A further study of the condensation products of resorcinol

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OF THE
CONDENSATION PRODUCTS
OF
RESORCINOL

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OUTLINE OF THESIS

Introduction ................................................. 1
Review of the Theories of Fluorescence ................... 3
Experimental part: ............................................. 12
   I. A Study of the Methods of Condensation ............ 12
   II. A Study of the Nature of the Fusion Product, with attempts to separate substances which could be analyzed. .......... 14
   III. Methods for the Synthesis of Resorcinol Ether ... 21
Conclusions; .................................................... 30
   I. Theoretical Consideration of Results ................ 30
   II. Relation of Experimental Results to the Theories of Fluorescence as Related to Structure .............................. 33
   III. General Importance of the Autocondensation of Resorcinol ........................................... 37
Bibliography ..................................................... 38
Acknowledgements .............................................. 40
INTRODUCTION

While working on the condensation of diphenic anhydride with resorcinol R. E. French found that resorcinol undergoes an autocondensation when heated with dehydrating agents. The product obtained in this condensation has a prominent green fluorescence which is strikingly similar to that of fluorescein. From the method of condensation it was assumed that the resulting compound was meta-hydroxy phenyl ether, and that this substance had fluorescent properties.

\[
\text{HO} \quad \text{O} \quad \text{OH}
\]

meta-hydroxy diphenyl ether
or resorcinol ether

If the above assumption is correct it would be of significance, for then we are dealing with a comparatively simple organic compound having fluorescent properties although its formula does not permit certain structures which are thought to be essential to the phenomenon of fluorescence. According to prominent theories on fluorescence and structure the following groups may cause fluorescence.

- Pyrone group
- Quinonoid structure
- Heterocyclic "Fluorophores"
None of these groups are found in the above resorcinol ether. On the other hand, the presence of a meta-hydroxy phenyl ether linkage in fluorescein as well as in the resorcinol ether, suggests that this arrangement is responsible for the fluorescence of these compounds. Thus in resorcinol ether we have a compound which cannot be classified under any of the existing theories of the relationship between fluorescence and structure. At the same time it suggests a definite structure to which its fluorescence may be due.

A study of the autocondensation of resorcinol and its relation to fluorescence was made by R. E. Flikkema(27), who submitted his thesis on this work in 1923. This paper dealt mostly with the separation of certain substances from the resorcinol fusion product although some synthetic work was tried.

The present investigation is a continuation of those mentioned above. The experimental work includes various methods of resorcinol condensation, a study of the nature of the resulting product, and chiefly the synthesis of resorcinol-ether compounds.
When rays of light fall upon a substance one or more of the following phenomena may occur: (1) The rays are reflected unchanged while, (2) some of the rays may be absorbed and this energy transformed into heat; (3) the substance may absorb certain rays and thereby exhibit color; (4) the rays may bring about a chemical change in the compound as in photosynthesis or, (5) some of the rays may be emitted by the substance in the form of light waves having a different wave length than the original light waves. If the latter case occurs and the emission of radiations continues even after the original source of light has been removed, the substance is said to be "phosphorescent". On the other hand, if the effect ceases with the removal of the exciting rays, the phenomenon is called "fluorescence".

Fluorescence is of interest not only in chemistry, where it involves a large variety of chemical compounds, but also in other fields of science. Thus, the physicist is interested in fluorescence as a physical phenomenon. The plant physiologist and botanist are attracted by the fluorescence of many plants and plant products, while the bacteriologist observes this phenomenon in many microorganisms. The close relation of fluorescence and photosynthesis was recently emphasized by Pringsheim, who has shown that in certain sensitive substances light from the same region of the spectrum is capable of producing a photochemical reaction as well as fluorescence. This author found further
support for his views in the observation that fluorescent substances may act as photocatalyzers in seed and bud development. Another investigator has reported that fluorescent substances have a destructive action on many bacteria.

