THESIS FOR THE DEGREE OF PH.D.

THE ACTION of DIPHENYLFORMAMIDINE on the PHENOLS.

BY

JOHN HALDANE, B.Sc.

Directed by Mr. John B. Shoesmith, M.Sc., under the
supervision of Professor Sir JAMES WALKER, F.R.S.

Chemistry Department,
University of EDINBURGH.

May, 1924.

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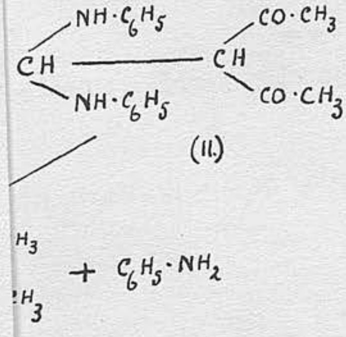

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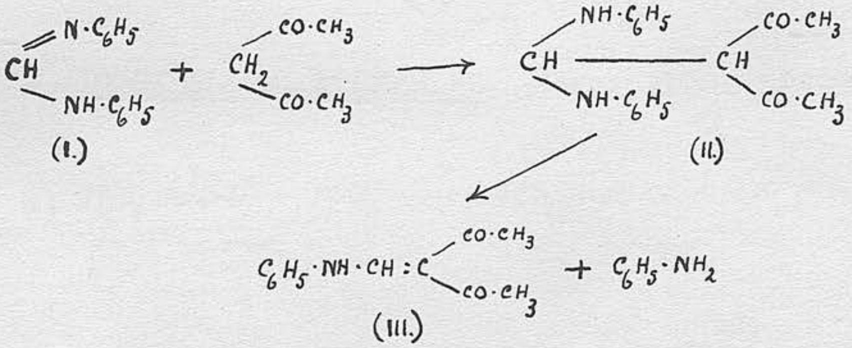
ERRATA.

PAGE 33, LINE 7: FOR "HAVE" READ "GAYE"
PAGE 58, LINE 4: PHYLOROGLUCINOL
" 59, " 3: "
PAGE 93, LINE 12: FOR 0·002002 gms. READ 0·02002 gms.
PAGE 7A, LINE 1: FOR ALDEHYDE READ β-RESORCYLALDEHYDE

Corrected

The condensation which takes place when diphenylformamidine is heated at a suitable temperature with compounds containing an active methylene group was first pointed out by Dains (Ber. 1902·35· 2504.). As an example of this, the condensation of the amidine (i) with acetyl acetone, which probably takes place in two stages, may be quoted. The intermediate compound (ii) is never isolated, aniline being liberated at once.



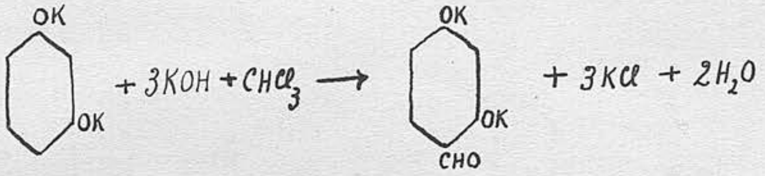
Anilinomethyleneacetylacetone (iii.) is isolated in almost quantitative yield.

This type of reaction appears to be a very general one and has been extended by DAINS and coworkers, (J. Amer.Chem.Soc., 1909 onwards.) to a large number of similar compounds.

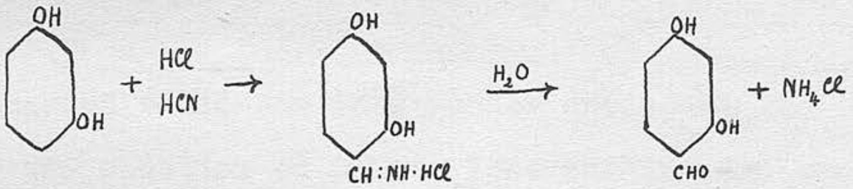
Such a condensation might be expected to take place with compounds in the aromatic series where/

where the nuclear hydrogens are most reactive. Similar condensations with splitting off of nuclear hydrogen are recorded in the following well known reactions.

(1) TIEMANN & REIMER (Ber., 1877·10·2212).



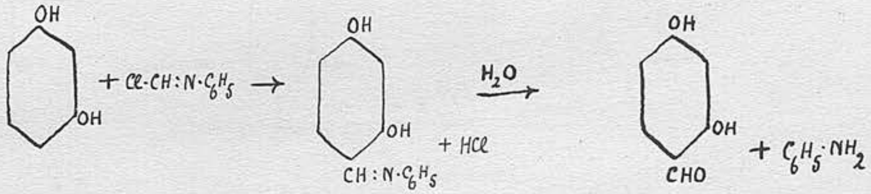
(2) GATTERMANN (Ber., 1899·32·278).



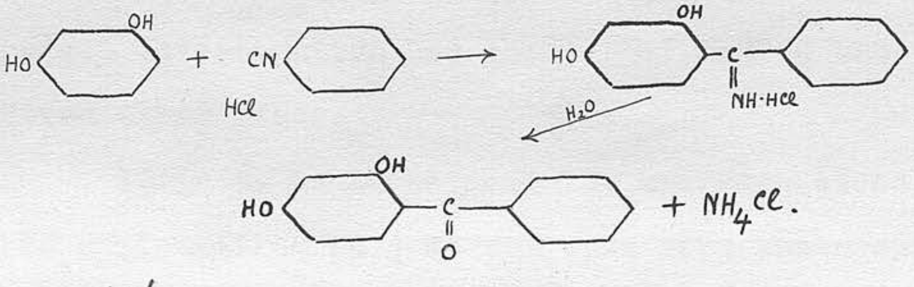
(3) DIMROTH & ZOEPFRITZ (Ber., 1902·35·993).

a) $3C_6H_5\cdot NH\cdot CHO + POCl_3 \longrightarrow 3C_6H_5\cdot N:CH\cdot Cl + H_3PO_4 + H_2O$

b)

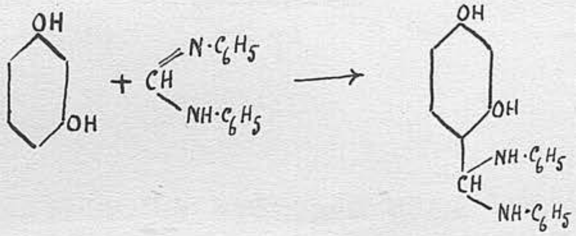


(4) HOESCH (Ber., 1915·48·1122).

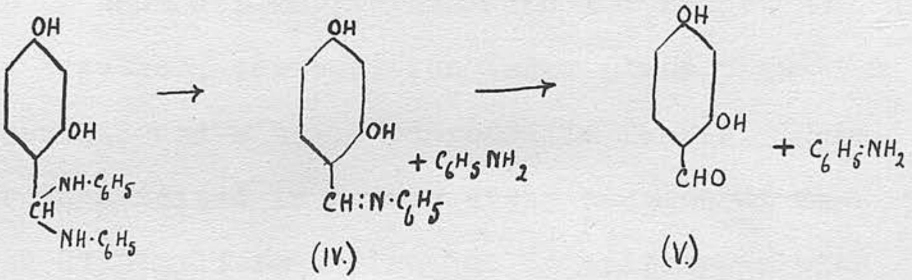


As/

As resorcinol is very reactive in all the condensations quoted above and easily obtained in a pure condition it was chosen for condensation with diphenylformamidine. The reaction expected to take place would be



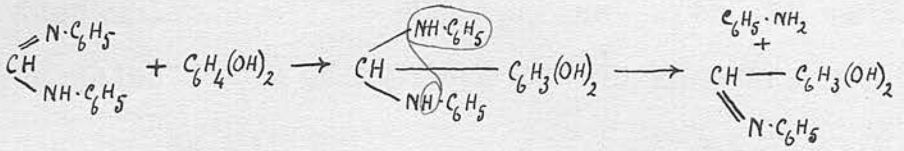
This compound would now in a manner analogous to that of the reaction of DAINS, lose aniline and produce the Schiff's base of β-resorcylaldehyde (iv.) which on hydrolysis would give the parent aldehyde namely β-resorcylaldehyde (v).



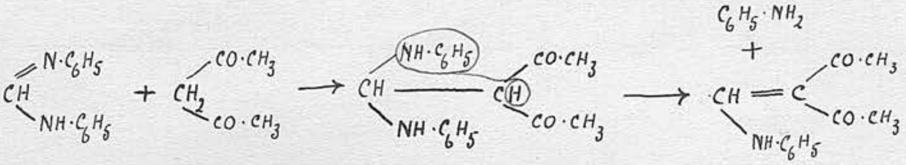
This would be a new synthesis of β-resorcylaldehyde. Investigation has shown that such a condensation takes place.

It is to be noted that the hydrogen atoms in this condensation (a.) do not come from analogous positions as those in Dains reaction (b.)

a.)



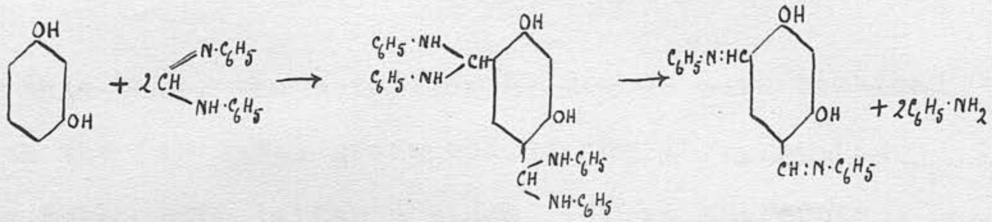
b.)



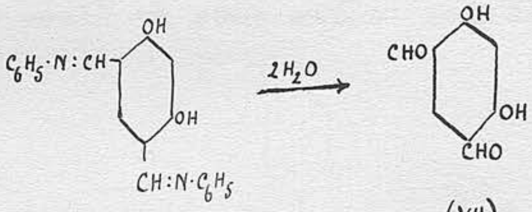
In Dains reaction the hydrogen atom leaves the original methylene carbon atom to combine with the $(\cdot NH\cdot C_6H_5)$ group whereas in the condensation with resorcinol the hydrogen atom leaves the second $(\cdot NH\cdot C_6H_5)$ group as shown above. This point is further discussed on pp.20

When diphenylformamidine and resorcinol are heated together, condensation takes place. Aniline is liberated and a solid compound is formed. This cannot be obtained in a pure state because of unchanged diphenylformamidine but on hydrolysis with alkali, aniline is liberated and from the acidified solution, β -resorcylaldehyde can be obtained in appreciable yield. The condensation under these conditions involves one molecule of diphenylformamidine and one molecule of resorcinol. Two molecules of/

of diphenylformamidine may condense with one molecule of resorcinol when the course of the reaction may be represented as follows.



The di - Schiff's base (vi.) on hydrolysis would yield 4;6-dihydroxyisophthalaldehyde (vii.) as prepared by TIEMANN and LEWY (Ber., 1877·10·2212).



(VI.) (VII.)

The 4:6-dihydroxyisophthalaldehyde has been isolated in a pure state from the condensation product,

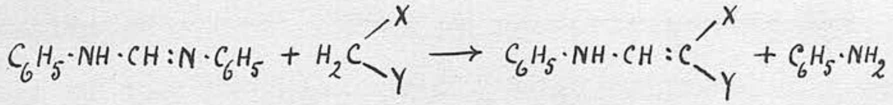
(a) when the resorcinol is moist

(b) on long heating

(c) when the temperature at which the condensation is carried out is very high

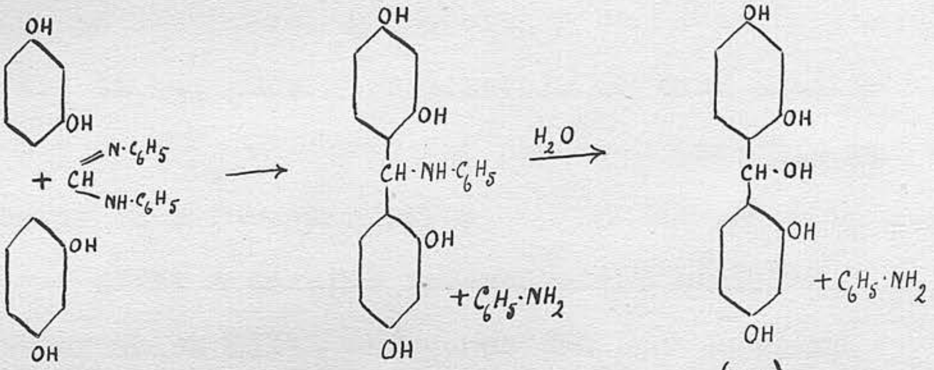
(d) when β-resorcylaldehyde and β-resorcylic acid are condensed with diphenylformamidine.

There is still one more possibility in this condensation. The action of diphenylformamidine on the methylene compounds may be looked on as double decomposition. i.e.



$$C_6H_5\cdot NH\cdot CH{:}N\cdot C_6H_5 + H_2C\begin{smallmatrix}\diagup X\\ \diagdown Y\end{smallmatrix} \longrightarrow C_6H_5\cdot NH\cdot CH{:}C\begin{smallmatrix}\diagup X\\ \diagdown Y\end{smallmatrix} + C_6H_5\cdot NH_2$$

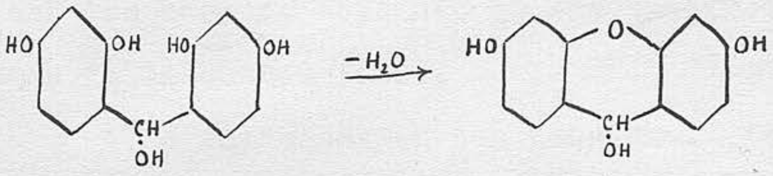
In this case, the methylene hydrogens have combined with the $(:N\cdot C_6H_5)$ group whilst the grouping $(:C\begin{smallmatrix}\diagup X\\ \diagdown Y\end{smallmatrix})$ has taken this latter's place. If we therefore looked on the two reactions namely diphenylformamidine + resorcinol and diphenylformamidine + methylene compound as analogous we should expect the condensation would to some extent follow the course.



(VIII.)

Tetrahydroxy-diphenyl-carbinol (viii.) should be present. From the condensation product β-resorcylaldehyde, 4:6-dihydroxyisophthalaldehyde and a red resinous substance have all been obtained. In addition all the solutions from which aldehyde was extracted showed a remarkable green fluorescence in/

in alkaline solution. This is probably due to the presence of the tetrahydroxydiphenylcarbinol, not as such, but as the corresponding xanthydrol (ix.)



(IX.)

because, when the compound was synthesised by the method given in Part II. of the thesis it was found in great dilution to show the same fluorescence as noticed in the solutions stated above. A small quantity of the xanthydrol is necessary to give the fluorescence. It has only been possible to show that it is formed in this reaction and not been possible to isolate it in a pure condition.

After a careful investigation of all the conditions which might influence the condensation, such as,

(1) temperature.

(2) presence of moisture.

(3) time.

β-resorcylaldehyde has been obtained in 45-50 per cent yield of the theoretical by this new method. Too long heating or too high a temperature causes the formation/

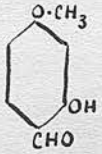
formation of much 4:6 - dihydroxy - isophthalaldehyde and resin. The presence of moisture has an effect similar to that noted in the higher temperature and longer heating experiments. This is remarkable and the bearing this has on the theory of the reaction is discussed later.

The condensation has been shown to take place between diphenylformamidine and a large number of phenols.

APPLICATION TO OTHER PHENOLS.

Diphenylformamidine has been condensed with various phenols. A summary of the results is given.

(1) Monomethyl resorcinol. The aldehyde isolated proved to be 4.-methoxy-2.-hydroxy-benzaldehyde.



(Ber., 1880.13.2367)

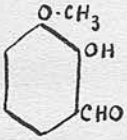
and was obtained in quantities representing 20 per cent of the expected yield.

(2) Dimethyl resorcinol. No condensation takes place.

(3) Catechol. Only a trace of an aldehyde could be isolated. An odour of carbylamine was preceptible in this condensation product.

(4) Guaiacol./

(4) Guaiacol. The aldehyde isolated proved to be 3.- methoxy- 2.- hydroxybenzaldehyde.

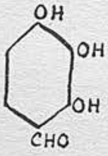


(Ber. 1881.14.2023.)

(5) Quinol. Only a trace of an aldehyde could be isolated. The condensation product had a pronounced odour of carbylamine.

(6) Phloroglucinol. Only a trace of an aldehyde could be isolated. There was a strong odour of carbylamine in this condensation product.

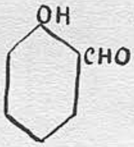
(7) Pyrogallol. The aldehyde isolated proved to be pyrogallol aldehyde.



(Ber., 1898.31.1768: Ber., 1899.32.281.)
(Ber., 1901.34.1445: Ber., 1902.35.997)

and was obtained in quantities representing 15-20 per cent of the expected yield.

(8) Phenol. The aldehyde isolated proved to be salicylaldehyde



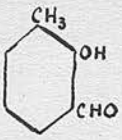
and was obtained in quantities representing 20 per cent of the expected yield.

(9)/o.

(9). o.Nitrophenol. Only a trace of an aldehyde could be isolated.

(10) p. Nitrophenol: The condensation product had a pronounced odour of carbylamine and only traces of an aldehyde could be isolated.

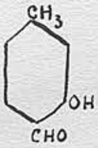
(11). o.Cresol. The aldehyde isolated proved to be 3.-methyl- 2.-hydroxybenzaldehyde.



(Ber., 1878.11.772)

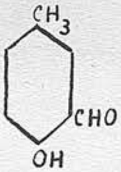
and was obtained in quantities representing 20 per cent of the expected yield.

(12) m.Cresol The aldehyde isolated proved to be 4.-methyl- 2;hydroxybenzaldehyde.



and was obtained in quantities representing 20per cent of the expected yield.

(13) p.Cresol. The aldehyde proved to be 5.-methyl 2.-hydroxybenzaldehyde.

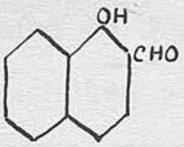


(Ber.,1878.11.773 & 785)
(Annalen.1907.357.322)

and/

and was obtained in quantities representing 15-20 per cent of the expected yield.

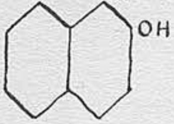
(14) α-Naphthol. The aldehyde isolated proved to be 1-hydroxy- 2-naphthaldehyde.



(Monatsh., 1909.30.277)

was obtained in quantities representing 30-40 per cent of the expected yield.

(15) β-Naphthol. The aldehyde isolated proved to be 2-hydroxy-1-naphthaldehyde

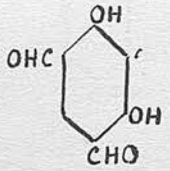


(Ber., 1882.15.804, Ber., 1899.32.284)
(Bull. Soc. chim 1896.(3). 25.374)

and was obtained in quantities representing 50. per cent of the expected yield.

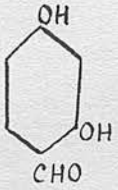
(16)/

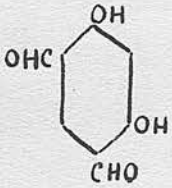
(16) β-Resorcylaldehyde. The aldehyde isolated proved to be 4:6-dihydroxyisophthalaldehyde.



and was obtained in quantities representing 30-40 per cent of the expected yield.

