 grams of hydroxylamine hydrochlorine, \( \text{H}_2\text{NOH.HCl} \) were dissolved in aniline. The two portions were mixed and allowed to stand for several days at room temperature. On standing a yellow compound, having very much the appearance of the original body, separated. This was removed and recrystallized several times from glacial acetic acid. A constant melting point was obtained at 284\(^\circ\) C. 0.2186 grams of this substance gave 20.5 cc. of nitrogen at 25.5\(^\circ\) and 743.5 mm.

<table>
<thead>
<tr>
<th>Calculated for</th>
<th>Obtained</th>
</tr>
</thead>
<tbody>
<tr>
<td>( C_{17}H_{23}N_5O_3 )</td>
<td>( C_{17}H_{23}N_5O_3 )</td>
</tr>
<tr>
<td>N.</td>
<td>15.05 %</td>
</tr>
</tbody>
</table>

This percentage of nitrogen corresponds to a dioxime and not a trioxime as we had expected.

Several attempts were made under the above conditions to obtained the trioxime of the 1: 3: 5 formamidio cyclohexamtrione, but
each time it came down as the didervative.

As hydroxylamine failed to give the trioxide, semicarbazid, a reagent which is known to condense readily with compounds containing the carbonyl grouping forming semicarbazones, was next employed as the condensing agent. The reaction was subjected to the same conditions as the above hydroxylamine. The formamidime derivative of phloroglucinol and semicarbazid chloride were dissolved in separate portions of aniline and mixed while warm and allowed to stand for several days. A substance separated having very much the appearance of the original body which it was found to be upon taking a melting point of the purified product. The unchanged body was again placed in the aniline solution and heated to 120° to 140° for two hours. This time, on cooling, a different compound came down which was due to a reaction that had taken place between the aniline and semicarbazid. Several attempts were made to get the semicarbazone derivative in aniline solution by heating at different temperatures, but all were fruitless.

If our theory of the formation of the diphenylformamidine derivative of phloroglucinol is correct, there should be double bonds between the nucleus carbon atom and the carbon atom of the formamidine group.

\[
\begin{align*}
\text{H}_2\text{C}_\text{CH}_\text{N} = \text{O} & \quad \text{(formamidine)} \\
\text{c} = \text{C}_\text{H}^{\text{N}} & \quad \text{(phloroglucinol)} \\
\text{c}_\text{O} & \quad \text{(semicarbazid)}
\end{align*}
\]

This theory being true it should add six bromines. The reactions went with great ease. 2.17 grams of the formamidine derivative were dissolved in hot chloroform, cooled and an excess
of the calculated amount of bromine gradually added, with constant shaking. Soon after the addition of bromine an oily liquid formed on the surface and immediately a reddish brown precipitate began to separate. The mixture was allowed to stand over night. This precipitate was insoluble in the common solvents, alcohol, chloroform, ether, petroleum ether, ligroin benzol and glacial acetic acid. It was purified by long extraction with chloroform which removed the unchanged phloroglucinol derivative and also the excess of bromine. It gave a constant melting point of 281°. On analysis 0.2121 grams of substance gave 0.2612 grams of AgBr.

<table>
<thead>
<tr>
<th>Calculated for</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{C}<em>{27} \text{H}</em>{21} \text{Br}_3 \text{O}_3 )</td>
<td>( \text{I} )</td>
</tr>
<tr>
<td>Br</td>
<td>52.45</td>
</tr>
</tbody>
</table>

Our attention was next turned to ethylphloroglucinol dicarboxylate which was prepared by Moore (1) by the action of sodium ethylate on malonic ester:

This body on treating with potassium hydroxide also forms phloroglucinol. Therefore the ketone structure was assigned to it