Before the theories of fluorescence are considered, it might be well to discuss some of the main factors involved in this phenomenon. Fluorescence is exhibited by a large variety of compounds, and is not restricted to any special group or class. It is not limited to any physical state of matter, being found in liquid, gaseous and solid substances. Examples that might be quoted are: fluorescein, aesculin, eosine in dilute solutions; iodine, mercury or anthracene in the vapor phase; Iceland spar and barium platinocyanide in the solid form. The emitted rays are not limited to any particular position of the spectrum. Stark and Meyer having found that numerous benzene derivatives give fluorescence only in the ultra-violet region. Therefore, although the common fluorescent substances are visibly fluorescent, many more may exist which are just as truly so although the fluorescence is not observable with the naked eye.

When light passes through two consecutive layers of the same fluorescent substances only the first layer shows fluorescence. This indicates that only certain rays are absorbed by the compound and that only these are capable of exciting fluorescence in the substance used. Stokes has shown that light of a definite wave length may excite a fluorescence consisting of different rays and also that a given ray in the fluorescent spectrum may be derived from the absorption of rays having a varied wave length. Usually the emitted ray has a greater wave length.
than the absorbed ray. This relationship, expressed in what is known as "Stokes' Law", does not hold very rigidly and substances showing exceptions may be mentioned, such as chlorophyl, fluorescein, and eosine.  

An increase in the intensity of the exciting light increases the absorption due to fluorescence up to a certain limiting and constant value. The concentration of the substance in solution also may vary the intensity of fluorescence. J. Perrin has formulated a mathematical equation for expressing the optimum concentration of a solution at which a maximum fluorescence is produced. An increase of concentration above the optimum value may decrease the fluorescence even to zero. Moderate variations in temperature in general have little effect on fluorescence. Certain substances which do not show this phenomenon at ordinary temperature do so at -180°C, while other substances show fluorescence only when heated.

Fluorescence may be markedly influenced by the solvent. Thus ortho-aminocinnamic ester fluoresces with a violet color in ligroin, blue in benzene and green in alcohol. Explanations of the solvent action are quite incomplete and indefinite. It is generally assumed that the solvent may prevent fluorescence by absorbing either the exciting or the emitted rays; or that it influences the electronic conditions of the substance thereby changing the conditions necessary for fluorescence.

Closely allied to the solvent effect is the relation of fluorescence to ionization. The ion, according to certain theories, is much more fluorescent than the molecule. Examples often quoted are
quinine sulphate in acid solution or fluorescein in weakly alkaline solution. H. C. Jones (11) explains the latter case in terms of the dissociation theory, as follows: The addition of alkali causes a greater dissociation of the weakly acid fluorescein thereby increasing the number of complex organic cations and giving a corresponding increase in the fluorescence. Thus, a maximum fluorescence is obtained at a maximum concentration at which dissociation is complete.

It should also be noted that fluorescence may be produced in many compounds by the action of X-rays. (12) On the other hand, the phenomenon is often destroyed, especially with solutions of organic substances, by the action of ultra-violet rays or ozone. (13)

With the above general considerations in mind we may now proceed to investigate some of the more prominent theories dealing with the phenomenon of fluorescence. As these are not of direct importance to the experimental part of this paper they will be briefly given. (14)

The first attempt at a fundamental explanation was made by Wiedemann in 1889, who later with Schmidt published a more detailed discussion in 1895. This theory holds that fluorescence and similar phenomena are due to a reversible molecular change; as for example, substance A changes to B and B to A. If the change is rapid and reverses immediately, fluorescence is observed; but if the reverse change (B to A) is slower than the first change (A to B), phosphorescence occurs. When heat must be applied to reverse the change the
substance shows "thermo-luminescence". Leonard somewhat extended the theory by assuming that the molecular change was essentially due to the transference of electrons from one atom to a neighboring atom. Thus an atom of fluorescent substance might give and take electrons from neighboring atoms of the solvent. These active atoms called "centers" form characteristic groupings, each of which gives a band in the spectrum.