(17) β-Resorcylic acid. The aldehydes isolated proved to be β-resorcylaldehyde and 4:6-dihydroxy-isophthalaldehyde.

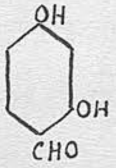




and were obtained in quantities representing 10 per cent and 40 per cent respectively of the expected yield/

yield.

(18). Ethyl-β-resorcylate. The aldehyde isolated proved to be β-resorcylaldehyde

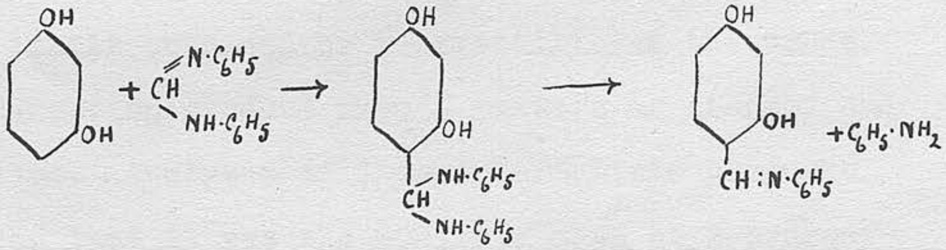


and was obtained in quantities representing 20-25 per cent of the expected yield.

ISOLATION of INTERMEDIATE COMPOUNDS.

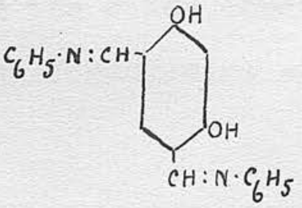
(The course of the reaction.)

In this condensation between diphenylformamidine and the phenols, the course of the reaction has so far been assumed to be

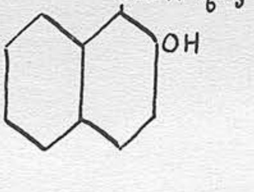


The isolation of intermediate condensation products from (a) resorcinol and (b) β-naphthol has proved the assumption to be correct. The intermediate product from the condensation of carefully dried resorcinal and diphenylformamidine could not be isolated/

isolated in a pure condition because of the presence of unchanged diphenylformamidine and resin in the condensation product. From the product obtained by the condensation of moist resorcinol and diphenylformamidine however, needle shaped crystals were easily isolated and purified. Analysis proved that they were the di-Schiff's base of 4:6-dihydroxyisophthalaldehyde.



The intermediate compound from the condensation of diphenylformamidine and β-naphthol was easily obtained by recrystallising the crude condensation product from a mixture of alcohol and aniline. Analysis of this intermediate compound proved that it was the Schiff's base of 2-hydroxy-1-naphthaldehyde.



Thus the condensations follow the course

Phenol + diphenylformamidine
↓
Schiff's base + aniline
↓ Hydrolysis
Aldehyde + aniline.

It has not been possible to isolate the intermediate compounds from the other condensations owing to unchanged diphenylformamidine and resin.

MECHANISM of the REACTION.

The reaction between diphenylformamidine and the phenols may be looked upon as one which involves.

(1) Direct substitution in accordance with the equations already given on pp.3 or

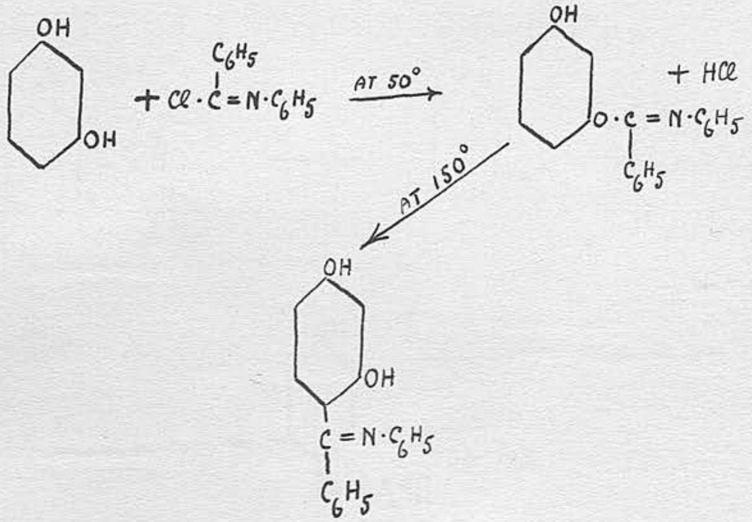
(2) isomeric change. or

(3) enol ⟶ keto transformation of the phenol.

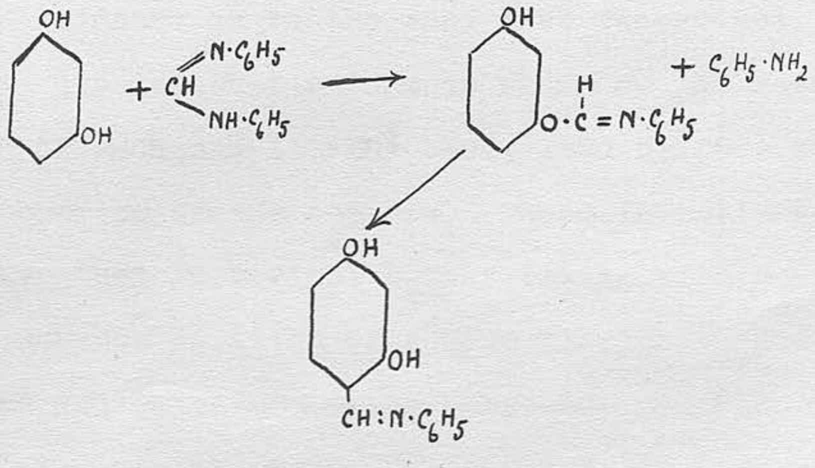
(1) That the reaction between diphenylformamidine and the phenols is not one of direct substitution is suggested by the fact that in the condensations carried out, where a reaction does take place, substitution always takes place in the ortho position to the hydroxyl group, under conditions entirely different from that of the Gattermann reaction where substitution takes place in the para position.

(2) STEPHEN (T., 1920.117.1529) recently suggested that the reaction between benzanilideiminochloride and/

and resorcinol takes place in the following manner.

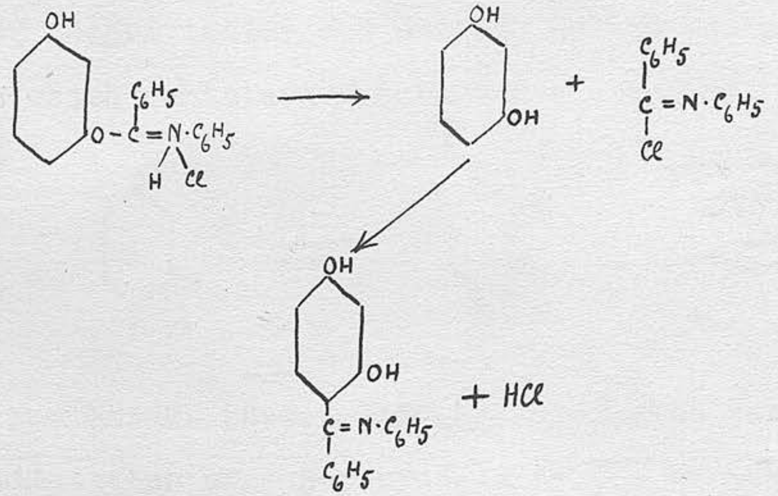


This reaction and the condensation between diphenylformamidine and resorcinol are very similar to one another and the reaction would be formulated as



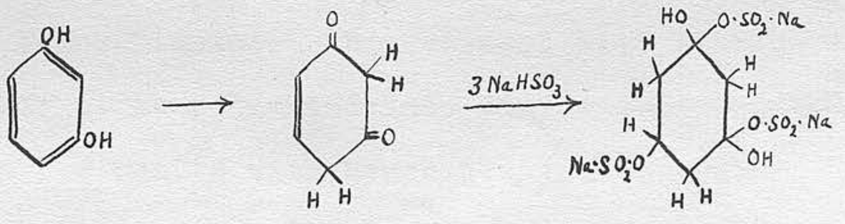
It does not appear probable that such wandering of the (– CH = N.C_6 H_5) group does take place however especially since Chapman (T., 1922. <u>121</u>.1676) has shown that the probable course of the reaction/

reaction suggested by **STEPHEN** (loc. cit.) is as follows:-



i.e., The preliminary decomposition is followed by direct substitution. Thus the third mechanism is the one which is the most probable.

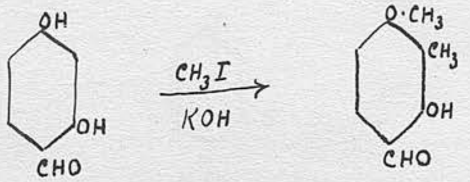
(3) Evidence as to the fact that resorcinol reacts in its tautomeric form is shown by the recent research of **FUCH** and ELSNER (Ber., 1920.53.886) on the tautomerism of the phenols. These investigators have shown that resorcinol slowly reacts with a boiling aqueous solution of sodium bisulphite and gives the following bisulphite compound.



Further evidence as to the tautomerism of resorcinol has/

has been put forward by PERKIN (T., 1895.<u>67</u>.993) who found that methylation of β-resoreylic acid by means of methyl iodide and caustic potash yielded a product which contained a methyl group in the nucleus

HERZIG and ZEISEL (Ber., 1920.<u>53</u>.1518) also found that methylation of β-resrocylaldehyde by means of methyliodide and caustic potash produced a compound which also contained a methyl group in the nucleus.

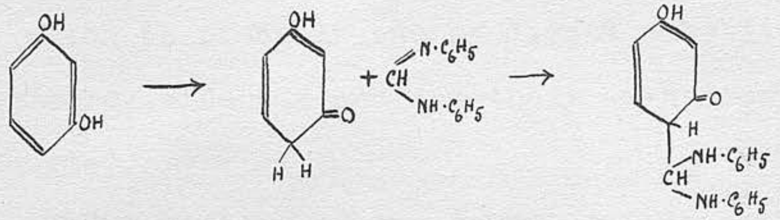


These investigators concluded that the wandering of the methyl group into the nucleus can only be explained by the fact that resorcinol reacts in its ketonic form. Again, it has been shown by BAEYER (Ber., 1886.<u>19</u>.163) that resorcinol does not react with hydroxylamine. On treatment with nitrous acid however it is converted into dinitrosoresorcinol which now reacts with hydroxylamine to yield diquinoyltetroxime (Kostanecki Ber., 1899.<u>22</u>.1345)

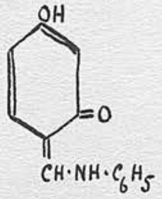
The condensation of diphenylformamidine

and/

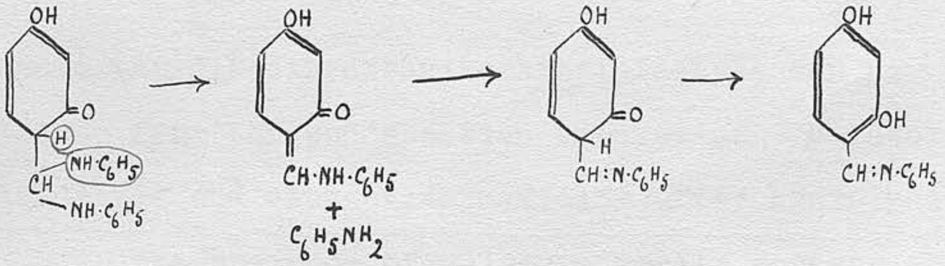
and carefully dried resorcinol according to such a theory is as follows:-



The close similarity between this reaction and that of DAINS is apparent if the hydrogen atom of the nucleus is regarded as the one which splits off from the molecule as aniline. The intermediate compound would then first exist as the ketonic form which is a very unstable configuration



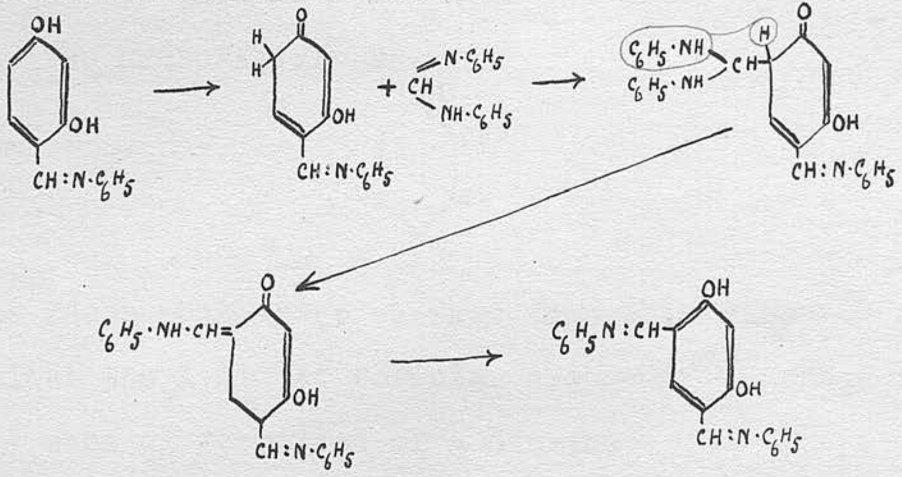
The full equation should thus be written



This would explain why diphenylformamidine condenses with resorcinol and monomethyl resorcinol respectively whilst no reaction takes place with dimethyl resorcinol. According to GATTERMANN (Ber/

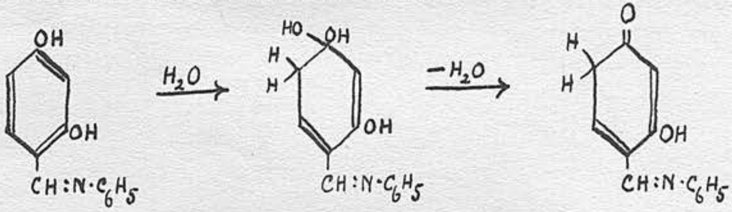
(Ber., 1898.31.1152.) the 2:4 - dimethoxybenzaldehyde is just as easily obtained by the hydrocyanic acid method, which is probably one of direct substitution, as β-resorcylaldehyde and 4-methoxy -2-hydroxybenzaldehyde.

The formation of the SCHIFF'S base of 4:6 dihydroxyisophthalaldehyde must be formulated as a result of the reaction of the mono-SCHIFF'S base and diphenylformamidine. i.e.,



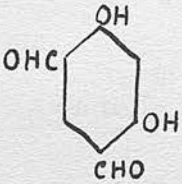
because the 4:6-dihydroxyisophthalaldehyde can be obtained from the condensation product of β-resorcylaldehyde and diphenylformamidine after hydrolysis.

The presence of moisture really assists the production of the ketonic form.

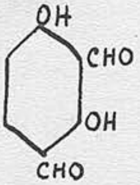


The fact must not be overlooked that the constitution/

constitution of the 4:6 dihydroxyisophthalaldehyde has not yet been definitely proved. It is formulated as.



by TIEMANN and LEWY (Ber., 1877.10.2212) where the CHO groups are ortho and para to the hydroxyl groups, but it may be that the second CHO group is between the two hydroxyl groups.

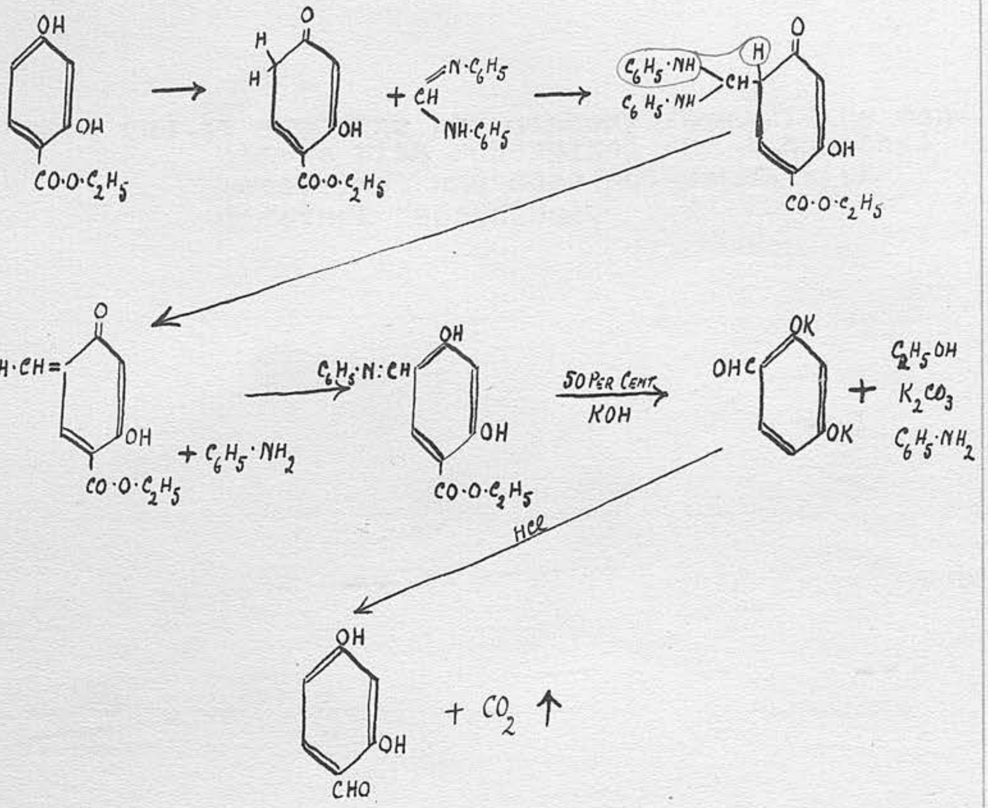


The facts which have emerged from this research against the 1:2:3:4: formula. are

(1) ease of formation of a dioxime.

(2) " " " " a p.nitrophenylhydrazone.

(3) the production of β-resoreylaldehyde when diphenylformamidine and ethyl-β-resorcylate are heated together. The production of β-resorcylaldehyde from this condensation must result from loss of carbon dioxide after hydrolysis of the crude condensation product.



The production of β-resorcylaldehyde and 4:6 dihydroxyisophthalaldehyde from β-resorcylic acid does not assist in this point because it is difficult to say whether carbon dioxide is split off before or after condensation.

This point however must be regarded as a debatable one but the ketonic form suggestion explains.

(1) the similarity of the condensation to the the action discovered by DAINS.

(2) the production of ortho substituted compounds and

(3) it suggests a reason for the production of 4:6-dihydroxyisophthalaldehyde in presence of moisture.

(4)/

(4) it explains why diphenylformamidine condenses with resorcinol and monomethyl resorcinol and does not react with dimethyl resorcinol.

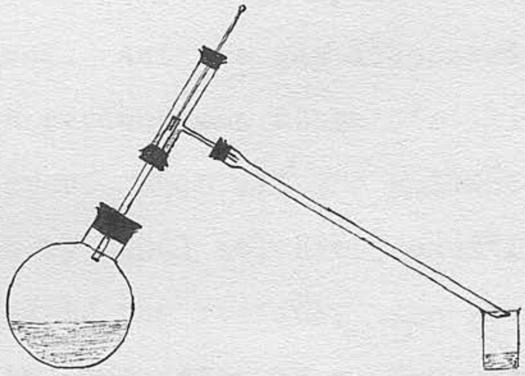
EXPERIMENTAL.