Moore brings proof that the body Baeyer synthesised was dicarboxylate instead of a tricarboxylate as he supposed. This substance should condense with diphenyl formamidine if it is in the ketone form to give a momoformamidine derivative. 1.13 grams of diphenylformamidine were dissolved in alcohol and 1.35 grams of ethyl phloroglucinol dicarboxylate added. The flask attached to a return flow condenser was heated for six hours but no reaction took place. Semicarbazid and hydroxylamine dissolved in aniline also failed to react. When heated with acetic acid no acet derivative was obtained. We next employed the fusion method to obtain a formamidine derivative of ethyl phloroglucinol dicarboxylate. One part of Moore's body and one part of diphenyl formamidine were heated to a temperature of 140° - 145° C. for 20 minutes. The brown mass was slightly soluble in alcohol and easily soluble in chloroform so a mixed solvent was used to recrystallized it. It crystallized in yellow crystals with a melting point of 202° - 203° C. The yellow color would lead one to believe it was a ketone splitting. The average of seven nitrogen determinations ranging from 8.80 to 11.80 gave 10.13% N. which is too much for one formamidine group. If the carboxylate groups had been removed and replaced by the
diphenyl formamidine groups we should have the same compound as when phloroglucinol was fused with diphenylformamidine with 9.70 % N. and melting point of 297°C. (uncorr.) We ran out of Moore's body and we did not have time enough left to repeat the above experiment. We believe that by the fusion method we could obtain a derivative of Moore's body.

Since we were unable to get the troxime of the 1: 3: 5 tri-formalilido-cyclohexantrione, nothing with semicarbazid, and nothing with Moore's body we next prepared the troxime of phloroglucinol according to Baeyer (1). One part of phloroglucinol in 45 parts of water with 1½ parts of hydroxylamine hydrochloride and 1½ parts of potassium carbonate were placed in a glass stoppered flask and kept in the dark at a temperature of about 0°C. for five or six days. The brown sandy precipitate which formed was filtered off from time to time. This sandy crystalline powder had all of the properties he described; that is, difficulty soluble in water, more soluble in chloroform, turned black at about 140°C. and exploded at 155°C. colored a pine shaven yellowish red.

Since the troxime forms so easily we concluded the semicarbazone should form in a like manner. 3.2 grams of phloroglucinol, 8.5 grams of semicarbazid hydrochloride, 7 grams of potassium carbonate, and 30 cc. of water were placed in a glass stoppered flask and kept away from the light at a temperature of about 0°C. for nine or ten days. Sandy cream colored crystals

Ber. 1886, 19, 159. (1)
were formed. The crystals were removed, washed with water, several times and recrystallized from absolute alcohol in flaky, cream colored crystals. Melting point 155-156°C. 0.2148 grams of substances gave 45.4 cc. of nitrogen at 747 mm. and 28°C.

\[
\text{calculated for } \quad C_7H_9N_3O_3
\]

\[
\begin{array}{c}
N_n \quad 22.95 \\
\text{Found} \quad 22.79
\end{array}
\]

This experiment was repeated several times under the above conditions with the expectation of putting in two and possibly three semicarbazone groups.
THE STRUCTURE OF RESORCINOL AND SOME NEW DERIVATIVES.

Resorcinol $\text{H}_2\text{C} = \text{C} = \text{C} = \text{C} = \text{C} - \text{H}_{2} - \text{C} - \text{C} - \text{H}_{2}$ is usually considered a dihydric phenol, when fused with potassium hydroxyl yields phloroglucinol; therefore it too may exist in the ketone structure

This formula contains the $-\text{C} = \text{C} - \text{C} - \text{C} - \text{C} - $ grouping which is known to react with the formamidines. Jones and Stagner attempted to condense diphenyl formamidine with resorcinol by heating a mixture of the two in alcohol as a solvent. Both were unsuccessful. We endeavored to bring about the reaction by heating under pressure. Two parts of diphenyl formamidine and one part of resorcinol were dissolved in alcohol and heated in a sealed tube in a brine bath at $104^0$ to $105^0\text{C.}$ for ten hours. This method was also unsuccessful. We next resorted to the fusion method. 1.1 grams of resorcinol and 2.9 grams of diphenyl formamidine were heated in a flask at a temperature of $145^0$-$160^0\text{C.}$ for three hours. The brown mass was soluble in a mixture of alcohol and chloroform from which it was recrystallized several times and finally dried on a porous plate. The yellow compound melted at $197\text{C.}$ 0.2746 grams of substance gave 21.4 cc. of N. at $15^0\text{C.}$ and 742.7 mm. pressure.