Kowalski assumed that fluorescence and phosphorescence are caused by certain electronic systems made up of molecules or groups of molecules of two different types. One type, having "electrogenous centers", is capable of emitting electrons, and therefore, of showing photoactivity under the influence of light. The other type, having a "luminophore center", is capable of emission only when its internal energy exceeds a certain value. In some cases the solvent may furnish the "electrogens" (centers) for supplying the necessary electrons to a luminophore group. This theory explains the exceptions to Stokes' Law quite satisfactorily by the assumption that thermal agitation may increase the speed of the emitted electrons and so shorten the wave length of the emitted ray in some cases. Experiments at reduced temperatures verify these views.

Another theory advanced by Baly pictures the atoms of the molecules as forming a "closed field" in regard to their electric and magnetic properties. Through various agents such as solvents, light, X-rays, the fields may be "opened up" to a greater or less
extent. In so doing the compound becomes capable of a considerable number of modes of vibrations each of which has its own frequency. Light is absorbed or emitted only at some one, or more, of these frequencies. This view indicates a relation between fluorescence and photochemical activity in that the distended atom, a condition produced by light, etc., would be more reactive.

The last theory to be mentioned is the "photochemical" theory of Perrin and, as the name implies, its explanation involves chemical reactions rather than physical changes. The electronic changes which are generally accepted as the fundamental cause of fluorescence may be considered either physically or chemically. From the chemical viewpoint this change, causing a difference in the behavior of the atom, is essential; while from the physical point of view it is incidental. In other words, the physical phenomenon (light emission) is produced by a chemical reaction in which definite chemical compounds, different in properties from the original substance, are formed. The reaction is fundamental and the light phenomenon its accompaniment. According to this theory the fluorescence is due to the destruction of the molecule and its intensity depends on the rate at which this destruction occurs. Perrin explained the condition of "optimum concentration" by saying that up to a certain concentration the molecules are decomposed by a certain amount of energy, but that at a higher concentration the active molecules mutually protect each other. The destruction of molecules may be brought about by light, $\alpha$-rays or ultra-violet rays, depending on the nature of the substance. Photo-chemical reactions may be explained in a similar way. Thus oxygen is changed to ozone by ultra-violet rays in the "Schumann" region, while
the reverse process occurs with longer ultra-violet rays.

The theories just mentioned all attempt a fundamental explanation of the phenomenon of fluorescence. Much work has also been done in trying to establish the relationship of fluorescence to structure. (15) While these theories do not try to explain the mechanism involved they have served, nevertheless, in classifying a large number of fluorescent substance, and have aided in the discovery of new fluorescent compounds. A more extensive resume of these theories may be found in the thesis of Mr. R. E. Flikkema (M. A. C., 1923).

In 1897 R. Meyer advanced a theory that the fluorescence of a compound is due to the presence of certain six-membered cyclic systems which he named "fluorophores". Examples may be given as follows:

\[
\begin{align*}
\text{CH} & \quad \text{H} & \quad \text{O} & \quad \text{N} & \quad \text{O} & \quad \text{S} \\
\text{CH} & \quad \text{CH} & \quad \text{CO} & \quad \text{N} & \quad \text{N} & \quad \text{N}
\end{align*}
\]

These systems, however, must be associated with other groups or complex arrangements including benzene nuclei. The theory does not attempt to explain the action of introduced atoms which destroy fluorescence or shift its spectrum. When Stark discovered ultra-violet fluorescence in 1907, Meyer came to a new conclusion, viz., that the benzene nucleus, rather than the special "fluorophores", was the seat of the fluorescent properties. This broadens the theory so much that it is of little use in classifying fluorescent compounds.
Kaufmann, after an extensive investigation, concluded that fluorescence was due to:

1. The presence of a benzene nucleus.
2. Its arrangement of valence bonds similar to the Dewar formula, giving a "luminophore".
3. The presence of "auxochromes" (groups added to a benzene ring to give the luminophore) and "fluorogens" (groups added to the luminophore to give fluorescence).
4. A favorable arrangement of the fluorogens in respect to the other groups present. Where two auxochromes and one fluorogen occur the arrangement must be symmetrical, but if three auxochromes and one fluorogen are present, two of the auxochromes must not be adjacent to the fluorogen. In cases where the fluorogen is a side chain, its effect (strength) depends on the residual affinity between the group and the ring. Thus the affinity, according to Thiele's theory of partial valence, is greater in dimethoxy acetophenone (I) than in dimethoxy benzophenone (II).