PREPARATION of DIPHENYLFORMAMIDINE.

This was prepared by boiling together aniline and formic acid. WEITH, (Ber., 1876.9.454).

$$\mathrm{HC}\begin{array}{l}=\mathrm{O}\\ -\mathrm{OH}\end{array} + \begin{array}{l}\mathrm{H_2N.C_6H_5}\\ \mathrm{H_2N.C_6H_5}\end{array} \longrightarrow \mathrm{CH}\begin{array}{l}=\mathrm{N.C_6H_5}\\ -\mathrm{NH.C_6H_5}\end{array} + 2H_2O$$

40 gms. (1 mol.) of 80 per cent formic acid were mixed with 160 gms. ($2\frac{1}{2}$ mols.) of aniline. The water, which was present in the original acid together with that produced in the reaction, was distilled away through a fractionating column. The head of the column was fitted with a device for trapping the water as soon as it reached the top.



After four hours gentle boiling, the temperature was raised until 60ccs. of aniline had distilled over. The residual diphenylformamidine solidified/

solidified on cooling and was recrystallised from a small quantity of alcohol when it possessed a melting point of 137°. The yield was approximately 60 per cent of the theoretically expected quantity.

CONDENSATION of DIPHENYLFORMAMIDINE with RESORCINOL.

PRELIMINARY EXPERIMENTS and IDENTIFICATION of CONDENSATION PRODUCTS.

The condensation of the diphenylformamidine and resorcinol was carried out at a temperature of approximately 130° for 1½ hours, 14 gms. and 28 gms. of resorcinol and diphenylformamidine respectively being used. Aniline was liberated in quantity. The reaction product was steam distilled when aniline passed over. When all the aniline had passed over, as shown by NaOCl solution, caustic soda in excess was added to the residue. The whole went into solution with production of a wine red coloration and aniline was liberated. This showed that all the diphenylformamidine had reacted. The aniline was again /

again distilled away in steam and the solution cooled and acidified. Points noticed were,

(1) The red colour disappeared.

(2) A mixture of a red resin and yellow needles was obtained.

The solid products of the reaction were filtered from the acid liquor which was then extracted with ether. These ethereal extractions were now used for the continuous extraction of the solid products for 15 hours. The ethereal solution was in turn extracted six times with saturated sodium bisulphite solution.

TREATMENT of BISULPHITE EXTRACTIONS.

The solution was acidified with concentrated hydrochloric acid and steam distilled. A yellow crystalline solid distilled over and a brown red resinous substance appeared in the flask. The yellow needle shaped crystals were filtered off and recrystallised from water when they melted at 126°-127°. The yield was approximately 25-30 per cent of the theoretical quantity.

The solution which remained from the steam distillation was cooled, filtered from the brown red resin (1.4 gms.) and extracted four times with ether. The/

The solution left after extraction with ether, produced a deep green fluorescence on the addition of alkali. When the ether was distilled off, a crystalline substance remained which was boiled for four hours with water and animal charcoal, and the almost white crystals so obtained recrystallised from water when they possessed a melting point of 134°-135°. (Yield 0.5 gms.)

TREATMENT of ETHEREAL SOLUTION which had been EXTRACTED with SATURATED SODIUM BISULPHITE.

The ether was distilled off. The syrupy liquid which remained formed a phenylhydrazone, oxamazone, carbazone, and gave a peculiar yellow opalescence, deepening in strong solutions to a precipitation with SCHIFF'S reagent.(1) Presence of an aldehyde was therefore indicated.

ESTIMATION/

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(1) This point has been further investigated by other workers in these laboratories and is due to the precipitation of a hydrated SCHIFF'S base in which the rosaniline is combined with several molecules of the aldehyde.

ESTIMATION of the AMOUNT of ALDEHYDE in SYRUPY LIQUID.

The syrupy liquid was treated with semioxamazide. A semioxamazone (1.5 gms.) was formed. Therefore, approximately 0.7 gms of aldehyde remained in the ether due to incomplete extraction by saturated sodium bisulphite.

PRODUCTS SEPARATED.

(1) Yellow needle shaped crystals, (M.Pt 126°-127°), volatile in steam.

(2) White crystalline compound (M.Pt. 134°-135°) non-volatile in steam.

(3) A brown red resinous substance.

To obtain a sufficient quantity of these products for identification and analysis, a few condensations were carried out under the same conditions, the methods of separation of the condensation products being similar to that employed in the previous condensation.

RESULTS/

RESULTS. Condensation of, diphenylformamidine and resorcinol.

RESOR-CINOL.	DIPHENYL-FORMAMIDINE.	VOLATILE COMPOUND.	NON-VOLATILE COMPOUND.	RESIN.
10 gms	20 gms.	1.5 gms	0.3 gms	3.7 gms
10 gms	20 gms.	2.2 gms	0.3 gms	1.5 gms
10 gms	20 gms	2.2 gms	0.5 gms	0.9 gms
20 gms	40 gms	3.1 gms	1.2 gms	6.2 gms

The disparity of yields is due to the difficulty of maintaining a constant temperature of 130^{0} which was afterwards remedied.

The constitution of the yellow needles (M.P+ 126^{0}-127^{0}) was now investigated.

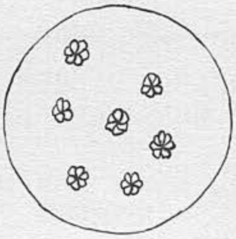
(1) When recrystallised from water they possessed a melting point of 126^{0}-127^{0}.

(2) An aqueous solution was coloured red brown with $FeCl_3$.

(3) With SCHIFF'S reagent, they gave in aqueous solution a peculiar yellow opalescence which deepened in strong solutions to precipitation.

(4) A nitrogen test was carried out with a negative result.

(5) An alcoholic solution was taken and a few drops of phenylhydrazine added. The mixture was warmed and drops of water added until turbidity was seen. When the solution was cooled a well defined phenylhydrazone crystallised out which under the microscope had the appearance.



This classified the substance immediately as an aldehyde.

The 4:6-dihydroxyisophthalaldehyde $C_6H_4(OH)_2(CHO)_2$ has been described by TIEMANN and LEWY (Ber. 1877.<u>10</u>.2211) and a comparison of the compound there described and the yellow needles (M.Pt 126°-1279) reads.

REAGENT/

REAGENT.	DESCRIBED 4:6-DIHYDROXYISOPHTHALALDEHYDE.	REACTION PRODUCT.
NaOH.	Dissolves with yellow colour.	The same.
HCl	Ppts. from alkaline solution.	" "
NH_4OH	Dissolves with yellow colour	" "
Action of NH_4OH solution with (a) PbAc	White ppte.	" "
(b) $CuSO_4$	Green ppts.	" "
H_2SO_4	Dissolves but on addition of H_2O ppts.	" "
Steam	Volatile.	" "
$FeCl_3$	Red brown colour.	" "
SCHIFF'S reagent.	Not given.	Yellow opal or ppte.
Solubility.	H_2O: sol. in hot, almost insol. in cold: soluble in alcohol.	The same " "
M.Pt.	127°	126°-127°
NH_2OH.	Forms a dioxime M.Pt. 209°	208°-209°

An estimation of the nitrogen in the compound formed by the action of hydroxylamine on the yellow needles gave the following result.

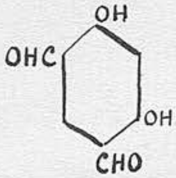
0·1026 gms of substance gave 12·45cc. at 17·5° & 750 mm.

This represents N = 14·06 per cent.

$C_8H_8O_4N_2$ requires **N** = 14·23 per cent.

Thus/

Thus the compound was classified as the 4:6-dihydroxyisophthalaldehyde.



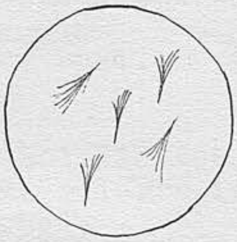
The constitution of the non-volatile substance (M.Pt 134°-135°) was now investigated.

(1) An aqueous solution gave a deep brown coloration with $FeCl_3$.

(2) SCHIFF'S reagent gave a peculiar opalescence or precipitate.

(3) A nitrogen test was carried out with a negative result.

(4) An alcoholic solution was taken and a few drops of phenylhydrazine added. The mixture was warmed and drops of water added until turbidity was apparent. A well defined phenylhydrazone crystallised out which under the microscope had the appearance.



This classified the compound immediately as an aldehyde. The mono-phenylhydrazone of β-resorcylaldehyde has been described by MARCUS (Ber., 1891. 24.3650) as yellow needles (M.Pt 158°-159°), easily soluble/

soluble in ether and alcohol and coloured brown with a solution of $FeCl_3$. The phenylhydrazone obtained possessed all these properties.

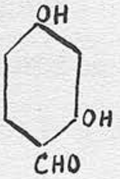
The properties of β-resorcylaldehyde. (TIEMANN and LEWY, Ber., 1877·10·2216; GATTERMANN. Ber., 1899·32·278; SCHOLL and BERTSCH Ber., 1901·34·1441; DIMROTH and ZOEPPRITZ, Ber., 1902·35·993; KARRER, Helv. Chim. Acta. 1919·11·39; D.R.P. 105.798 and 155. 731). prepared by GATTERMANN'S method (loc.cit.) were compared with those of the reaction product and reads;

REAGENT	DESCRIBED β-RESORCYLALDEHYDE.	REACTION PRODUCT.
NaOH.	Soluble with slight coloration.	The same
HCl	Pptes. from alkaline solution.	" "
Steam.	Non-volatile	" "
$FeCl_3$	Deep brown coloration.	" "
SCHIFF'S REAGENT .	Yellow opal. or ppte.	" "
Solubility.	H_2O: Sol, in hot, in sol in cold. soluble in ether and alcohol.	" "
M.Pt	134°-135°	M.Pt 134°-135°
Mixed. M.Pt	134°-135°	
NH_2OH	Forms an oxime (M.Pt 191°)	M.Pt 191°

The/

The oxime of β-resorcylaldehyde has been described by MARCUS (Ber., 1891·24·3651) as white needle shaped crystals (M.Pt 191°), easily soluble in alcohol and ether, gives a brown red coloration with $FeCl_3$ and a green precipitate with FEHLING'S solution. The reaction product with hydroxylamine gave a white needle shaped crystalline compound which possessed all the properties of the oxime of β-resorcylaldehyde as stated above.

The compound, therefore, is β-resorcylaldehyde.



The brown red amorphous powder isolated in the condensation of diphenylformamidine and resorcinol probably contains a little of the 3:6-di-hydroxyxanthydrol as shown by the synthesis of this compound (Part II of this thesis). How much is present cannot be stated but a very small quantity of the compound only is necessary to give the deep green fluorescence. The two aldehydes, namely, β-resorcylaldehyde and 4:6-dihydroxyisophthalaldehyde are the only reaction products which may be isolated in a pure condition.

Attempts/

Attempts were now made to increase the yield of β-resorcylaldehyde, by using aniline hydrochloride as a precipitating agent.

In previous condensations, saturated sodium bisulphite was used as a means of separation of the aldehydes formed in the reaction. As the extraction was incomplete the following method was adopted. The crude condensation product was first hydrolysed with alkali and the liberated aniline steam distilled over. The unchanged diphenylformamidine was filtered off and the alkaline solution acidified which was then steam distilled until all 4:6-dihydroxyisophthalaldehyde had passed over. The steam distilled solution was cooled, resin filtered off and saturated solution of aniline hydrochloride added when a precipitate of the hydrated Schiff's base of β-resorcylaldehyde was obtained. The Schiff's base was collected and hydrolysed with alkali. Any resin formed during the hydrolysis was filtered off and the alkaline solution acidified and extracted with ether. β-resorcylaldehyde was thus obtained almost quantitatively from its solution in a fairly pure condition.

METHOD/

METHOD. Molecular quantities of resorcinol and diphenylformamidine were heated at a temperature of 130° for 1-5 hours. To the reaction product, the requisite amount of caustic soda solution was added, and the whole steam distilled until all the aniline had passed over as shown by bleaching solution. Any unchanged diphenylformamidine was filtered off from the deep red solution. The alkaline solution was acidified with concentrated hydrochloric acid and then steam distilled when the 4:6-dihydroxyisophthalaldehyde collected in the condenser. After three hours steam distillation, the solution was cooled and resin filtered off. To the slightly acid filtrate, 20cc. of a saturated solution of aniline hydrochloride were added when β-resorcylaldehyde was precipitated as the crude hydrated Schiff's base hydrochloride. $C_6H_3(OH)_2 \cdot CH \cdot OH \cdot NH \cdot C_6H_5 \cdot HCl$. This was allowed to stand for one hour to complete precipitation. The hydrochloride was then filtered off. According to the excess of hydrochloride acid used in acidifying the caustic soda solution there remained in solution a corresponding quantity of the Schiff's base hydrochloride. This was, therefore, separated as the insoluble free base by the addition of a saturated solution of sodium acetate. The free base was filtered off/

off, mixed with the hydrochloride and the whole hydrolysed with caustic soda solution. The liberated aniline was again distilled over in steam. The bright red solution was acidified and the aldehyde extracted with ether from the acid solution. β-resorcylaldehyde was obtained from the ethereal extract in a fairly pure condition.

RESULTS of CONDENSATIONS at APPROX. 130° for 1½ hours, in which the above method of separation of the reaction products was employed.

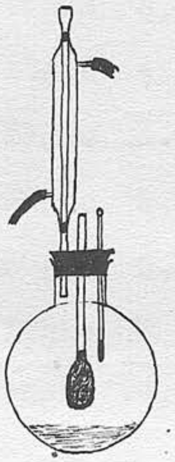
RESORCINOL.	DIPHENYLFORMAMIDINE.	UNCHANGED DIPHENYLFORMAMIDINE.	4:6-DIHYDROXYISOPHTHALALDEHYDE.	β-RESORCYLALDEHYDE.	RESIN.
20 gms.	40 gms	5.2 gms	3,2 gms	1.5 gms	8.5gms.
15 gms.	30 gms	3.4 gms	2.7 gms	2.55gms	5.2gms
10 gms	20 gms	4.9 gms	0.9 gms	2.9 gms	2,7gms
10 gms	20 gms	0.4 gms	1.9 gms	1.75gms	4.1gms
10 gms	20 gms	4.9 gms	1.3 gms	2,6 gms	2.2gms
10 gms	20 gms	0.9 gms	1.1 gms	0.8 gms	6.4gms

From the above table, the yield of β-resorcylaldehyde has been increased to approximately 20 per cent in some of the condensations. This indicates that the method of separation and purification is very/

very much better than any which involves the use of sodium bisulphite. The table of results also indicated that as the yield of resin increased the yield of β-resorcylaldehyde decreased.

A series of condensations were now carried out in which the temperature and time were varied. The object was to increase the yield of β-resorcylaldehyde and lower that of the resin.

In previous condensations, a castor oil bath was used. It was now proposed to carry out the condensations at a constant temperature. The following apparatus, which consisted essentially of a litre flask with a three holed stopper through which passed the condenser, thermometer and condensation tube, was employed. The boiling point of the liquid in the litre flask determined the temperature of the experiment.



For a temperature of 100°, water was used.

" " " " 110°. toluene " "

" " " " 116°, glacial acetic acid was used.

" " " " 130°, ethylene dibromide " "

" " " " 138°, m-xylene " " "

RESULTS of CONDENSATION of DIPHENYLFORMAMIDINE & RESORCINOL.

TEMP.	TIME.	RESORCINOL.	DIPHENYLFORMAMIDINE.	UNCHANGED DIPHENYLFORMAMIDINE.	4:6-DIHYDROXYISOPHTHALALDEHYDE.	β-RESORCYLALDEHYDE.	RESIN.
100°	5 hrs.	7.5gms	15gms	1.4gms	1.25gms	1.1gms	0.8gms.
110°	½ hr.	5 gms.	9 gms	5.2gms	Trace.	Trace	0.4"
110°	4 hrs.	7.5gms	15gms	5.6gms	1.15gms	2.1gms	1.5"
110°	4 hrs.	5 gms	10gms	2.9gms	0.7gms	1.1gms	0.85"
110°	6 hrs.	5 gms	10gms	1.2gms	1.22gms	0.9gms	0.8"
110°	9 hrs.	6.25gms	12.5gms	3gms.	0.8gms	1.1gms	2 "
110°	20 hrs.	7.5gms	15gms	3.2gms	1.3gms	0.9gms	4.6"
116°	2½ hrs.	7 gms	14gms	4.1gms	1.2gms	1.3gms	1.4"
116°	4 hrs.	7.5gms	15gms	4.5gms	1.5gms	1.6gms	1.6"
130°	¾ hr.	5 gms	9 gms	2.8gms	0.4gms	Trace	2.8"
130°	1½ hrs.	5 gms	10 gms	0.2gms	1.2gms	1.25gms	2.3"
130°	2 hrs.	7 gms	14gms	3 gms	1.25gms	1.5gms	2.6"
138°	2 hrs.	7.5gms	15gms	3.6gms	1.8 gms	0.45gms	2.1"

From/

From these results, it is evident that time and temperature are important factors in resin formation.

The yield of combined aldehydes in the majority of above condensations is approximately 40-50 per cent whilst the resin is greatest when the temperature is above 110°.

In the previous condensations, ordinary reagent bottle resorcinol which had not been dried in any way was used. A series of condensations was now carried out in which the resorcinol and diphenylformamidine were carefully dried at 100° before use, and the following results were obtained.

TEMP.	TIME.	RESORCINOL.	DIPHENYLFORMAMIDINE.	UNCHANGED DIPHENYLFORMAMIDINE.	2:4-DIHYDROXYISOPHTHALALDEHYDE.	β-RESORCYLALDEHYDE.	RESIN
100°	6hrs	5gms	9gms	1.5gms	-	2.4gms	0.4gms
100°	6hrs	5gms	9gms	1.2gms	-	2.3gms	0.6gms
100°	9hrs	5gms	9gms	0.8gms	Trace	2.1gms	0.9gms
110°	6hrs	5gms	9gms	1.5gms	-	2.35gms	0.5gms
110°	6hrs	5gms	9gms	1.7gms	-	1.8gms	1.3gms
110°	6hrs	5gms	9gms	0.4gms	-	1.75gms	0.9gms
110°	6hrs	6gms	9gms	1.1gms	-	3gms	0.8gms
110°	6hrs	6gms	9gms	0.4gms	-	137gms	1.2gms
130°	1½hrs	5gms	9gms	1.8gms	1.1gms	1.3gms	1.2gms
130°	1½hrs	5gms	9gms	2gms	0.6gms	1.2gms	1.9gms

The/

CONDENSATION OF DIPHENYLFORMAMIDINE WITH PHENOLS. PART I. A NEW SYNTHESIS OF β-RESORCYLALDEHYDE.

BY

JOHN BALDWIN SHOESMITH

AND

JOHN HALDANE.

From the Transactions of the Chemical Society, 1923. Vol. 123.