$\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_2$

\[\begin{array}{c}
\text{N} \\
8.86 \\
8.88
\end{array}\]
To remove any doubt we used a different formamidine, ethyl
diparaphenetidine:

\[
\text{H}_2\text{N}\text{C}_6\text{H}_4\text{O}_2\text{H}_2 \to \text{H}_2\text{N}\text{C}_6\text{H}_4\text{O}_2\text{H}_2
\]

This was prepared according to Walther (1) by heating for \( \frac{3}{4} \)hours two parts of phenetidine \( H_2NCH_6HOCH_2 \) with one part of
orthoformic ester \( H.C.\) in a flask attached to a return flow condenser. Purified by recrystallizing from
alcohol. 5.68 grams were placed with 1.1 grams of resorcinol in a flask and heated in \( H_2SO_4 \) bath for two hours at
a temperature between 150\(^0\) - 160\(^0\)C. The product was recrystallized from benzol in reddish yellow crystals giving a
melting point of 146\(^0\)C. 0.3036 grams gave 16.2 cc. of
nitrogen at 21\(^0\) and 756 mm. pressure.

\[
\text{Calculated for} \quad \text{Found} \\
C_{24}H_{24}N_2O_2 \\
N. \quad 6.93 \quad 6.73
\]

\[
\text{(I) J. Prakt. Chem. 55, 41.}
\]
SUMMARY

Jones and Stagner, in their respective researches, show that only substances containing the \( \text{\textit{caco}} \text{\textit{co}} \text{\textit{-group will condense with the formamidines of the type } } \text{\textit{HCO}}\text{\textit{NH}}\text{\textit{R}} \) \textit{.} We succeeded in bringing about a condensation between phloroglucinol and diphenyl formamide by simply fusing the two at a temperature of \( 220 - 225 \text{\textdegree} \) for 30 minutes, giving evidence of the keto structure of phloroglucinol. This method also gives a much better yield than when a solvent is used. This formamide derivative of phloroglucinol did react, as our experimental evidence shows, with phenyl hydrazine and hydroxyl amine, reagents that are known to condense with bodies containing the keto grouping, giving further evidence of the keto structure. When treated with semicarbazid, no reaction took place. The reasons why this reaction did not take place is due to the slight solubility of semicarbazid hydrochloride in aniline, to the reaction that takes place between semicarbazid and aniline on heating, and to steric hinderance caused by the nature of the groups in the molecule. The fact that semicarbazid does react with phloroglucinol giving a monosemicarbazone is proof that the negative result of the triformamide derivative of phloroglucinol with semicarbazid is not due to the inactivity of the two substances.

From these results of phloroglucinol and its derivatives we conclude that phloroglucinol has a large per cent of the ketone structure as we were able to get reactions with every reagent tried on the diphenyl formamide derivative of phloroglucinol except semicarbazid.
Resorcinol, usually considered as a dihydroxy phenol, exists in the ketone structure as is shown by its condensation with formamidines in the absence of a solvent by fusing at a temperature of 145°-160° C. for three hours. Calvert and Jones and Calvert and Stagner attempted to condense resorcinol with diphenyl formamidine in alcoholic solution, but were unsuccessful. We also endeavored to bring about a reaction by heating the alcoholic solution under pressure, but failed to get a reaction. The enolic structure of resorcinol in alcoholic solution seems to be the more stable form, and for this reason no reaction takes place with the formamidines in that solvent.

From these results we conclude that resorcinol exists partially in the ketone structure when not in an ionizing solvent. The evidence seems to show that substances which are tautomeric in regard to enolic and ketonic structure will in non-ionizing solvents give reactions supporting the keto structure if a reagent, like the formidines, is used which causes no shifting within the molecule.

This work was undertaken at the suggestion of Professor Sidney Calvert, Professor Organic Chemistry, at the University of Missouri. I here take the opportunity to express my thanks for his sound counsel and hearty encouragement through the course of this work. I also wish to thank Professor Webster Newton Jones for his valuable suggestions and kindly interest shown me.

Approved: W. N. Jones

Chemistry Laboratory,
University of Missouri.