![Chemical structures](image)

Fluorescent | Non-fluorescent
---|---
(I) | (II)

Those substituents which increase fluorescence by their addition to a compound Kaufmann has named "auxoflores" (NH₂,NHR,CH,COOH), while those which depress it he called "bathoflores" (I,Br,NO₂,COCH₃).
Hewitt advanced a theory which considers fluorescence as due to two interchangeable forms of the same substance. This change is not brought about by dissociation or similar phenomena for this would require too much energy. It is due rather to a symmetrical rearrangement of a labile atom-like hydrogen, or to a rearrangement of the valence bonds. This theory may be quite satisfactorily applied to a great many fluorescent compounds, and also affords an explanation as to why substances like diphenyl pyrone fluoresce only in concentrated acid solution.

The theory fails to explain why certain symmetrical compounds such as phenolphthalein and tetra nitrofluorescein fail to show fluorescence. Also when the labile hydrogen is replaced by an alkyl group, which is considered non-mobile, the compound does not lose its fluorescent properties.

The most recent work in relating fluorescence to chemical constitution has been done by James Moir. According to this author fluorescence depends on the presence of a benzene ring and upon the nature and position of the groups attached to the ring. With one aromatic ring, one of these groups must be an auxochrome, and the fluorescence depends more on the nature of these groups than upon their relative arrangement. In the case of two groups in the ortho
position, one must be an auxochrome and the other must be attached to the ring by an unsaturated bond if the substance shows fluorescence. With two aromatic rings, no auxochrome is necessary. Whenever two rings are joined in two places by two groups fluorescence is observed. Because xanthene cannot have a quinonoid structure

\[ \text{Xanthene green fluorescence} \]

in concentrated sulphuric acid, the author concluded that fluorescence in this case is due to the special arrangement of the compound, the groups holding the rings in a rigid position.
EXPERIMENTAL PART

The experimental work of this investigation was divided into three parts, viz.; I, A study of the methods for the condensation of resorcinal; II, A study of the product, attempting to isolate a pure substance suitable for analysis; III, A study of various methods for synthesizing meta-phenyl ether derivatives in order to establish the structure of the resorcinal fusion product.

I. The Condensation of Resorcinal

According to Beilstein resorcinal ether may be prepared by treating resorcinal with concentrated sulphuric acid, with carbonic acid and sodium or by heating with concentrated hydrochloric acid in a sealed tube. It may also be prepared by condensing resorcinal with resorcinal disulphonic acid, or with phenanthrene disulphonic acid. R. B. French first condensed resorcinal in this laboratory by means of zinc chloride, while R. E. Flikkena also used aluminium chloride and phosphorus pentoxide.

In the present investigation it was found that sulphuric acid was the most satisfactory dehydrating agent for condensing resorcinal. When either zinc chloride or aluminium chloride is used, the fusion product cannot be easily extracted with an alkaline solution due to the formation of flocculent metallic hydroxides which interfere with filtration. The extraction must then be made by means
of alcohol, reprecipitating the fluorescent substance by addition of a small amount of hydrochloric acid or by diluting the alcoholic solution with water. The acid fusion product was first dissolved in an alkaline solution and then reprecipitated by addition of hydrochloric acid. The precipitate was washed several times on a filter paper to remove the acid and sodium salt. A very nearly pure product can be obtained by neutralizing the sulphuric acid with barium carbonate and then extracting the dried mass with alcohol.

It was found that the fluorescent resorcinol ether could also be prepared by melting a quantity of resorcinol and treating it with metallic sodium. Hydrogen is freely evolved in the reaction. When the resulting product is dissolved in water the fluorescence is readily observed. When a 10 per cent sodium hydroxide solution, containing resorcinol is evaporated on a steam bath, the same fluorescent product is obtained. It is thought that the sodium hydroxide at this temperature has enough dehydrating effect to cause the condensation of the resorcinol.