CCCIX.—*Condensation of Diphenylformamidine with Phenols. Part I. A New Synthesis of β-Resorcylaldehyde.*

By John Baldwin Shoesmith and John Haldane.

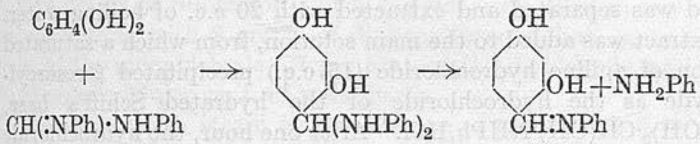
The condensation which takes place when diphenylformamidine is heated with compounds containing an active methylene group was first pointed out by Dains (*Ber.*, 1902, **35**, 2504). As an example of this may be quoted the condensation of the amidine (I) with acetylacetone, which probably takes place in two stages. The intermediate compound (II) is never isolated, aniline being liberated at once.

$$\text{(I.)}\ CH(\colon NPh){\cdot}NHPh + CH_2(COMe)_2 \longrightarrow CH(NHPh)_2{\cdot}CH(COMe)_2\ \text{(II.)}$$
$$\longrightarrow CH(NHPh)\colon C(COMe)_2\ \text{(III.)} + NH_2Ph.$$

Anilinomethyleneacetylacetone (III) is isolated in almost quantitative yield.

This type of reaction appears to be a very general one and has been extended by Dains and his co-workers (*J. Amer. Chem. Soc.*, 1909, onwards) to a large number of similar compounds.

The present investigation has shown that condensation also takes place between diphenylformamidine and resorcinol. Aniline is liberated and a solid compound results. The course of the reaction is represented thus:



(IV.)

The crude condensation product, which consists essentially of the Schiff's base (IV) of β-resorcylaldehyde, unchanged resorcinol, and diphenylformamidine, is hydrolysed by boiling caustic soda and β-resorcylaldehyde can thus be obtained in a very simple manner.

It is, however, necessary to say that the structure to be assigned to compound (IV) is not yet decided. Its physical and chemical properties show that it is slightly different from the Schiff's base of the aldehyde which was prepared by Dimroth and Zoeppritz (*Ber.*, 1902, **35**, 995) by another method.

The present communication details the method of preparing β-resorcylaldehyde in appreciable yield; the extension of the method to other phenols and the constitution of the intermediate compound are reserved for further investigation.

EXPERIMENTAL.

Diphenylformamidine.—This was prepared by boiling together aniline and formic acid (Weith, *Ber.*, 1876, 9, 454). Forty grams (1 mol.) of 80 per cent. formic acid were mixed with 160 grams (2½ mols.) of aniline. The water which was present in the original acid together with that produced in the reaction was distilled away through a fractionating column. The head of the column was fitted with a device for trapping the water so soon as it reached the top. After four hours' gentle boiling, the temperature was raised until 60 c.c. of aniline had distilled over. The residual diphenylformamidine solidified on cooling and after recrystallisation from alcohol melted at 137° (yield 63 grams).

Condensation of Diphenylformamidine with Resorcinol.—A long series of experiments has shown the following to be the best conditions for the preparation of β-resorcylaldehyde by this method.

A finely powdered mixture of 5 grams (1 mol.) of carefully dried resorcinol with 9 grams (1 mol.) of diphenylformamidine was heated in a small, thin-walled flask,* totally immersed in the vapour of boiling water to ensure a temperature of 100°. The mixture first liquefied; solid appeared after five hours' heating. At the end of six hours, the condensation product was dissolved in 50 c.c. of hot 12—15 per cent. caustic soda solution, the liberated aniline distilled with steam, and the cooled filtered solution made slightly acid with dilute hydrochloric acid. The small quantity of resin here precipitated was separated and extracted with 20 c.c. of boiling water. The extract was added to the main solution, from which a saturated solution of aniline hydrochloride (15 c.c.) precipitated β-resorcylaldehyde as the hydrochloride of the hydrated Schiff's base, $C_6H_3(OH)_2\cdot CH(OH)\cdot NHPh,HCl$. After one hour, the hydrochloride was collected and the base remaining in the filtrate was precipitated by adding a saturated solution of sodium acetate. The free base was filtered off, mixed with the hydrochloride, and the whole hydrolysed with caustic soda solution. The liberated aniline was removed with steam, the bright red solution acidified, and the aldehyde, extracted with ether (yield 45—50 per cent. of the theoretical), was recrystallised from hot water. It was identified by mixed melting-point determinations (135—136°), the deep brown colour given by ferric chloride to its aqueous solution, the feathery needles of its phenylhydrazone, the oxime of melting point 192°, and the peculiar yellow precipitate which it gives with Schiff's reagent.

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* It is hoped to publish details of this simple thermostat shortly.

The method of purification adopted is very much better than any involving the use of sodium bisulphite solution.

Condensation under other Conditions.—The same quantities of resorcinol and diphenylformamidine were heated at 130° for one and a half hours, and the hydrolysis was carried out as before. Acid, however, precipitated a considerable quantity of red needles, which were characterised as the dialdehyde of resorcinol, $C_6H_2(OH)_2(CHO)_2$, m. p. 126° (Tiemann and Lewy, *Ber.*, 1877, **10**, 2211). They represented 25 per cent. of the resorcinol; a smaller quantity (25—30 per cent.) of monaldehyde was isolated from the acid solution, whilst the resin present represented 30—40 per cent. The aldehyde was difficult to purify.

When the condensation was effected at 100° for nine hours, 40 per cent. of the expected monaldehyde, a trace of dialdehyde, and 25—30 per cent. of the resinous compound were produced.

An increase in the quantity of resorcinol used caused a corresponding increase in the amount of aldehyde produced.

The effect of moisture on this condensation is remarkable. The free hydrated Schiff's base which is probably formed in the condensation in presence of moisture was found to decompose at 100° in the impure condition into aniline and a resin. This caused the yield of monaldehyde to be very poor whenever precautions were not taken to dry the resorcinol before use. Under these conditions, it is interesting to point out the as yet inexplicable formation of dialdehyde.

Five grams of resorcinol (which had not been dried in any way), on condensing with 9 grams of diphenylformamidine, gave 25 per cent. of the monaldehyde, 27 per cent. of the dialdehyde, and resin representing 20 per cent. of resorcinol.

Distillation with steam in the absence of caustic alkali is not a practicable method of removing the aniline from the Schiff's base produced in the condensation. This is due to the decomposition of the hydrated Schiff's base by moisture at 100°, as already stated. The resin obtained dissolves afterwards in caustic alkali with a deep red colour, but does not appear to be a definite compound.

Summary.

(1) Diphenylformamidine and resorcinol condense together on heating with liberation of aniline. The condensation product, hydrolysed by caustic alkali, yields aniline and β-resorcylaldehyde.

(2) The method by which the best yields of β-resorcylaldehyde may be obtained is described and the deleterious effect of moisture, too long heating, and condensation at too high a temperature pointed out.

The authors wish to state that the suggestion that such a condensation might take place was due to Prof. A. Lapworth, F.R.S. They also wish to thank the Advisory Council of the Department of Scientific and Industrial Research for grants which enabled each of them in turn to undertake these investigations.

CHEMISTRY DEPARTMENT,
EDINBURGH UNIVERSITY.

[*Received, July* 31*st*, 1923.]

PRINTED IN GREAT BRITAIN BY RICHARD CLAY & SONS, LIMITED,
BUNGAY, SUFFOLK.

The yield of β-resorcylaldehyde in certain of the above condensations has been increased to 45-50 per cent of the theoretically expected quantity and the quantity of resin correspondingly lowered.

The experiments which have been undertaken in order to prepare β-resorcylaldehyde by this new method are summarised in the following account which has already appeared in the transactions of the Chemical Society. (1923.<u>124</u>.2704).

A finely powdered mixture of 5 gms. (1 mol.) of carefully dried resorcinol with 9 gms. (1 mol.) of diphenylformamidine was introduced into a small thin walled flask which was then immersed in the vapour of boiling water to ensure a temperature of 100°. The mixture first liquified; solid appeared after 5 hours heating. At the end of 6 hours, the condensation product was dissolved in 50cc. of 12-15 per cent caustic soda solution. The condensation product only goes completely into solution in hot alkali. The liberated aniline was steam distilled away from the bright red alkaline solution. When the solution was cold, the unchanged diphenylformamidine was filtered off and the alkaline solution acidified with dilute hydrochloric acid. The small quantity of resin here precipitated/

precipitated was separated and extracted with 20cc. of boiling water. The extract was added to the main solution from which a saturated solution of aniline hydrochloride (15cc.) precipitated the β-resorcylaldehyde as the hydrated Schiff's base hydrochloride. $C_6H_3(OH)_2 \cdot CH \cdot OH \cdot NH \cdot C_6H_5 \cdot HCl$. After this had stood for an hour to complete precipitation, the hydrochloride was filtered off. According to the excess of hydrochloric acid used in acidifying the alkaline solution, there remained in solution a corresponding quantity of the Schiff's base hydrochloride. This was therefore separated as the insoluble free base by the addition of a saturated solution of sodium acetate. The free base was filtered off, mixed with the hydrochloride and the whole hydrolysed with caustic soda solution. The liberated aniline was again distilled over in steam. The bright red solution was acidified and the aldehyde extracted with ether from the acid solution. From the ethereal extract, the aldehyde was obtained in 45-50 per cent of the theoretically expected quantity.

EFFECT of CARRYING out the CONDENSATION at a HIGHER TEMPERATURE.

The same quantities of resorcinol and diphenylformamidine were heated at a temperature of 130° for 1½ hours. The hydrolysis was carried out as before. Acid, however, precipitated a considerable quantity of reddish needles. These were filtered off and purified by distillation in steam after which they were characterised as 4:6-dihydroxyisophthalaldehyde. $C_6H_2\ (OH)_2 \cdot (CHO)_2$ and possessed a melting point of 126°-127°. (TIEMANN and LEWY. Ber., 1877·10·2211). They represented 25 per cent of the resorcinol. A smaller quantity of β-resorcylaldehyde was isolated from the acid solution, only 25-30 per cent being obtainable whilst the resin was present in an amount representing 25-30 per cent of the resorcinol. The β-resorcylaldehyde so obtained was difficult to purify.

EFFECT of PROLONGING the TIME of HEATING.

Carefully dried resorcinol (5gms.) and diphenylformamidine (9gms.) when heated at a temperature of 100° for 9 hours gave 40 per cent of the expected β-resorcylaldehyde, a trace of 4:6-dihydroxyisophthalaldehyde and 20 per cent of the resinous compound.

EFFECT of VARYING the QUANTITIES of the REACTANTS.

An increase in the quantity of resorcinol used, caused a corresponding increase in the amount of aldehyde produced.

EFFECT of MOISTURE on the CONDENSATION.

The effect of moisture on this condensation is remarkable. The free hydrated Schiff's base which is probably formed in the condensation in presence of moisture was found to decompose at 100° in the impure condition into aniline and a resin. This caused the yield of β-resorcylaldehyde to be very poor whenever precautions were not taken to dry the resorcinol before use. Under these conditions, it is interesting to point out the formation of 4 :6-dihydroxyisophthalaldehyde.

Ordinary reagent bottle resorcinol (5gms.) which had not been dried in any way, when heated with diphenylformamidine (9gms.) at a temperature of 100° for 6 hours, gave 25 per cent of β-resorcylaldehyde, 27 per cent of 4:6-dihydroxyisophthalaldehyde, and resin representing 20 per cent of resorcinol.

APPLICATION to other PHENOLS.

I. CONDENSATION of DIPHENYLFORMAMIDINE and MONOMETHYL-RESORCINOL.

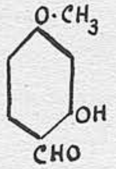
Preparation of monomethyl-resorcinol. This was prepared according to the directions given by ULLMANN. (Annalen., 1903.327.116). A solution of resorcinol in the requisite amount of caustic soda was agitated with dimethylsulphate until the solution was neutral. An oil separated. From the latter on treatment with alkali dimethyl-resorcinol was obtained in approximately 60 per cent yield of the theoretical quantity. The alkaline solution when acidified and extracted with ether yielded the monomethyl derivative in approximately 30 per cent yield of the theoretical quantity.

PRELIMINARY CONDENSATION.

Diphenylformamidine (7 gms.) and monomethyl-resorcinol (3 gms.) were heated at a temperature of 210° for 6 hours. To the crude condensation/

condensation product the requisite quantity of 50 per cent sulphuric acid was added and the solution steam distilled. The distillate had a distinct odour not unlike that of vanillin and readily gave a p-nitrophenylhydrazone, which indicated the presence of an aldehyde. The aldehyde present in the distillate was extracted by the sodium bisulphite method. (Yield 0.5 gms.) This substance when recrystallised from dilute alcohol possessed a melting point of 41° and readily formed a phenylhydrazone (M.P+.137°). It dissolved in alkalies with an intense yellow coloration and an alcoholic solution of the aldehyde gave an intense red coloration with $FeCl_3$.

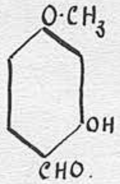
4-Methoxy-2-hydroxybenzaldehyde has been



prepared by TIEMANN (Ber., 1880.<u>13</u>.2637) and OTT (Ber., 1922.<u>55B</u>.920) and a comparison of the compound there described and the reaction product reads.

REAGENT.	DESCRIBED 4-METHOXY-2-HYDROXYBENZALDEHYDE.	REACTION PRODUCT.
NaOH.	Dissolves with yellow colour	The same.
$FeCl_3$	Deep reddish brown coloration	" "
Heam	Volatile	" "
Solubility	Insol in H_2O: easily soluble in alcohol ether, benzene and ligroin	" "
NH_4OH Solution	Yellow	" "
with (1) Pb AC	Crystalline Pb compound	" "
(2) $CuSO_4$	Yellow green ppte.	" "
$C_6H_5.NH.NH_2$	Phenylhydrazone M.P+137°	M.P+137°
M.P+	41°-42°	41°

The compound is therefore 4-methoxy-2-hydroxybenzaldehyde



The/

The following results were obtained when an attempt was made to increase the yield of 4-methoxy-2-hydroxybenzaldehyde by the condensation of diphenylformamidine with monomethyl-resorcinol. The method employed for the separation of this aldehyde in the following condensations was as follows:-

To the crude condensation product, the requisite quantity of a caustic soda solution was added and the solution steam distilled until all aniline had passed over. The unchanged diphenylformamidine was filtered off and the alkaline solution acidified with dilute hydrochloric acid. The acid solution was extracted with ether and 10c.c. of saturated sodium bisulphite solution added to the ethereal extracts. The ether was then distilled away and the remaining bisulphite solution was extracted with ether before it was decomposed with 50 per cent sulphuric acid. The 4-methoxy-2-hydroxybenzaldehyde was obtained in almost a pure condition when the acid solution was extracted with ether.

Results/

RESULTS of CONDENSATION of DIPHENYLFORMAMIDINE and MONOMETHYL RESORCINOL.

Temp.	Time.	Monomethyl Resorcinol	Diphenylformamidine	Unchanged Diphenylformamidine.	Resin	4-Methoxy-2-Hydroxybenzaldehyde.
116°	7 hrs	4 gms	7 gms.	3.2 gms.	—	0.4 gms.
130°	6 hrs	3 gms.	7 gms	2.8 gms.	—	0.4 gms.
138°	7 hrs	4 gms.	7 gms.	2 gms.	1 gm.	0.5 gms.
138°	6 hrs	4 gms.	7 gms.	1.8 gms.	0.8gms.	0.7 gms.
150°	4 hrs	3 gms.	6 gms.	2.4 gms.	0.6gms.	0.7 gms.
183°	1 hr.	3.5gms	7 gms.	1 gm.	1.2 gms	0.8 gms.
183°	2 hrs	3.5gms	7 gms.	0.8 gms.	1.4 gms	0.9 gms.
183°	1½hrs	3 gms.	6 gms.	0.4 gms.	2 gms	0.6 gms.
183°	2 hrs	3.5gms	7 gms	1 gm	1.3 gms	0.8 gms.
193°	1½hrs	3 gms	7 gms	—	3.5 gms	Trace.

From the above results, it is evident that the best yield of 4-methoxy-2-hydroxybenzaldehyde. i.e., approximately 20 per cent of the theoretical quantity, is obtained when diphenylformamidine and monomethyl resorcinol are heated at a temperature of 183° for 2 hours.

2/

2. CONDENSATION of DIPHENYLFORMAMIDINE and DIMETHYL RESORCINOL.

A preliminary condensation of molecular quantities of diphenylformamidine and dimethy resorcinol was carried out at a temperature of 210° for 6 hours. When the reaction product was worked up in a similar manner to that employed in the previous condensation, namely diphenylformamidine and monomethyl resorcinol, a small quantity of an aldehyde was isolated and which was proved to be 4-methoxy-2-hydroxybenzaldehyde. An examination of the dimethyl resorcinol however proved the presence of a small quantity of the monomethyl derivative which was very resistant to alkali extraction and had reacted with the diphenylformamidine at 210°. That the monomethyl resorcinol had reacted with the diphenylformamidine was proved when dimethyl resorcinol which had been freed from the monomethyl derivative by many extractions with alkali in ethereal solution was heated with diphenylformamidine at a temperature of 210° for 6 hrs. In this condensation, no trace of an/

an aldehyde could be detected.

Therefore, dimethyl resorcinol does not react with diphenylformamidine.

3. CONDENSATION of DIPHENYLFORMAMIDINE and CATECHOL.

Molecular quantities of diphenylformamidine and catechol were heated at a temperature of 110° and 130° respectively for six hours. The condensation product in each case had a strong odour of carbylamine. When the condensation products were hydrolysed with the necessary quantity of caustic soda solution, only a trace of aniline was liberated in each case. From the amount of unchanged diphenylformamidine recovered it was concluded that the reaction had only proceeded to a very slight extent. When the alkaline solutions were acidified however, a small quantity of aldehyde was obtained in each case by the bisulphite method of separation. The very impure product readily gave a p-nitrophenylhydrazone and a green coloration with $FeCl_3$ changing to red on the addition of sodium carbonate which is a characteristic reaction of protocatechuic aldehyde.

4. CONDENSATION of DIPHENYLFORMAMIDINE and GUAIACOL.

Guaiacol (4 gms.) and diphenylformamidine (7 gms.) were heated at a temperature of 183° for two hours. The necessary quantity of caustic soda solution was added to the condensation product and the solution steam distilled until all aniline had passed over. The unchanged diphenylformamidine (5.4 gms.) was filtered off and the alkaline solution acidified with dilute Hydrochloric acid. In order to isolate any aldehyde formed, the bisulphite method was employed. Actually, a small quantity of an oil with an odour not unlike that of vanillin and which gave all the reactions of an aldehyde was obtained.

As a result of the large amount of unchanged diphenylformamidine recovered in the first experiment, the following condensations were carried out at a higher temperature, the method of separation being as follows:-

The crude condensation product was hydrolysed with the requisite quantity of caustic soda/

soda solution and the solution steam distilled until all aniline had passed over. The unchanged diphenylformamidine was filtered off and the alkaline solution acidified. The acid solution was then steam distilled until the distillate gave no p-nitrophenylhydrazone. The distillate was extracted with ether and the aldehyde purified by the bisulphite method. The best yield of the aldehyde obtained was approximately 10 per cent of the theoretically expected quantity.