From the above methods it is obvious that the autocondensation of resorcinol is easily brought about. Work which will be described later points to the fact that, while the products obtained from the various methods show similar fluorescence, there is reason to believe that the condensation may take place to different degrees, i.e., two, three, or more benzene rings may be united into one molecule by the ether linkage. The number of resorcinol molecules thus united into one system depends on the nature of the dehydrating agent used, the temperature employed, and the time of the fusion.
II. The Isolation of Pure Products from the Fusion Mass

Flikkema made an extensive study of the different substances obtained in a fusion of resorcinol with zinc chloride and the results agreed quite closely with those reported by previous investigators. He claims to have separated three different compounds from a single fusion product: one agreeing with the composition \( (C_6H_4OH)_2O \), and undoubtedly having the structure:

\[
\text{HO} - O - \text{OH}
\]

another, a crystalline compound, to which a structural formula cannot be satisfactorily applied, had the composition of \( C_{14}H_{13}O_3 \); and a third substance having the formula \( C_{24}H_{18}O_6 \) which probably has the structure:

\[
\text{HO} - \text{O} - \text{O} - \text{O} - \text{O} - \text{OH}
\]

The crude fusion product is completely soluble in dilute alkali solution, quite soluble in alcohol, and slightly soluble in warm glycerol. It shows fluorescence in each of these solvents. The product is not soluble in ether, acetone, ligroin, benzene, chloroform, or carbon tetrachloride. According to previous investigators the compound \( C_{14}H_{13}O_3 \) is soluble in ether, alcohol, chloroform and acetone. It was found, however, that these solvents did not extract this substance directly from a fusion product. As the compound \( C_{14}H_{13}O_3 \) was extracted from the fusion mass by means of boiling water, and because the yield was small, it is probable that
the method of extraction employed by these investigators, is responsible for its formation. If this is so, it should be considered as a derivative of the original fusion product and not as one of the direct products of the condensation of resorcinol.

The other two products which are reported to have been isolated are

\[
\text{HO-} \overset{-\text{O}}{\text{O}} \text{OH} \quad \text{and} \quad \text{HO-} \overset{\text{-O}}{\text{O}} \overset{\text{-O}}{\text{O}} \overset{\text{-O}}{\text{O}} \text{OH}
\]

It will be noticed that the two formulas represent different degrees of condensation; that is, in the first case we have only two molecules of resorcinol combined (di-phenyl ether) while in the later case four molecules have united in a phenyl ether formation (a tetra-phenyl ether).

Evidence obtained during the present investigation leads to the conclusion that the condensation may consist of a varied number of resorcinol molecules. When resorcinol was condensed with concentrated sulphuric acid (sp. gr. 1.8) it was found that the product differed somewhat if the fusion took place at 160° (approximately) for 6 hours than when the fusion occurred at 130° for 4 hours. In the latter case the product softens to a sticky tar when boiled in water, while the product from a high temperature fusion did not soften in boiling water. Furthermore, the product obtained when fused resorcinol is treated with metallic sodium shows a pale yellow solution color when dissolved, while the more intensive fusion products, such as obtained from resorcinol sulphuric acid fusion at 160°, show a deep red solution color. The more intensive fusion product is much more easily precipitated from a neutralized solution by the addition of electrolytes. This again points to a variation
in the nature of the products although their fluorescence is practically the same.

From the above results we may now conclude that the fusions under varied conditions yield similar but not identical products. The low temperature fusions, or when comparatively weak dehydrating agents are used, would be expected to yield compounds representing a lower degree of condensation. On the other hand the more intensive condensations with a higher temperature or stronger dehydrating agents, would yield products showing a more extensive condensation of resorcinol molecules. The larger condensed molecules would undoubtedly have a higher melting point and thus, only the low temperature fusion product melts in boiling water. That the solution color is darkened by a more intensive condensation might also be expected. If the product is of a colloidal nature, the more highly condensed products would undoubtedly show more pronounced colloidal phenomena and, therefore, be more easily precipitated by the addition of electrolytes.

When it was found that electrolytes would precipitate at least part of the fusion product, experiments were tried with semi-permeable membranes in the hope of gaining some definite knowledge regarding the physical nature of the fusion product. Two membrane sacks of collodion were each attached to a one-hole rubber stopper containing a glass tube about three feet in length. One of the sacks was filled with a weakly alkaline solution saturated with an average fusion product and the other with the same solution just neutralized
with hydrochloric acid. The sacks were immersed in separate water baths through which there was a continual flow of fresh water.

Dialysis was continued for a period of three weeks during which time the sacks were once replaced. At the end of this time 15 c.c. samples of each solution were evaporated in crystallizing dishes and the residue examined under a microscope. No inorganic crystals could be found, showing that complete dialysis of these substances had taken place.

During the dialysis the alkaline solution showed a marked osmotic pressure while the neutralized solution did not. It was assumed that in the latter case the product was in a form of suspension, for a further addition of acid caused precipitation, and in this case no osmotic pressure would be possible. The alkaline solution being in a true solution form could exhibit osmotic pressure. It was plainly observable that the fluorescent substance readily passed through the collodion membrane, and after the period of dialysis, the product remaining in the sack showed no fluorescence, even in alkaline solution. The acid solution which showed no osmotic pressure, retained its fluorescent property. This was undoubtedly because the substance being in a form of suspension could not dialyze through the membrane. The behavior of the alkaline solution would indicate that the constituents of a fusion are not the same as to their colloidal nature or their fluorescent properties.

If we now revert to the hypothesis that the condensation may take place to a varied degree we can partly explain these results. In the first place, it is reasonable to assume that, especially in the highly condensed products, certain anhydride systems may be formed;
According to the various theories of fluorescence these compounds would not show fluorescence. Being complex, benzene ring compounds they would be expected to show osmotic pressure. Thus we might assume that the substance remaining in the collodion sack after dialysis consists of certain anhydride systems; while the fluorescent compounds which passed through the membrane were of the dihydroxy-phenyl ether type. Whether or not the collodion membrane would retain the more highly condensed di-hydroxy systems of the phenyl ether compounds is hard to say. Experimental work of this nature is highly technical and would constitute a problem of research in itself.

The colloidal nature of the resorcinol condensation product undoubtedly explains the failure of all attempts to obtain crystalline substances directly from the fusion mass. The preparation of crystalline compounds either directly or indirectly from the fusion product would be very desirable as these might be made suitable for analysis.

Direct crystallization being unsuccessful, it was next attempted to alter the product in such a way as to give crystalline derivatives or substances which could be analyzed. Previous investigators have reported that the lead salt of resorcinol ether may be precipitated from an alcoholic solution. A saturated alcoholic solution of the condensation product was treated with an alcoholic solution of lead acetate. Precipitation readily occurs and the red flocculent mass was separated by filtration. It was first washed with alcohol to remove any part which was not combined with lead, and it was
then washed with a large quantity of water to take out the excess lead acetate. The last washings gave no lead test with H₂SO₄.

After washing out the water with alcohol the precipitate was dried at 110⁰. A weighed quantity of the dry substance was treated with small amounts of nitric acid and heated until only the white lead nitrate remained. This was dissolved and the lead precipitated as lead sulphate from the solution diluted with alcohol. The results of duplicate analyses gave an average of 34.98 per cent lead in the substance. The theoretical percentage of lead in a four-ring compound

\[ \text{Pb} - O - O - O - O - O - O \]

is 35.03 per cent. While these figures compare rather closely there is no proof that only the four-ring system is precipitated. It is more likely that the result obtained represents an average of several compounds with a varied number of benzone rings. In the above determination the purified product from a resorcinol-sulphuric acid fusion was used.