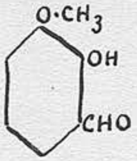
RESULTS of CONDENSATION of DIPHENYLFORMAMIDINE and GUAIACOL.

Temp.	Time	Guaiacol	Diphenyl formamidine	Unchanged Diphenylformamidine	Resin	Aldehyde
210°	6 hrs	4 gms	7 gms	3.8 gms	1.6 gms	0.5 gms
210°	7 hrs	4 gms	7 gms	4.4 gms	1.3 gms	0.4 gms
210°	7 hrs	4 gms	7 gms	4 gms	1.2 gms	0.6 gms
239°	4 hrs	4 gms	7 gms	4 gms	1.6 gms	0.4 gms

This aldehyde was suspected to be 3-methoxy-2-hydroxybenzaldehyde and a comparison of its properties and those of 3-methoxy-2-hydroxybenzaldehyde as stated by TIEMANN (Ber., 1881.14.2023) reads:-

REAGENT.	3-METHOXY-2-HYDROXY-BENZALDEHYDE.	REACTION PRODUCT.
	Oil	The same.
NaOH.	Soluble with an intense yellow colour.	" "
$FeCl_3$	Alcoholic solution - deep green.	" "
Heam	Volatile.	" "
Solubility	Insol in H_2O, easily soluble in alcohol, ether, and benzene.	" "
$NaHSO_3$	Forms a double compound very easily.	" "

Therefore, guaiacol and diphenylformamidine condense and after hydrolysis, 3-methoxy-2-hydroxybenzaldehyde can be isolated.



5./

5. CONDENSATION of DIPHENYLFORMAMIDINE and QUINOL.

Two condensations were carried out at a temperature of 183° and 150° for two hours and four hours respectively and in each case the condensation product possessed a strong odour of carbylamine. When the condensation products were hydrolysed with the requisite quantity of caustic soda solution merely a trace of aniline was liberated in each case. This showed that the reaction had proceeded only to a very slight extent. When the alkaline solution was acidified a trace of aldehyde, as detected by p-nitrophenylhydrazine, could be separated by the bisulphite method.

6. CONDENSATION of DIPHENYLFORMAMIDINE and PHLOROGLUCINOL.

A finely powdered mixture of anhydrous ph~~y~~loroglucinol (2.5 gms.) and diphenylformamidine (4.5 gms.) were heated at a temperature of 130° for four hours. The deep red condensation product readily dissolved in caustic soda solution. The alkaline solution had a distinct odour of carbylamine. When this solution was steam distilled, only a trace of aniline passed over as shown by bleaching solution. The unchanged diphenylformamidine was filtered off and the solution acidified with dilute hydrochloric acid. A dark resin was precipitated and no trace of an aldehyde could be obtained.

The condensation was repeated at 130° for 10 minutes but again there was a distinct odour of carbylamine and the only product isolated was a resin.

EFFECT/

EFFECT of CARRYING OUT the REACTION in SOLUTION.

(a) Anhydrous ph~~y~~loroglucinol (2 gms.) was mixed with diphenylformamidine (4 gms.) and 10 c.c. of aniline and heated at a temperature of 130° for four hours. From the amount of unchanged diphenylformamidine recovered after hydrolysis with alkali, it appeared that no reaction had taken place under these conditions.

(b) Anhydrous phloroglucinol (2 gms.) and diphenylformamidine (4 gms.) were dissolved in 40 c.c. of m-xylene and the solution was boiled for six hours. When the solution was steam distilled a small quantity of aniline passed over. The distilled solution was cooled and unchanged diphenylformamidine filtered off. A dark red resinous substance appeared on the addition of acid. The acid solution was extracted with ether and was found to contain a trace of aldehyde as detected by p-nitrophenylhydrazine.

7/

7. CONDENSATION of DIPHENYLFORMAMIDINE and PYROGALLOL.

A preliminary investigation showed that diphenylformamidine and pyrogallol reacted only to a slight extent when heated at a temperature of 100° At a temperature of 138° the condensation product was chiefly a tar which had a strong odour of carbylaminine.

At the intermediate temperature of 110° the two compounds condensed together and after hydrolysis, an aldehyde which recrystallised from water and possessed a melting point of 157° was obtained in approximately 15-20 per cent of the theoretically expected quantity. The aldehyde was isolated by the bisulphite method.

RESULTS of CONDENSATION of DIPHENYLFORMAMIDINE with PYROGALLOL.

Temp.	Time.	Pyrogallol	Diphenylformamidine.	Unchanged Diphenylformamidine.	Aldehyde.
100°	1½hrs	5 gms	6.5 gms	3.5 gms	Trace
110°	2 hrs	4.5gms	6 gms	2.4 gms	0.4 gms
110°	2 hrs	4.5 gms	6 gms	2 gms	0.7 gms
110°	4 hrs	4.5 gms	6 gms	1.4 gms	0.9 gms

The/

The reaction product recrystallised from water and possessed a melting point of 157° and readily formed a phenylhydrazone (M.P+.161°). GATTERMANN (Ber., 1899.32.281.) prepared pyrogallol aldehyde by the HCN method and the melting points of the aldehyde and phenylhydrazone are given as 157°-158° and 161° respectively which agree with those of the aldehyde isolated from the condensation of diphenylformamidine and pyrogallol. Therefore pyrogallol aldehyde can be obtained in approximately 15-20 per cent of the theoretically expected quantity by the condensation of diphenylformamidine and pyrogallol.

It was found in the condensations carried out at a temperature of 110° for more than two hours that the solution, obtained after the condensation product had been hydrolysed with alkali and then acidified, was difficult to extract with ether as a result of the formation of an emulsion.

8./

8. CONDENSATION of DIPHENYLFORMAMIDINE with PHENOL.

Phenol and diphenylformamidine were found to condense together and salicylaldehyde was isolated. In the hope of making the yield comparable with that obtained by other methods, a long series of condensations were carried out. The following were found to be the best conditions for obtaining salicylaldehyde from the condensation of diphenylformamidine and phenol.

Molecular quantities of phenol and diphenylformamidine were heated at a temperature of 200° for six hours. To the crude condensation product, the requisite quantity of caustic soda solution was added and all the aniline distilled over in steam. The unchanged diphenylformamidine, if any, was filtered off and the alkaline solution acidified with dilute hydrochloric acid. The acid solution was extracted with ether and this ethereal solution ~~extraca~~ extracted with saturated sodium bisulphite (15c.c.). The bisulphite solution was in turn extracted with ether

to/

to remove phenol and then decomposed with 25 per cent sulphuric acid. Salicylaldehyde was obtained by the extraction of the acid solution in approximately 20 per cent of the theoretically expected quantity.

CONDENSATION RESULTS.

Temp.	Time	Phenol	Diphenylformamidine.	Unchanged Diphenylformamidine.	Resin	Salicyl Aldehyde.
183°	6hrs	4.5gms	9 gms	5 gms	–	0.4gms
193°	6hrs	4.5gms	9 gms	3 gms	–	0.6gms
193°	10hrs	4.5gms	9 gms	–	2gms	0.8gms
199°	4hrs	4.5gms	9 gms	1 gm.	1.4gms	0.8gms
199°	5hrs	4.5gms	9 gms	0.4 gms	2gms	0.8gms
199°	4hrs	4.5gms	9 gms	1.4 gms	1.2gms	0.7gms
199°	6hrs	4.5gms	9 gms	–	3.8gms	0.8gms
199°	6hrs	4.5gms	9 gms	–	4gms	0.9gms
199°	6hrs	4.5gms	9 gms	–	3.9gms	0.9gms
199°	6hrs	4.5gms	9 gms	–	4.2gms	0.7gms
210°	4hrs	5gms	10gms	Trace	4gms	0.9gms
210°	6hrs	4.5gms	9 gms	–	5gms	Trace
210°	6hrs	4.5gms	9 gms	–	5gms	Trace

As/

As is seen from the table, resin formation is the chief difficulty and it does not appear possible to eliminate it. At a lower condensation temperature e.g., 183° no resin is formed but the reaction does not go to completion and the salicylaldehyde formed after hydrolysis of the condensation product was difficult to purify as a result of unchanged phenol.

9/

9. CONDENSATION of o-NITROPHENOL with DIPHENYLFORMAMIDINE.

Molecular quantities of o-nitrophenol and diphenylformamidine were heated at a temperature of 183° for six hours. When the condensation product was hydrolysed with the requisite quantity of caustic soda solution only a trace of aniline was liberated. The unchanged diphenylformamidine was filtered off and the alkaline solution acidified. Only a trace of an aldehyde as detected by p-nitrophenylhydrazine could be separated from the acid solution by the bisulphite method.

10/

10. CONDENSATION of p-NITROPHENOL with DIPHENYLFORMAMIDINE.

Molecular quantities of p-nitrophenol and diphenylformamidine were heated at a temperature of 183° for six hours. There was a pronounced odour of carbylamine in the condensation product. When the crude condensation product was hydrolysed with the necessary quantity of caustic soda solution only a trace of aniline was liberated. The unchanged diphenylformamidine was filtered off and the alkaline solution acidified when only traces of an aldehyde, as detected by p-nitrophenylhydrazine, could be separated by the bisulphite method.

11. CONDENSATION of DIPHENYLFORMAMIDINE and o-CRESOL.

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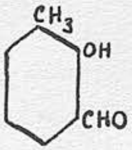
o-Cresol (4 gms) and diphenylformamidine (8 gms) were heated at a temperature of 183° for six hours. The crude condensation product was steam distilled until all aniline and unchanged o-cresol had passed over. The requisite quantity of caustic soda solution was then added and the solution steam distilled when a further quantity of aniline passed over. The unchanged diphenylformamidine was filtered off and the alkaline solution acidified with dilute hydrochloric acid. The acid solution was then steam distilled. The distillate had an odour not unlike that of salicylaldehyde which indicated the presence of an aldehyde in the distillate. The distillate was therefore extracted with ether and the ethereal extracts dried over calcium chloride. When the ether was distilled away, an oil which had a distinct odour resembling that of salicylaldehyde was obtained. The oil gradually solidified (Yield 1.1 gms)

As this aldehyde was suspected to be

3-methyl-2-hydroxybenzaldehyde,

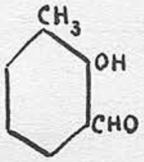


its properties were compared with those of 3-methyl-2-hydroxybenzaldehyde as stated by TIEMANN. (Ber., 1878.11.772) - The comparison reads:-

REAGENT.	Described. 3-Methyl-2-Hydroxybenzaldehyde.	REACTION PRODUCT.
	Oil at 20° with an odour resembling that of of salicylaldehyde.	The same " " " "
NaOH.	Dissolves with yellow colour.	" "
$FeCl_3$	Alcoholicsoln gives deep blue colour	" "
Steam	Volatile	" "
Alcoh. soln $+NH_4OH$	Yellow	" "
$+$(a)$AgNo_3$	White ppte	" "
(b)$Pb\overline{AC}$	White ppte	" "
(c)$CuSO_4$	Green ppte. insol in in XS. of NH_4OH.	" "
$C_6H_5.NH.NH_2$	Phenylhydrazone. M.P+.95°	M.P+.95°

Therefore/

Therefore the aldehyde is 3-methyl-2-hydroxybenzaldehyde.



12. CONDENSATION of DIPHENYLFORMAMIDINE with m-CRESOL.

m-Cresol (4 gms) and diphenylformamidine (8 gms) were heated at a temperature of 210° for six hours. The requisite quantity of caustic soda solution was added to the condensation product and the alkaline solution steam distilled until all aniline had passed over. There was no unchanged diphenylformamidine. The alkaline solution was acidified and steam distilled when an oil, which gradually solidified, appeared in the condenser. The acid solution was steam distilled until no trace of an aldehyde could be detected by means of p-nitrophenylhydrazine. The solid product in the distillate was filtered off and the filtrate extracted for a further quantity of the aldehyde. This aldehyde recrystallised from slightly diluted alcohol in long yellow needles (M.P+59°), and formed a phenylhydrazone (M•P+160°) which recrystallised in long needles from alcohol. As this aldehyde was suspected to be 4-methyl-2-hydroxybenzaldehyde its properties were compared with those/

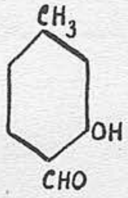
those of 4-methyl-2-hydroxybenzaldehyde as stated by CHUIT and BOLSING (Bull.Soc.chim.1906.(3)·<u>35</u>·82.)

The comparison reads:-

REAGENT.	Described 4-Methyl-2-Hydroxy-benzaldehyde.	REACTION PRODUCT.
NaOH.	Soluble with yellow colour.	The same
$FeCl_3$	Violet colour.	" "
Steam	Very volatile	" "
Alcohol. soln + NH_4OH	Yellow	" "
+(a)$AgNO_3$	White ppte.	" "
(b)$Pb\overline{AC}$	White ppte.	" "
(c)$CuSO_4$	Green ppte. insol in XS, of NH_4OH.	" "
Solubility	Recrystallises from E+OH in yellow needles: fairly soluble in warm H_2O	" "
$C_6H_5 \cdot NH \cdot NH_2$	Forms a phenylhydrazone M.P+160°	M.P+160°
M.P+.	59°	59°

Therefore/

Therefore, the aldehyde is 4-methyl-2-hydroxybenzaldehyde.



In a condensation carried out at a temperature of 199° for six hours in which 4 gms of m-cresol and 8 gms of diphenylformamidine were used, 1·2 gms 4-methyl-2-hydroxybenzaldehyde and 2·4 gms of resin were separated. The method of separation was similar to that employed in the previous condensation.

13/

13. CONDENSATION of DIPHENYLFORMAMIDINE with p-CRESOL.

p-Cresol (4 gms) and diphenylformamidine (8 gms) were heated at a temperature of 193° for six hours. The condensation product which had a distinct odour of aniline was steam distilled until all p-cresol and aniline had passed over. The requisite quantity of caustic soda was then added and the solution again steam distilled until all the liberated aniline had passed over. There was no unchanged diphenylformamidine. The alkaline solution was acidified with dilute hydrochloric acid and the acid solution steam distilled. A volatile aldehyde, as detected by p-nitrophenylhydrazine, passed over and 2·5 gms of resin remained in the distilling flask. The solid aldehyde in the distillate was filtered off and a further quantity of the aldehyde was obtained form the filtrate by the bisulphite method of purification The total yield of aldehyde was 0·8 gms.

The aldehyde recrystallised from diluted alcohol/

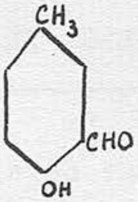
alcohol and possessed a melting point of 55°. It formed a phenylhydrazone very readily which recrystallised from alcohol in long yellow needles (M.Pt. 149°).

As the aldehyde was suspected to be 5-methyl-2-hydroxybenzaldehyde its properties were compared with those of 5-methyl-2-hydroxybenzaldehyde as stated by TIEMANN. (Ber., 1878·11·777 & 785). The comparison reads.

REAGENT.	DESCRIBED 5-METHYL-2-HYDROXYBENZALDEHYDE.	REACTION PRODUCT.
NaOH	Soluble with yellow colour	The same.
$FeCl_3$	Deep blue coloration.	" "
Steam	Easily volatile	" "
Alcoh.soln. +NH_4OH	Yellow.	" "
+a)$Pb\overline{AC}$	White ppte.	" "
b)$AgNO_3$	White ppte.	" "
c)$CuSO_4$	Green ppte. insol in XS. of NH_4OH	" "
Solubility	Sparingly soluble in H_2O, easily in alcohol, ether & chloroform.	" "
M.Pt.	56°	55°
$C_6H_5\cdot NH\cdot NH_2$	Forms a phenylhydrazone M.Pt. 149° .	M.Pt. 149°

Therefore/

Therefore, the aldehyde is 5-methyl-2-hydroxybenzaldehyde.



14/.

14. CONDENSATION of DIPHENYLFORMAMIDINE & α-NAPHTHOL.

PRELIMINARY CONDENSATION.

A finely powdered mixture of α-naphthol (4 gms.) and diphenylformamidine (5.25gms.) was heated at a temperature of 130° for four hours. Aniline was liberated. The necessary quantity of caustic soda solution was added to the crude condensation product and the liberated aniline steam distilled over. During the steam distillation a dark green resin appeared in the flask. The resin (5gms.) was filtered off and the solution acidified when a precipitate containing unchanged α-naphthol was obtained. The precipitate, however, gave an oxime, oxamazone and an orange coloured p-nitrophenylhydrazone. It was hoped, at this point, to separate the aldehyde as the bisulphite compound, a method by which GATTERMANN (Ber., 1899.32.284) had isolated the aldehyde from α-naphthol and hydrocyanic acid. It was found, however, that this aldehyde only formed a bisulphite compound very slowly. However, when the acid solution of the aldehyde was steam distilled, a yellow oil which slowly solidified, appeared in the condenser. This volatile product when recrystallised from dilute alcohol/

alcohol possessed a melting point of 58°-59°, readily gave an oxime (M.Pt., 145°), a semioxamazone and an orange coloured p-nitrophenylhydrazone. It was decided to prepare a small quantity of the 1-hydroxy-4-naphthaldehyde according to GATTERMANN'S method (Ber., 1899·32·284) for comparison with this reaction product.

PREPARATION of 1-HYDROXY-4-NAPHTHALDEHYDE.

α-Naphthol (7.5 gms.) was dissolved in 20 c.c. of ether and to the solution 5 c.c. of liquid hydrogen cyanide and 7.5 gms. $ZnCl_2$ were added. The solution was then saturated with dry hydrogen chloride and the imine hydrochloride precipitated from the ethereal solution was decomposed with water.

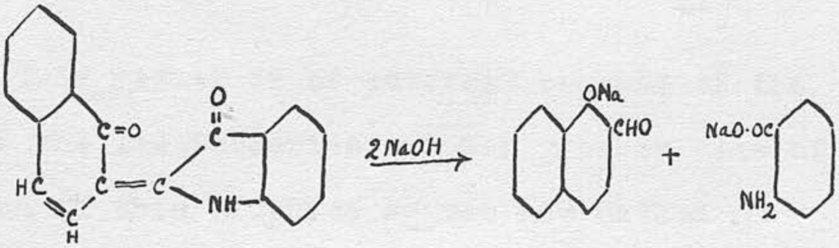
A comparison of the properties of the reaction product (M.Pt 58-59) and the 1-hydroxy-4-naphthaldehyde reads.

REAGENT	1-HYDROXY-4-NAPHTHALDEHYDE.	REACTION PRODUCT.
M.Pt.	181°	58°-59°
Steam.	Non-volatile.	Volatile
$NaHSO_3$	Forms a double compound very easily.	Only very slowly.
p·NO_2 phenylhydrazine.	Forms a dirty brown phenylhydrazone.	gives an orange P. nitrophenylhydrazone.

The/

The reaction product is not the 1-hydroxy-4-naphthaldehyde.

FRIEDLANDER (Ber., 1908·41·1037) has prepared the 1-hydroxy-2-naphthaldehyde by boiling the 1-hydroxy-2-indoxylnaphthalene with 10 per cent caustic soda.