The barium salt was prepared in a similar way, but the yield was small and a satisfactory analysis could not be made. The copper and magnesium salts were also made, but the sodium salt could not be isolated. The solution which supposedly contained the sodium salt showed an intense green fluorescence, stronger than any other fluorescent solution obtained in this research. A more extended study of these compounds might be made to ascertain whether only the
four-ring system is precipitated by lead or whether the different fusion products would yield different compounds. It is possible that the precipitation method could be applied in separating the various compounds obtained in a single fusion. The precipitated salts are not crystallizable so that it is difficult to know definitely whether or not a pure compound is obtained.

In extending the search for crystalline derivatives from a resorcinol fusion product attempts to methylate and acetylate the product were made, but without success. A dilute alkaline solution of the fusion product was treated with di-methyl sulphate, adding small amounts with continual stirring. Small amounts of 10 per cent sodium hydroxide were added simultaneously to keep the solution alkaline. When all was added the solution was distilled. Water contaminated with di-methyl sulphate distilled over 100° - 105° C. No other product could be distilled from the solution. The residue was treated with various solvents but no organic crystalline substance could be extracted. Acetylation was attempted by boiling the product in acetic anhydride and also in acetyl chloride under a reflux condenser. The boiling was continued for 30 hours, but no apparent change took place. The use of copper as a probable catalyst in the reaction did not alter the result.
III. The Synthesis of meta-Phenyl Ether Derivatives

When it was found that crystalline substances could not be obtained from the resorcinol fusion product, attention was directed toward the synthesis of compounds which would correspond to those thought to result in the resorcinol condensation. If the synthetic methods did not involve the use of resorcinol and the products obtained corresponded, especially in their fluorescence, to the resorcinol condensation product, proof would be established in regard to the structure of the fluorescent substance. With this in view various methods for the synthesis of phenyl ether derivatives were studied and developed.

The first method was the condensation of phenol compounds by means of dehydrating agents. A quantity of meta-amino phenol was treated with twice the weight of concentrated sulphuric acid (sp. gr. 1.84). The acid was carefully added as a reaction, probably salt formation, takes place liberating considerable heat. The mixture was then heated in an oil bath at about 160°C. for two hours. The product was placed in about 500 cc. of water and dissolved by heating. A distinct green fluorescence was shown by the acid solution, while an alkali solution destroys the phenomenon. Upon cooling, white, rectangular, crystals separated from the solution. The purified crystals have a very high melting point, are easily soluble in basic solution or in hot water, but exhibit no
fluorescence. Qualitative tests indicated that the substance was a sulphonlic acid derivative. The fluorescent, acid filtrate was cooled to 0°C and diazotized in the usual way by careful addition of sodium nitrite. After the diazotization, fluorescence was observed in alkaline solution, but not in an acid solution. This corresponds to the behavior of the resorcinol fusion product. The fluorescence of the original resorcinol fusion and that of the synthetic product here prepared is identical in all respects. The reactions involved in this method are as follows:

![](image)

Fluorescent in acid solution

Fluorescent in basic solution

It may be thought that because amino phenol is generally prepared directly from resorcinol, that the resorcinol contamination could be responsible for the fluorescence. This cannot be the case for the resorcinol fusion shows fluorescence only in a basic solution while here the phenomenon is observed only in an acid solution, except after diazotization. This also excludes the possibility of the sulphuric acid first changing the amino phenol into resorcinol, and then causing its condensation.

Fusions were carried out in a similar way in which the meta-amino phenol was condensed by means of zinc chloride. The temperature in this case was kept at 175 degrees for about 8 hours. The product had identical properties with the substance prepared in
the acid fusion although the fluorescence both before and after
diazoetization was much stronger. This indicates that the zinc
chloride fusion gives a better yield of the fluorescent substance
while in the sulphuric acid fusion, the main product is a sulph-
phonic acid derivative.

Several attempts were made to condense meta-amino phenol
by means of phosphorus pentoxide, but these were unsuccessful.