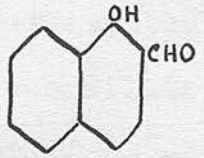


A comparison of the properties of the 1-hydroxy-2-naphthaldehyde as stated by FRIEDLANDER (loc.cit.) and the reaction product reads

REAGENT	1-HYDROXY-2-NAPHTHALDEHYDE	REACTION PRODUCT.
$FeCl_3$	Dark green coloration	The same
Steam	Volatile.	" "
$NaHSO_3$	Forms a bisulphite compound very slowly.	" "
Solubility	Only very slightly soluble in warm water; easily soluble in alcohol.	" "
NH_2OH.	Forms an oxime M.Pt. 145°.	M.Pt. 145°
M.Pt.	59°	58°-59°

The/

The comparison shows, therefore, that α-naphthol and diphenylformamidine condense and the aldehyde which may be isolated is 1-hydroxy-2-naphthaldehyde.

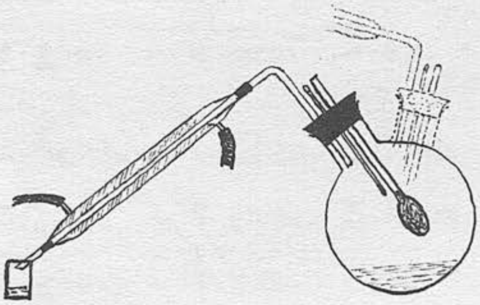


This result is of interest because of the absence of the 1:4 isomeride and the greater ease of preparation of this aldehyde by the new method as compared with that of FRIEDLANDER (loc. cit.) This condensation was investigated very fully because of the relative importance of such an easy method for obtaining the aldehyde.

In all the experiments, after the α-naphthol and diphenylformamidine had been heated together, the product was hydrolysed with the requisite quantity of 10 per cent caustic soda solution and the liberated aniline steam distilled off. A dark green resin generally made its appearance in the flask during the steam distillation. When all the aniline had passed over, the resin was filtered off and a saturated solution of sodium chloride added to the yellow green alkaline solution. A paste of the sodium salt of the aldehyde/

aldehyde separated in yellow green leafy crystals which was washed with a small quantity of saturated sodium chloride and then decomposed with hydrochloric acid. The 1-hydroxy-2-naphthaldehyde so obtained was recrystallised from dilute alcohol, when it possessed a melting point of 58°-59°.

The condensation is adversely affected by a high temperature but does not go at all at a lower temperature. A series of condensations were carried out at 80°; 85°; 90°; 95° and 110°. These temperatures were obtained by using benzene, toluene or a mixture of these two. By means of the following apparatus, any temperature between 80° and 110° could be obtained.



The/

The mixture of benzene and toluene was boiled until the thermometer registered the required temperature when the whole apparatus was tilted as shown by dotted lines. During the condensations, it was noticed that the temperature only rose 0.5° after a period of six hours.

RESULTS of CONDENSATION of DIPHENYLFORMAMIDINE and α-NAPHTHOL.

TEMP.	TIME.	α-NAPHTHOL	DIPHENYL-FORMAMI-DINE.	RESIN	ALDE-HYDE.
77°	4 hrs.	5 gms.	7 gms.	6gms. Form	Trace
85°	4 hrs.	5 gms.	7 gms.	1.8 gms.	1.2gms
90°	4 hrs.	5 gms.	7 gms.	1.9 gms.	1.3gms
95°	2 hrs.	5 gms.	7 gms.	1.6 gms.	0.8gms
95°	6 hrs.	5 gms.	7 gms.	2.9 gms	1.2gms
95°	6 hrs.	5 gms.	7 gms.	2.1 gms.	1.8gms
95°	6 hrs.	5.5gms.	7.75gms	1.9gms.	2.1gms
95°	6 hrs.	5 gms.	7 gms.	1.9 gms.	1.9gms
100°	2 hrs.	4 gms.	6 gms.	3.4g. Form + Resin	0.7gms
100°	4 hrs.	4.5gms.	6.5gms.	3.5gms.	1.3gms
100°	4 hrs.	5 gms.	7 gms.	3.9gms.	1.5gms.
100°	4 hrs.	5 gms.	7 gms.	3.5gms.	1.4gms.
110°	2 hrs.	5 gms.	7 gms.	2.8gms.	1.5gms.
110°	2 hrs.	5 gms.	7 gms.	3.1gms.	1.4gms.
130°	4 hrs.	4.5gms.	6.5gms.	5 gms.	Trace.

From/

From results, at 77° there is no resin formed in the condensation but the reaction does not go exceedingly well as can be seen from the amount of unchanged diphenylformamidine. At a temperature of 130° the reaction seems to go to completion from the amount of aniline liberated but the main product isolated was a dark green resin insoluble in caustic soda solution.

The best yield of the aldehyde, i.e., approximately 30-40 per cent of the theoretically expected quantity, is obtained when the condensation is carried out at a temperature of 90-95° for six hours.

15/.

15. CONDENSATION of DIPHENYLFORMAMIDINE WITH β- NAPHTHOL.

A preliminary investigation showed the following to be the best conditions for obtaining 2-hydroxy-1-naphthaldehyde by the condensation of diphenylformamidine and β-naphthol.

Molecular quantities of β-naphthol and diphenylformamidine were heated at a temperature of 130° for six hours. The requisite quantity of caustic soda solution was added to the condensation product and the alkaline solution steam distilled until all the aniline had passed over. The alkaline solution was cooled and the unchanged diphenylformamidine filtered off. The alkaline solution was then acidified when unchanged β-naphthol and aldehyde were precipitated. The aldehyde was obtained free from β-naphthol by a modification of the method employed in the separation of β-resorcylaldehyde. β-naphthol is appreciably soluble in dilute alcohol while the Schiff's base of the aldehyde is only slightly soluble in this solvent. The precipitate was, therefore, dissolved in alcohol and boiled with 5 c.c. of aniline for 15 minutes. The solution was cooled and/

and diluted when yellow needles were precipitated. These were recrystallised from dilute alcohol and found to possess a melting point of 99°. The Schiff's base, so obtained was hydrolysed with 20 c.c. of 10-15 per cent caustic soda and the liberated aniline steam distilled over. The alkaline solution was then acidified when a yellow brown precipitate was obtained which recrystallised from dilute alcohol in prisms, (M.P+.81°). This compound readily gave a p-nitrophenylhydrazone, phenylhydrazone and oxime. It was found to be the expected 2-hydroxy-1-naphthaldehyde. The following summary of results of condensations of diphenylformamidine with β -naphthol at a temperature of 130° for six hours, shows the readiness with which this aldehyde can be obtained.

β-NAPHTHOL.	DIPHENYL-FORMAMIDINE.	UNCHANGED DIPHENYL-FORMAMIDINE.	2-HYDROXY-1-NAPHTHALDEHYDE.
4 gms.	5.5 gms.	1.2 gms.	2.2 gms.
4 gms.	7 gms.	1.8 gms.	2.3 gms.
4 gms.	7 gms.	2.1 gms.	2.1 gms.
4 gms.	6 gms.	1 gm.	2.4 gms.
5 gms.	7 gms.	0.6 gms.	2.9 gms.

In/

In these condensations, no resin was formed. The yield of aldehyde was approximately 50 per cent of the theoretically expected quantity. From the condensation product, it was afterwards possible to isolate the intermediate compound which is described on pp.94.

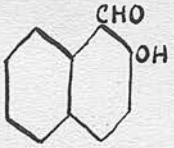
In order to make quite sure of the identity of the aldehyde, 2-hydroxy-1-naphthaldehyde was prepared according to directions given by GATTERMANN (Ber., 1899·32·284) and its properties compared with the reaction product.

PREPARATION of 2-HYDROXY-1-NAPHTHALDEHYDE.

β-Naphthol (7.5 gms.) was dissolved in 30 c.c of ether and 7.5 gms. $ZnCl_2$ and 5 CC. of liquid hydrocyanic acid added to the ethereal solution. Dry hydrogen chloride was passed into the solution for 2½ hours. The imine hydrochloride which had been precipitated from the ethereal solution, was washed with a small quantity of dry ether and decomposed with warm water. The aldehyde so obtained was filtered off and recrystallised from dilute alcohol. A comparison of the properties of the 2-hydroxy-1-naphthaldehyde so obtained and the aldehyde isolated from the condensation product of β-naphthol and diphenylformamidine reads.

REAGENT	2-HYDROXY-1-NAPHTHALDEHYDE	REACTION PRODUCT.
NaOH	Forms a Na.compound insol. in cold but more so on warming	The same
Schiff's reagent.	No reaction.	" "
$FeCl_3$	Alcohol soln. gives a brown coloration.	" "
$AgNO_3$	Reduced.	" "
Liebermann react.	Dirty green.	" "
$CHCl_3+NaOH$	No coloration	" "
NH_2OH	Forms an oxime M.P+.157°	M.P+.156°-157°.
$C_6H_5\cdot NH\cdot NH_2$	Forms a phenylhydrazone. M.P+. 205°	M.P$^+$.205°
$C_6H5\cdot NH_2$	Schiff's base M.P+. 99°	M.P+. 99°
$NaHSO_3$	Forms a bisulphite compound very slowly.	The same
M.P+.	81°	81°

Thus the compound is 2-hydroxy-1-naphthaldehyde.



16/

16. CONDENSATION of DIPHENYLFORMAMIDINE with β-RESORCYLALDEHYDE.

β-Resorcylaldehyde (2 gms), prepared by GATTERMANN'S method (Ber., 1899·32·278.) and diphenylformamidine (4 gms) were heated at a temperature of 110° for two hours. Aniline was liberated. The requisite quantity of caustic soda solution was added to the crude condensation product and the alkaline solution steam distilled. When all the aniline had passed over, the alkaline solution was acidified. The acid solution was now steam distilled and an aldehyde which proved to be 4:6-dihydroxyisophthalaldehyde collected in the condenser. The yield was 30-40 per cent of the expected quantity.

17. CONDENSATION of DIPHENYLFORMAMIDINE with β-RESORCYLIC ACID.

β-Resorcylic acid was prepared according to the directions given by KOSTANECKI (Ber., 1885·18· 1985). A solution of 20 gms of resorcinol and 100 gms of potassium bicarbonate in 200c.c. of water was warmed in the steam bath for 1½ hours. When the solution was cooled and then acidified, β-resorcylic acid was precipitated which after recrystallisation from water decomposed at 216°-217° with evolution of carbon dioxide.

A preliminary investigation showed that when diphenylformamidine and β-resorcylic acid in molecular quantities are heated together at a temperature of 183° carbon dioxide is evolved very vigourously. The crude condensation product when worked up in a similar manner to that employed in the separation of β-resorcylaldehyde, yielded 40 per cent and 10 per cent of 4:6-dihydroxyisophthalaldehyde and β-resorcylaldehyde respectively.

Under these conditions, therefore,

β-resorcylic/

β-resorcylic acid when heated with diphenylformamidine yields β-resorcylaldehyde and 4:6-dihydroxyisophthalaldehyde. A test tube experiment showed that when β-resorcylic acid is warmed with aniline, carbon dioxide is evolved.

The condensation was repeated

(1) at a temperature of 150° and

(2) with boiling butyl alcohol (B.P+.116°.) as solvent but again carbon dioxide was evolved and the only aldehydes isolated were β-resorcylaldehyde and 4:6 dihydroxyisophthalaldehyde.

Therefore, under these conditions, it is impossible to obtain an acid aldehyde by the condensation of diphenylformamidine with β-resorcylic acid.

18. CONDENSATION of DIPHENYLFORMAMIDINE and ETHYL-β-RESORCYLATE.

Ethyl-β-resorcylate was prepared according to directions given by KAUFMANN and ADAMS (J.Amer. Chem.Soc. 1923·45·1744.). It was obtained from β-resorcylic acid by boiling it under an inverted condenser for ten hours with absolute alcohol, saturated with dry hydrochloric acid. The alcohol was then distilled off, the residue washed with dilute sodium bicarbonate solution and the red oil so obtained distilled under diminished pressure. (B.P+.(13-15m.m.) 170°-175°). The distillate solidified and was purified further by crystallisation from water and possessed a melting point of 69°-70°.

Molecular quantities of diphenylformamidine & ethyl-β-resorcylate were heated at a temperature of 138° for six hours. No carbon dioxide was evolved. The crude condensation product had a pronounced odour of aniline. When the condensation product was hydrolysed with 50 per cent caustic potash solution and steam distilled aniline/

aniline passed over. A small quantity of unchanged diphenylformamidine was filtered off and the alkaline solution acidified. During the addition of the acid to the alkaline solution marked frothing (due to the evolution of carbon dioxide) took place. β-Resorcylaldehyde was obtained from the acid solution in approximately 20-25 per cent yield of the theoretically expected quantity by the same method as that employed in the isolation of β-resorcylaldehyde formed by the condensation of diphenylformamidine and resorcinol.

By further investigation, it is hoped to obtain an interesting acid aldehyde by the condensation of diphenylformamidine with ethyl-β-resorcylate.

ISOLATION of INTERMEDIATE COMPOUNDS.

THE DI-SCHIFF'S BASE OF 4:6-DIHYDROXY-ISOPHTHALALDEHYDE.

As previously stated, during the condensation of dry or moist resorcinol with diphenylformamidine at a temperature of 100°, a solid product is formed after five hours heating. An examination of the solid product formed in the condensations with moist resorcinol showed the presence of yellow needle shaped crystals and these have been isolated by the following method.

The crude condensation product was washed three times with a small quantity of aniline in order to dissolve out any unchanged diphenylformamidine. The resulting product was found to consist of yellow needle shaped crystals which were recrystallised twice from absolute alcohol. They melted at 202°-203°. These crystals were practically insoluble in water and caustic soda solution but easily soluble in alcohol and ether. On hydrolysis, aniline was liberated and the resulting product gave all the reactions of 4:6-dihydroxyisophthalaldehyde (see pp. 32.).

TIEMANN/

TIEMANN and LEWY (Ber., 1877·10·2212) prepared the di-Schiff's base of 4:6-dihydroxyisophthalaldehyde from a boiling saturated alcoholic solution of the aldehyde and aniline. The melting point of the Schiff's base is given as 199°.

An analysis of the intermediate product proved definitely that it was the suspected di-Schiff's base.

0.1853 gms. gave 0.5156 gms. CO_2 & 0.0853 gms. H_2O.

This represents, C = 75.92, and

H = 5.16 per cent.

0.2229 gms. contained 0.002002 gms. N (by Kjeldahl).

This represents, N = 8.98 per cent.

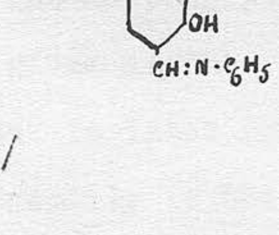
$C_{20}H_{16}N_2O_2$ requires.

C = 75.95,

H = 5.07, and

N = 8.88 per cent.

Therefore one of the intermediate compounds formed on condensing moist resorcinol with diphenylformamidine is the di-Schiff's base of 4:6-dihydroxyisophthalaldehyde.



Many/

Many attempts were made to isolate the intermediate compound formed in condensations carried out with dry resorcinol with the object of separation of the corresponding mono-Schiff's base. It was found impossible to obtain a pure product in this manner because of the similar solubilities of the impurities such as, unchanged diphehylformamidine, tarry material and the Schiff's base in all solvents.

THE SCHIFF'S BASE of 2-HYDROXY-1-NAPHTHALDEHYDE.

The intermediate compound formed by the condensation of diphenylformamidine and β-naphthol was separated as follows.

The crude condensation product was boiled with alcohol and a small quantity of aniline to keep the unchanged diphenylformamidine in solution. From the cold solution yellow needles separated which were recrystallised again from alcohol. They possessed a melting point of 99°. GATTERMANN (Ber., 1899·32·284) prepared the Schiff's base of 2-hydroxy-1-naphthaldehyde by boiling an alcoholic solution of the aldehyde with aniline. The melting point of the Schiff's base so obtained is given as 99°. The yellow needles of melting point 99° isolated from the condensation product dissolved readily in boiling caustic soda solution/

solution and the aniline liberated was steam distilled off. The alkaline solution was acidified when the 2-hydroxy-1-naphthaldehyde was obtained pure.

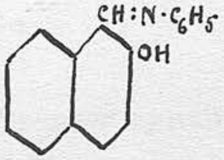
An analysis of the intermediate product proved definitely that it was the suspected Schiff's base of 2-hydroxy-1-naphthaldehyde.

0.1326 gms. gave 6.35c.c. N. at 10.5° & 752 m.m.

This represents N = 5.72 per cent.

$C_{17}H_{13}NO$ requires N = 5.66 per cent.

Therefore, the intermediate compound formed by the condensation of diphenylformamidine and β-naphthol is the Schiff's base of 2-hydroxy-1-naphthaldehyde.



SUMMARY/

SUMMARY.

(I) It has been proved by the isolation of the intermediate compounds from the condensation product of diphenylformamidine with moist resorcinol and β-naphthol respectively, that certain phenols when heated with diphenylformamidine, react according to the following equation.

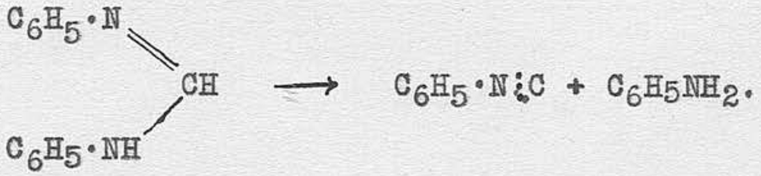
phenol + diphenylformamidine
↓
Schiff's base + aniline
↓ hydrolysis
aldehyde + aniline.

(II) By this new synthesis, the following aldehydes have been isolated in a pure condition.

(1) β-resorcylaldehyde
(2) 4:6-dihydroxyisophthalaldehyde.
(3) 4-methoxy-2-hydroxybenzaldehyde.
(4) 3-methoxy-2-hydroxybenzaldehyde.
(5) pyrogallol aldehyde.
(6) salicylaldehyde.
(7) 3-methyl-2 hydroxybenzaldehyde.
(8) 4-methyl-2-hydroxybenzaldehyde.
(9) 5-methyl-2 hydroxybenzaldehyde.
(10) 1-hydroxy-2-naphthaldehyde.
(11) 2-hydroxy-1-naphthaldehyde.

Only traces of an aldehyde could be isolated from the condensation product of catechol, quinol, phloroglucinol,/

phloroglucinol, o-nitrophenol, p-nitrophenol respectively with diphenylformamidine, but the crude condensation product from these phenols, except o-nitrophenol, had a pronounced odour of carbylamine due to the decomposition of diphenylformamidine into aniline and carbylamine.



$$\begin{matrix} C_6H_5\cdot N \\ C_6H_5\cdot NH \end{matrix} > CH \longrightarrow C_6H_5\cdot N{:}C + C_6H_5NH_2.$$

No trace of an aldehyde could be isolated from the condensation product of dimethyl resorcinol and diphenylformamidine.

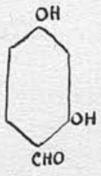
(III) The formation of 3:6-dihydroxyxanthydrol in the condensation of resorcinol with diphenylformamidine has been investigated and an account of this is given in Part II. of the thesis.

(IV) The suggestion is put forward that this reaction takes place between diphenylformamidine and the ketonic form of the phenols.

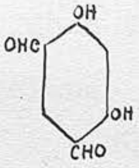
PART II.

SYNTHESIS of 3:6-dihydroxyxanthydrol.

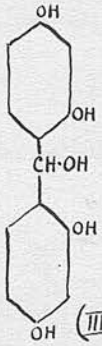
As already stated, the condensation of resorcinol with diphenylformamidine might be expected to go in such a manner that the following three substances could be obtained.



(I.)

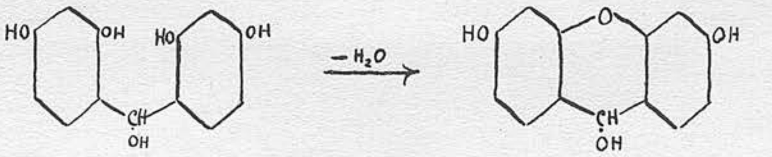


(II.)



(III.)

Actually, β-resorcylaldehyde (1) and the 4:6-dihydroxyisophthalaldehyde (ii) may be isolated along with a brown red resinous substance which contained the expected 2:4:2':4'-tetrahydroxy-diphenylcarbinol. This is borne out by the fact that the addition of alkali to the acid solutions from which the condensation products had been separated, produced a marked green fluorescence. This would be due to a further change of the carbinol to the corresponding 3:6-dihydroxyxanthydrol (iv), during the process of separation of β-resorcylaldehyde.

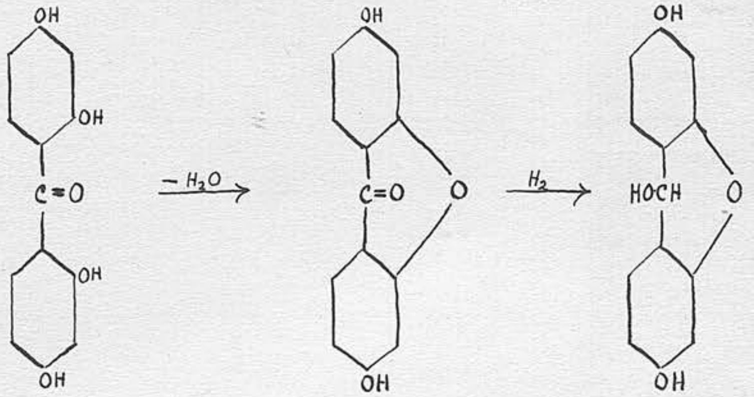


(IV.)

In order to discover whether this actually occurs, it was proposed to compare the known 3:6-dihydroxyxanthydrol with the third reaction product.

The/

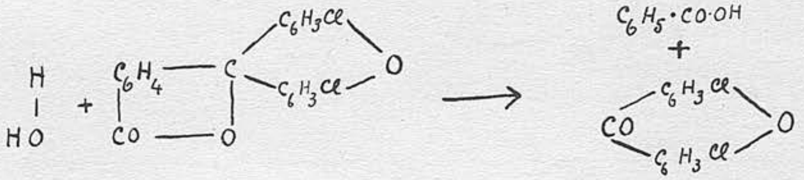
The xanthydrol has already been obtained from the corresponding 2:4:2':4'- tetra~~hydr~~hydroxy-benzophenone (v.) which is first dehydrated to the 3:6-dihydroxyxanthone (vi.) (Meyer & Conzetti. Ber., 1897.30. 971.) and is then reduced to the 3:6-dihydroxyxanthydrol. (Kehrmann. Annalen., 1909.371.287.)



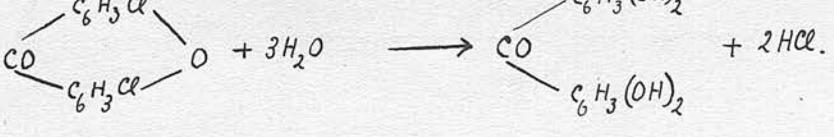
(v) (vi)

2:4:2':4'-Tetrahydroxybenzophenone has been prepared by Meyer & Conzetti (Ber., 1897.30.971) who fused fluorescein chloride with caustic soda at a temperature of 270°-280°.

(a)



(b)



The yield of the tetrahydroxybenzophenone obtained by Meyer/

PREPARATION OF 2 : 4 : 2′ : 4′-TETRAHYDROXYBENZOPHENONE.

BY

JOHN BALDWIN SHOESMITH

AND

JOHN HALDANE.

From the Transactions of the Chemical Society, 1924. Vol. 125.

XV.—*Preparation of 2 : 4 : 2′ : 4′-Tetrahydroxybenzophenone.*

By JOHN BALDWIN SHOESMITH and JOHN HALDANE.

2 : 4 : 2′ : 4′-TETRAHYDROXYBENZOPHENONE was first prepared by Meyer and Conzetti (*Ber.*, 1897, **30**, 971), who fused fluorescein chloride with caustic soda at 270—280°. The present investigation has shown that the method used first by Hoesch (*Ber.*, 1915, **48**, 1122) to prepare aromatic hydroxyketones is also applicable to the synthesis of this ketone.

2 : 4-Diacetoxybenzonitrile, $C_6H_3(OAc)_2{\cdot}CN$, and resorcinol condense in presence of hydrochloric acid. 2 : 4-Diacetoxy-2′ : 4′-dihydroxybenzophenoneimine hydrochloride,

$$(OAc)_2C_6H_3{\cdot}C(\text{:}NH,HCl){\cdot}C_6H_3(OH)_2,$$

thus formed, is moderately easily hydrolysed in acid solution to the expected benzophenone. From the reaction product, resacetophenone, $C_6H_3(OH)_2{\cdot}CO{\cdot}CH_3$, and β-resorcylamide may also be isolated. The former is produced by the condensation of acetyl chloride (from diacetoxybenzonitrile and hydrochloric acid) with resorcinol, and the latter by the hydrolysis of unchanged diacetoxybenzonitrile.

The compound described by Marcus (*Ber.*, 1891, **24**, 3652) as β-resorcylonitrile will not condense with resorcinol.

EXPERIMENTAL.

2 : 4-Diacetoxybenzonitrile (7 grams), prepared as described by Marcus (*loc. cit.*), and carefully dried resorcinol (2·5 grams) were

dissolved in 40 c.c. of dry ether, powdered anhydrous zinc chloride (1 gram) was added, and a slow stream of hydrogen chloride gas passed into the reaction mixture. Turbidity was apparent after four hours, and a crystalline precipitate formed almost immediately afterwards. The hydrogen chloride gas was passed for eight hours and after that the mixture allowed to stand for another twelve hours. The ether was then poured off from the crystals and from it, after standing some days, an additional quantity of the crystals separated out. The crystals were dissolved in cold water and precipitated with concentrated hydrochloric acid. The solid was purified by the repetition of this process at least twice, and after having been dried decomposed at 195° and proved to be 2 : 4-*diacetoxy-2′ : 4′-dihydroxybenzophenoneimine hydrochloride* (Found : Cl = 9·7. $C_{17}H_{16}O_6NCl$ requires Cl = 9·5 per cent.). The hydrochloride was hydrolysed by boiling 25 per cent. aqueous sulphuric acid, the operation being complete in about fifteen minutes. The cooled solution deposited a syrup which was then boiled with dilute sodium carbonate solution for half an hour. From this solution yellow crystals separated (2 grams) which were recrystallised from boiling water and animal charcoal and possessed all the properties of the 2 : 4 : 2′ : 4′-tetrahydroxybenzophenone obtained by the method of Meyer and Conzetti (*loc. cit.*).

β-*Resorcylamide*.—The acid solution from the hydrolysis of the imine hydrochloride was extracted with ether several times and the combined extracts were mixed with the ether from which the imine hydrochloride had separated. When the ether was distilled away from the extract, a syrup remained from which white, needle-shaped crystals were at once precipitated on the addition of water. This solid was recrystallised from water, when it melted at 221—222°. Its aqueous solution gave a reddish-brown coloration with ferric chloride. Ammonia was evolved (*a*) slowly from a boiling caustic soda solution of the solid, (*b*) more rapidly if the solid was first hydrolysed with 50 per cent. sulphuric acid and then boiled with caustic soda, (*c*) immediately when the solid was heated alone. The compound was classified as β-resorcylamide (Found : C = 55·14 ; H = 5·02 ; N = 9·03. Calc. for $C_7H_8O_3N$, C = 54·90 ; H = 4·58 ; N = 9·15 per cent.). After the hydrolysis of the amide a small quantity of β-resorcylic acid was isolated from the solution.

Resacetophenone.—The aqueous solution from which the β-resorcylamide had been precipitated was extracted with ether and the syrup remaining after the ether had been distilled off boiled with dilute hydrochloric acid and animal charcoal. From this solution, white needles crystallised out which when purified melted at 141—142° and easily gave a phenylhydrazone with melting point 158°.

This ketone did not depress the melting point of an authentic specimen of resacetophenone.

Attempts were made to prepare β-resorcylonitrile. 2 : 4-Diacetoxybenzonitrile was boiled with caustic alkali (or dilute sulphuric acid) of different concentrations for varying periods of time. The hydrolysed mixtures were extracted with ether and the solid fractionally precipitated by the addition of ligroin. Analysis showed that the nitrogen content varied with the conditions of hydrolysis and pure β-resorcylonitrile could not be isolated. The white needles obtained would not condense with resorcinol under the same conditions as those used in the condensation of 2 : 4-diacetoxybenzonitrile.

The authors wish to thank the Advisory Council of the Department for Scientific and Industrial Research for a grant to one of them (J. H.) which enabled this investigation to be carried out.

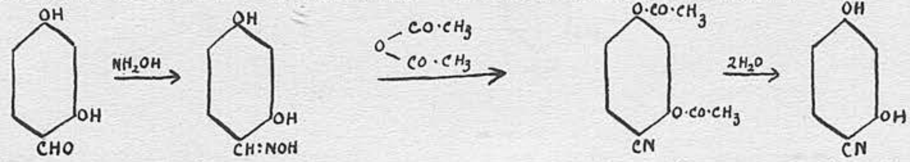
DEPARTMENT OF CHEMISTRY,
EDINBURGH UNIVERSITY.

[*Received, November 23rd*, 1923.]

PRINTED IN GREAT BRITAIN BY RICHARD CLAY & SONS, LIMITED,
BUNGAY, SUFFOLK.

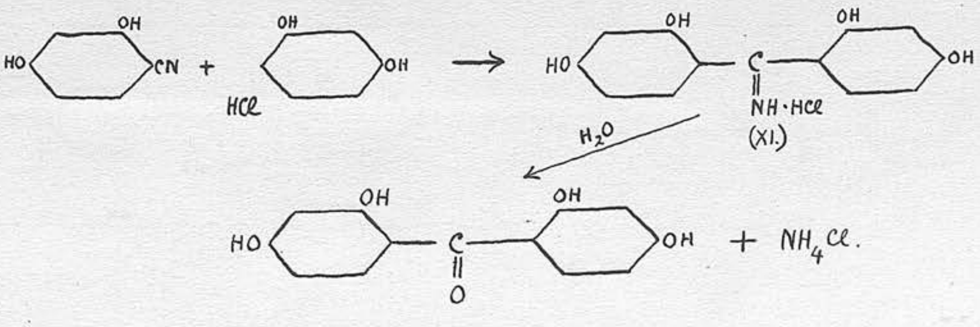
Meyer & Conzetti's method, however, is exceedingly poor and it was proposed to synthesise the tetrahydroxybenzophenone by the following series of reactions.

β-Resorcylaldehyde (vii) is first converted into the oxime (viii.) which with boiling acetic anhydride gives the 2:4-diacetoxy-benzonitrile. (ix.) This compound on hydrolysis should give β-resorcylonitrile (x.) (Marcus) Ber.1891.24.3651.)



(vii.) (viii.) (ix.) (x.)

By the condensation of β-resorcylonitrile (x.) with resorcinol in accordance with the general method devised by Hoesch (Ber., 1915.48.1122), 2:4:2':4'-tetrahydroxybenzophenoneimine hydrochloride (xi.) was expected to be formed which on hydrolysis would readily yield the expected 2:4:2':4'-tetrahydroxybenzophenone.



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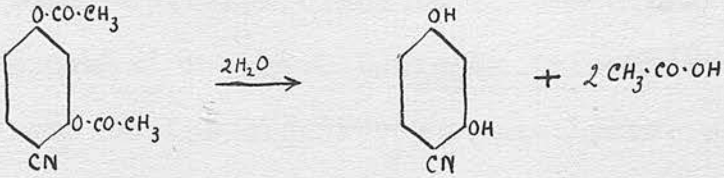
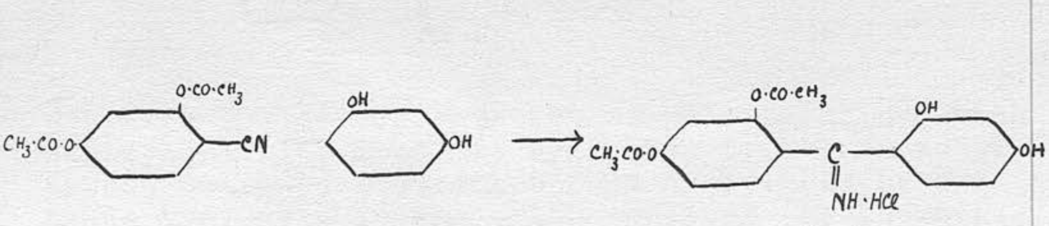
This, when dehydrated, would yield the 3:6- dihydroxyxanthone and the latter on reduction the 3:6-dihydroxyxanthydrol as shown on page 2A .

In the proposed synthesis, no difficulty was met with until attempts were made to hydrolyse the 2:4-diacetoxybenzonitrile to β-resorcylonitrile



It was then discovered that the pure β-resorcylonitrile cannot be obtained by this method and the mixture which might contain a little of the nitrile will not condense in the usual manner.

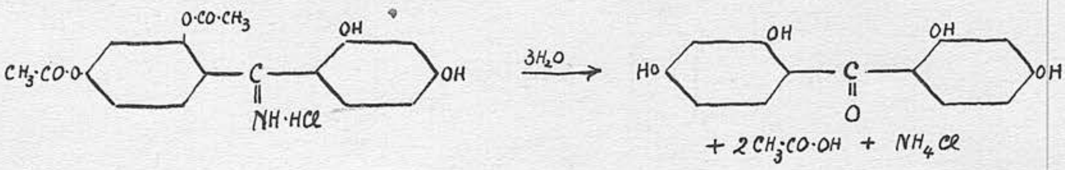
Condensation, however, takes place when the 2:4-diacetoxybenzonitrile is used and the intermediate compound 2:4-diacetoxy-2':4'-dihydroxybenzophenoneimine hydrochloride (xii.) may be isolated in a pure condition.



(XII)

This/

This is hydrolysed* to the expected 2:4:2':4'-tetrahydroxybenzophenone



The 3:6-dihydroxyxanthydrol obtained from the 2:4:2':4'-tetrahydroxybenzophenone which is first dehydrated to the 3:6-dihydroxyxanthone and then reduced to the 3:6-dihydroxyxanthydrol showed the same fluorescence as that of the solutions from which aldehyde was extracted in the condensation of diphenylformamidine and resorcinol.

From the condensation product of 2:4-diacetoxybenzonitrile and resorcinol resacetophenone and β-resorcylamide may be isolated. The former must/

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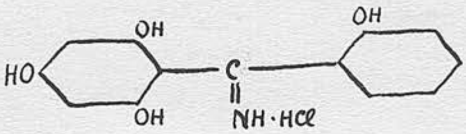
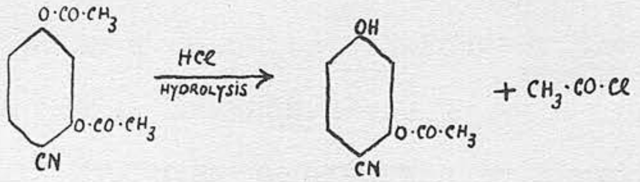
* This fact is interesting since the compound 2:4:6:2'-tetrahydroxybenzophenoneimine hydrochloride

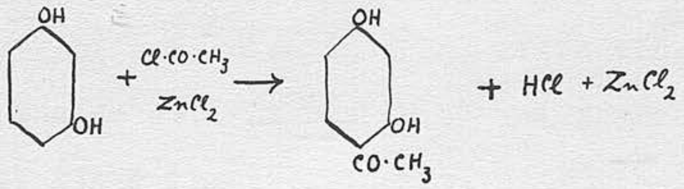


prepared by the condensation of phloroglucinol with salicylonitrile does not hydrolyse to the expected ketone owing to protection from hydrolysis by the three hydroxyls in the ortho position (Robinson.I., 1922.120.839.)

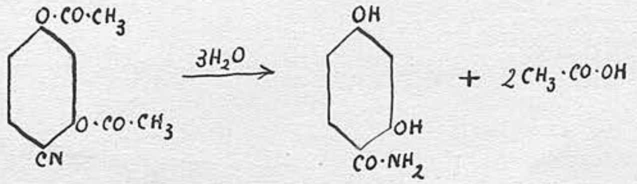
must result from the production of a small quantity of acetyl chloride during the synthesis as follows.



This is present under ideal conditions under which the usual Freidal Craft's reaction takes place. Hence resacetophenone is formed.



β-Resorcylamide must result from the hydrolysis of unchanged 2:4-diacetoxybenzonitrile.

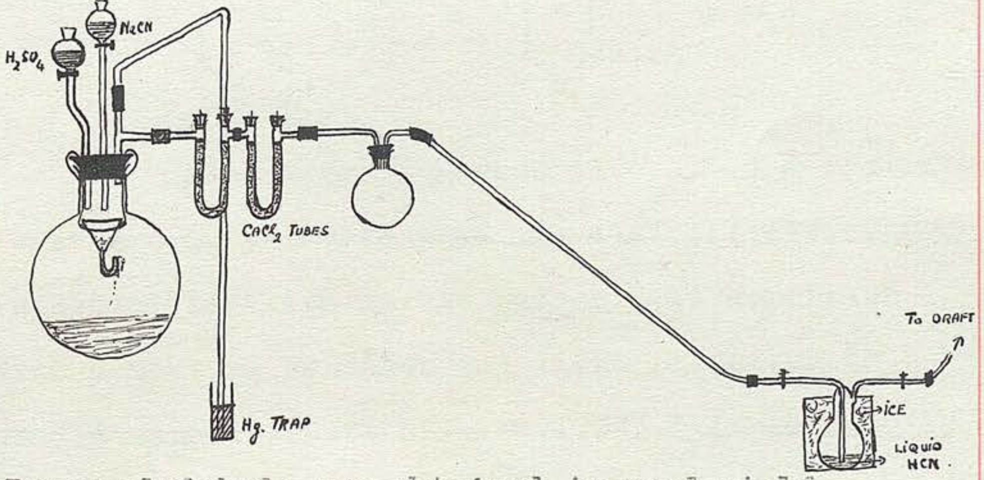


The hydrolysis takes place during the working up of the condensation product.

EXPERIMENTAL.

β-RESORCYL Aldehyde obtained in previous condensations was supplemented by a quantity obtained by the Gattermann method (Ber., 1899.32.278.)

Liquid hydrogen cyanide was prepared by the method devised by Ziegler (Ber., 1921.54.110.) A saturated solution of sodium cyanide and a 60 per cent solution of sulphuric acid were allowed to drop into a small funnel suspended in a one litre flask. The hydrogen cyanide evolved was dried and passed into a 100 c.c. flask immersed in ice.

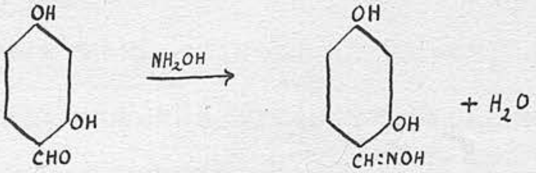


β-Resorcyladehyde was obtained in good yield.

PREPARATION of the OXIME of β-RESORCYLALDEHYDE.

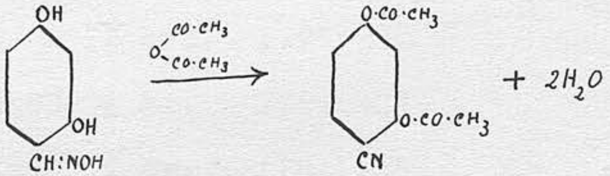
Marcus. (Ber., 1891.24.3651.) β-resorcylaldehyde was dissolved in warm water and the requisite amount of hydroxylamine hydrochloride added. After/

After the addition of a saturated solution of sodium acetate the oxime was obtained from the cold solution in approx. a theoretical yield. (M.Pt.191°)



PREPARATION of the 2:4-diacetoxybenzonitrile.

Marcus, (loc.cit.) The oxime was boiled with the requisite volume of acetic anhydride for two hours. The diacetate crystallised from the cold solution and was purified by crystallisation from alcohol. (M.Pt.72°). The yield was 70-80 per cent of the theoretical quantity.



According to Marcus (loc.cit.) β-resorcylonitrile is produced when the diacetyl derivative is hydrolysed with dilute potash. It separates from a mixture of ether and light petroleum in needle shaped crystals (M.Pt.175°). It is readily soluble in water, alcohol and ether and its aqueous solution gives a red coloration with Fecl$_3$.

A series of hydrolyses on the 2:4-diacetoxybenzonitrile were carried out but the final product in every case gave off ammonia on heating alone, (a property ascribed to the presence of

β-/

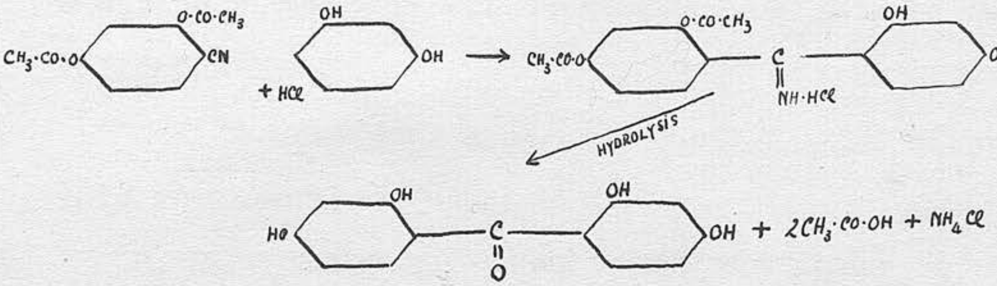
β-resorcylamide. See pp.20A), a purple red coloration with Fecl$_3$, and melting points which ranged between 175° and 185°. The white needle shaped crystalline substances were very soluble in water, alcohol and ether. Analysis of the products obtained from the hydrolyses of 2:4-diacetoxybenzonitrile showed that the expected nitrile could not be obtained pure.

$C_7H_5O_2N$ requires N=10.38 per cent.

HYDROLYSIS AGENT	TIME	M.P+.	PER CENT NITROGEN.
8 per cent NaOH	2 hrs.	177-178.5°	7.1
2 " KOH	1 hr.	180-182°	7.63
* N/10 NaOH	2 hrs.	177°	7.66
N/10 NaOH	½ hr.	178-180°	7.36
N/10 NaOH	½ hr.	176-178°	7.14
N/10 NaOH	½ hr.	176-178°	7.36
N/10 NaOH	½ hr.	176-178°	7.22
5 per cent KOH	Till oil disappears approx. 4 mins.	180-182°	9.2

* The hydrolysis product in this case after having been precipitated from its ether solution by light petroleum was recrystallised from m-xylene. The mixture softened at 170° became yellow in colour and melted at 177°. The hydrolyses products would not condense with resorcinol under the necessary conditions. (See below).

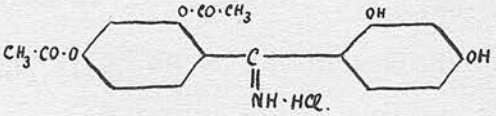
As β-resorcylonitrile could not be obtained, 2:4-diacetoxybenzonitrile was condensed with resorcinol according to the method devised by Hoesch, (Ber., 1915.48.1122.)



HOESCH SYNTHESIS. 2:4-Diacetoxybenzonitrile (7 gms) and anhydrous resorcinol (3.5 gms.) were dissolved in dry ether (40 c.c.), mixed with fused and powdered $ZnCl_2$ (1 gm) and a moderate stream of dry hydrogen chloride was passed through the liquid. Turbidity of the solution occurred after four hours and a crystalline precipitate soon appeared. After eight hours, the current of gas was stopped and the mixture allowed to stand overnight.

The ether solution was decanted off and the yellow crystals extracted with cold water. Concentrated hydrochloric acid was added to this solution when pale yellow crystals were precipitated. This operation was repeated three times and the resulting product which decomposed at approx. 195° carefully dried over sulphuric acid in a vacuum. As this substance was suspected to be the ketimine hydrochloride/

hydrochloride having the following constitution

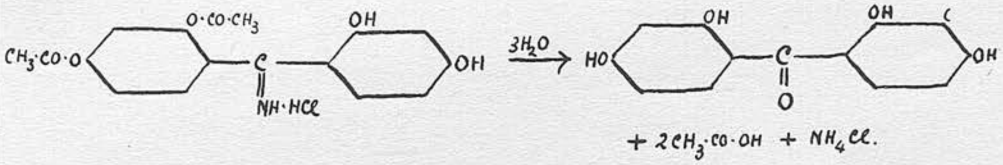


a Carius estimation, was carried out which gave the following result.

0.0696 gms. contained 0.00661 gms. chlorine This represents Cl = 9.5 per cent.

$C_{17}H_{16}O_6NCl$ requires cl = 9.7 per cent.

Further evidence that the above is the constitutional formula of this substance is borne out by the fact that on hydrolysis, as stated later, it yielded the 2:4:2':4'-tetrahydroxybenzophenone.



The hydrochloride thrown out of the ether solution was boiled with 25 c.c. of 25 per cent sulphuric acid for 15 mins. When the solution was cooled, a yellow syrup separated out. The acid solution was decanted from the syrup and put to one side for a later examination.

<u>TREATMENT of the YELLOW SYRUP</u>: It was washed twice with water and boiled for half an hour with very dilute sodium carbonate solution. Yellow crystals separated from the cold solution and were purified by boiling/

boiling with water and animal charcoal. The compound crystallised from water in long yellow needles (M.P+. 192°-194°), gave a brown coloration with $FeCl_3$, and a p-nitrophenylhydrazone on boiling an aqueous solution for some time. This indicated the presence of a ketonic group in this substance.

CONSTITUTION of the YELLOW NEEDLES (M.P+ 192°-194°) was now investigated.

As this compound was suspected to be the 2:4:2':4'-tetrahydroxybenzophenone, its properties were compared with those of the 2:4:2':4'-tetrahydroxybenzophenone as prepared and described by Meyer & Conzetti (Ber., 1897; 30. 971)

The comparison reads:-

REAGENT	DESCRIBED 2:4:2':4'-TETRAHYDROXYBENZOPHENONE.	REACTION PRODUCT.
NaOH	Dissolves with yellow colour	The same
HCl	Precipitates from alkaline solution	"
Conc. H_2SO_4.	Dissolves with a yellow colour. On warming solution goes colourless & finally darkens, very quickly. On cooling & making the solution alkaline, a deep blue violet fluorescence is produced due to the presence of 3:6-dihydroxyxanthone.	"
$FeCl_3$	Deep brown coloration	"
Solubility	H_2O: sol. in hot, insol. in cold. Sol. in E+OH & ether.	"
M.P+.	193°-195°	192°-194°
Mixed M.P+	192°-194°	

The slow formation of the p-nitrophenylhydrazone of the described 2:4:2':4'-tetrahydroxybenzophenone and the reaction product is due to the close proximity of the two hydroxyl groups i.e. an example of steric hindrance.

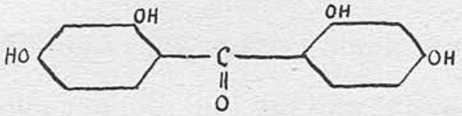
An analysis of the reaction product proved definitely that it was the suspected 2:4:2':4'-tetrahydroxybenzophenone.

0.0408 gms gave 0.0155 gms H_2O & 0.0940 gms. CO_2.

This/

This represents C=63.45 & H=4.22 per cent. $C_{13}H_{10}O_5$ requires C=63.45 & H=4.07 per cent. The compound did not contain nitrogen.

Thus the compound is 2:4:2':4'-tetrahydroxybenzophenone.



The 2:4:2':4'-tetrahydroxybenzophenone was heated at 210° i.e. in the vapour of boiling O-toluidine, for two hours. The reaction product when recrystallised from dilute alcohol melted at 243° and possessed all the properties of the 3:6-dihydroxyxanthone prepared by KOSTANECKI (Ber., 1885.18.1896) & MEYER & CONZETTI (Ber., 1897.30.971). It dissolved in a caustic soda solution with the production of a deep blue fluorescence.

The 3:6-dihydroxyxanthone thus obtained was reduced to the corresponding xanthydrol according to directions given by KEHRMANN (Annalen., 1909,371.287).

The xanthone was shaken with 3 per cent sodium amalgam in aqueous emulsion until there was a strong evolution of hydrogen. During this process the solution turned red and showed an intense green fluorescence. The solution was decanted from the sodium amalgam, acidified with dilute acetic acid whereby the/

the 3:6-dihydroxyxanthydrol was obtained as a red powdery mass which did not melt below 300°. The red powdery mass possessed all the properties of the xanthydrol as prepared by KEHRMANN. (Annalen 1909.371. 287.)

The 3:6-dihydroxyxanthydrol in alkaline solution showed the same fluorescence in great dilution as noticed in solutions from which aldehyde was extracted in the condensation of diphenylformamidine and resorcinol. A very small quantity of the xanthydrol is necessary to show such fluorescence. It is, therefore, formed in the condensation but cannot be isolated because of the resinous substances.

ISOLATION of RESACETOPHENONE.

The acid solution which was decanted from the syrup when the condensation product of resorcinol and 2:4-diacetoxybenzonitrile had been boiled for 15 minutes was in turn extracted with ether. When the ether was distilled away a syrup was left from which on the addition of a small quantity of water, a white solid was precipitated. This was separated for further investigation.

The/

The solution obtained by the addition of water to the syrup and after the white solid had been filtered off, gave a p-nitrophenylhydrazone very readily and a phenylhydrazone which crystallised from very dilute alcohol in yellow needles (M.Pt.158°.) From the fact that a p-nitrophenylhydrazone and a phe phenylhydrazone were formed so easily, it was concluded that the ketonic group in this substance could not be protected to such an extent as that in the 2:4:2':4'-tetrahydroxybenzophenone.

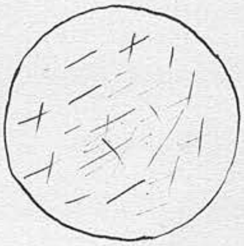
The solution which contained the ketonic substance was, therefore, extracted with ether. The syrup left after the ether had been distilled away was boiled with a small quantity of dilute hydrochloric acid and animal charcoal. White needle-shaped crystals were so obtained which were recrystallised from dilute hydrochloric acid when they possessed a melting point of 141°-142°. This substance readily gave a p-nitrophenylhydrazone and a phenylhydrazone (M.Pt.158°). The compound also possessed the following properties:-

(1) With $FeCl_3$, a deep brown coloration was obtained.

(2) A nitrogen test was carried out with a negative result.

(3) It readily gave a p.nitrophenylhydrazone.

(4) It readily gave a phenylhydrazone which under the microscope had the appearance



When recrystallised from very dilute alcohol it possessed a melting point of 158°. An analysis of the phenylhydrazone gave the following result:-

0.0529 gms gave 5.4c.c. of nitrogen at 15° and 729 m.m. This represents N = 11.6 per cent.
From the fact that the analysis gave such a high nitrogen content, it was concluded that the ketonic substance contained one benzone ring.

The phenylhydrazone of resacetophenone has been described by CRÉPIEUX (Bull.Soc.Chim.1891.(3).6. 154) as pale yellow needles (M.P+158°), exceedingly soluble in ether and alcohol and coloured brown with a solution of $FeCl_3$. When recrystallised from alcohol he says a large volume of water must be added to the cold solution. A whitish emulsion is first formed and from it the phenylhydrazone crystallises out in pale yellow needles. The phenylhydrazone from the reaction product possessed all these properties. As stated previously, an analysis showed the nitrogen content of the phenylhydrazone from the reaction product to be 11.6 per cent.

C/

$C_{14}H_{14}O_2N_2$ requires N = 11.57 per cent.

To complete the evidence regarding the constitution of the white needles (M.P+141°-142°) which formed a phenylhydrazone (M.P+.158°), resacetophenone and its phenylhydrazone were prepared and compared with the reaction product.

PREPARATION of RESACETOPHENONE for COMPARISON.

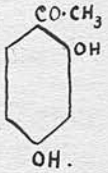
This was prepared according to directions given by NENCKI & SIEBER (J.pr.Chem.1881.23.147). Glacial acetic acid (1.5 parts) containing resorcinol (1 part) and 1.5 parts of $ZnCl_2$ as a dehydrating agent was boiled for a short time. The resacetophenone was precipitated when the mixture was poured into water and purified by repeated crystallisation from dilute hydrochloric acid and animal charcoal.

A comparison in properties of the reaction product and resacetophenone reads:-

REAGENT/

REAGENT	DESCRIBED. RESACETOPHENONE.	REACTION PRODUCT.
NaOH	Soluble with a deep violet coloration. On long heating, solution turns a dirty brown although acid precipitates the ketone unchanged.	The same.
$FeCl_3$	Brown coloration	"
$C_6H_5.NH.NH_2$	Forms a phenylhydrazone M.P+158°	M.P+.158°
	MIXED M.P+158°. N=11.57per cent	N=11.6%
M.P+	142°	141°-142°
MIXED M.P+	141°142°	

The compound is, therefore, resacetophenone.



ISOLATION of β-RESORCYLAMIDE.

The white solid which was precipitated from the crude resacetophenone by the addition of a small quantity of water, was recrystallised from water. The white needles thus obtained possessed the following properties.

(1) Recrystallised from water it melted at 221°-222°.

(2) An aqueous solution gave a brown red coloration with $FeCl_3$.

(3) A sodium test indicated the presence of nitrogen.

(4) Ammonia was evolved from an aqueous alkaline solution after long heating.

(5) When boiled with 50 per cent sulphuric acid for five minutes, making alkaline and warming, ammonia was evolved more rapidly.

(6) When heated alone, ammonia was evolved immediately.

An analysis of the white needles (M.P+221°-222°) gave the following results.

0.0690 gms. gave 0.1395 gms. CO_2 & 0.0310 gms. H_2O.

This represents C = 55.14 & H = 5.02 per cent. A micro-nitrogen* estimation gave the following result.

0.01485 gms gave 1.16 c.c. at 22° and 757 m.m.

This/

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*As this compound gave off ammonia so readily when heated a micro nitrogen was carried out with a view to ensure complete combustion.

This represents N = 9.00 per cent.

A Dumas nitrogen estimation gave the following result:-

0.0580 gms gave 4.5c.c. at 19° & 755 m.m.

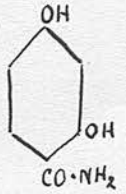
This represents N = 9.03 per cent.

Therefore the empirical formula is - $C_7H_8O_3N$. which agrees approximately with that of β-resorcylamide.

$C_7H_7O_3N$ requires C = 54.9, H = 4.58 & N = 9.15%.

If this substance is β-resorcylamide, the compound left after hydrolysis should give the specific tests for β-resorcylic acid i.e. a deep red coloration with $FeCl_3$, a purple coloration with a little bleaching solution, orange with excess. To test, therefore, this theory a small quantity of the suspected amide was boiled with 50 per cent sulphuric acid for five minutes, cooled and excess of alkali added. Ammonia came off very rapidly when the solution was warmed. When all the ammonia had been driven off the solution was acidified and extracted with ether. From the ethereal solution, a crystalline substance was obtained by distilling off the ether. This gave the specific tests for β-resorcylic acid as stated previously.

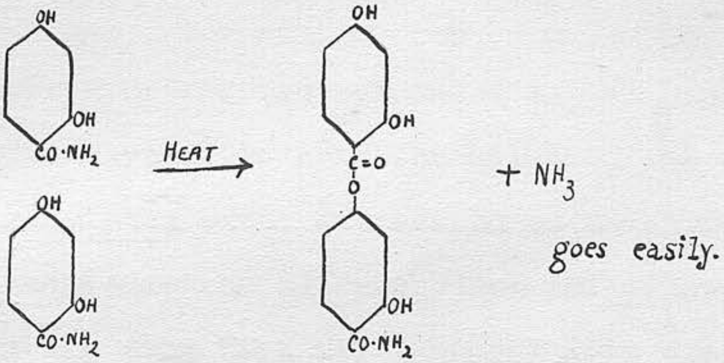
The compound, therefore, is β-resorcylamide.



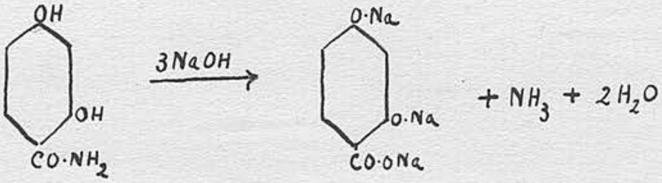
No reference to this compound having been prepared previous to this investigation could be found.

The fact that the amide gave off ammonia very rapidly when heated alone but only with difficulty when hydrolysed with alkali may be explained by the reaction.

1)



2)



Hydrolysis takes place slowly owing to the well known steric hindrance effect in such groups.

SUMMARY.

(1) 2:4:2':4'-Tetrahydroxybenzophenone may be prepared by the condensation of 2:4-diacetoxbenzonitrile and resorcinolin presence of dry hydrogen chloride. The ketone is obtained in 40 per cent of the theoretical quantity. β-Resorcylamide and resacetophenone may also be isolated from the condensation product.

(2) A comparison of the fluorescences of the 3:6-dihydroxyxanthydrol in alkaline solution and solutions remaining after extraction of aldehyde in the condensation of resorcinol and diphenyformamidine show that the xanthydrol is produced during the condensation.