Flikkerum\(^{(21)}\) tried to condense meta-nitro phenol by means
of zinc chloride, but the mass exploded at 150°C. Attempts were
made to use phosphorus pentoxide as the dehydrating agent, but with-
out positive results. Sulphuric acid would undoubtedly readily form
a sulphonic acid derivative as in the case of amino phenol so it was
not used. It was thought that upon reduction of the nitro group to
the amino groups, the compound would be similar to the product from
the meta-amino phenol condensation. According to certain theoretical
considerations, which will be considered later, the condensation of
meta-nitro phenol is not possible. For this reason further attempts
to use this method of synthesis were not made.

The next method used for the synthesis of meta-phenyl ether
derivatives depended upon the reaction between meta-substituted sodium
phenolates and meta-substituted benzene halides. Proof that a reaction
leading to phenyl ether derivatives had taken place would be indicated
by the formation of cubic sodium halide crystals upon evaporating the
water extract of the fusion product. These are easily detected under
a microscope.
The first problem presented in this part of the research was the preparation of a suitable meta-substituted sodium phenolate. It was mentioned previously that resorcinol does not form a definite sodium salt, but that condensation into fluorescent substances readily occurs. Likewise meta-amino phenol does not give a distinct sodium salt and auto-condensation may take place.

The only satisfactory sodium salt that was prepared was the meta-nitro sodium phenolate. After making a study on the preparation of phenolates it was found that the method given by Noyes for the preparation of the phenyl ether of salicylic acid is the most convenient. A weighed quantity of meta-nitro phenol was dissolved in methyl alcohol, while the calculated weight of metallic sodium was allowed to react with another portion of methyl alcohol. The two solutions were united and evaporated on a steam bath. It was necessary to stir continually during crystallization in order to prevent caking and to aid the evaporation of the methyl alcohol. The vermilion colored compound was pulverized and placed in a drying oven at 110°C. for about 20 minutes. The drying darkens the product somewhat, but does not char it in any way. The use of the meta-nitro sodium phenolate, prepared in this way will be described in some of the work that follows.

Various combinations of compounds were tried which involved the halogen-sodium reaction, and these will now be briefly given. In each case the meta compounds were used. When the fusions were made in sealed glass tubes, these were heated in a "Carius" combustion furnace.
Sealed tubes were generally necessary as the compounds used were frequently quite volatile at high temperatures.

1. The syrupy residue from the evaporation of amino-phenol sodium methyleate solution, viz., meta-amino sodium phenolate was heated with chloro aniline in a sealed tube at 150°C. for four hours.

\[
\text{NH}_2 - \text{O}(\text{Na} + \text{Cl}) \text{NH}_2 \quad \text{and} \quad \text{NH}_2 - \text{C}_6\text{H}_5\text{O}(\text{Na} + \text{Br})\text{C}_6\text{H}_5\text{NH}_2
\]

The product was fluorescent in acid solution. No sodium halide crystals could be found in any residues from the various extractions so it is evident that the above reaction had not taken place. The fluorescent substance undoubtedly resulted from an auto-condensation of the amino phenol, corresponding to the condensations previously described in this paper.

\[
\text{NH}_2 - \text{O}(\text{H} + \text{H-O}) \text{NH}_2
\]

2. That this autocondensation occurs is further established by the result obtained in heating meta-amino phenol with meta-chloro aniline in the presence of excess sodium carbonate.

\[
\text{Na}_2\text{CO}_3
\]

\[
\text{NH}_2 - \text{O}(\text{H} + \text{Cl}) \text{NH}_2 \quad \text{or} \quad \text{NH}_2 - \text{O}(\text{H} + \text{H-O}) \text{NH}_2
\]

\[
\text{NaCl} \quad \text{formed} \quad \text{auto-condensation}
\]

\[
\text{CO}_2 \quad \text{A} \quad \text{B}
\]

The mixture was heated at about 150°C. for four hours. If the reaction took place according to formula A the hydrochloric acid
would liberate a certain amount of carbon dioxide. No increased pressure was detected when the tube was opened. Furthermore, no sodium chloride crystals could be observed in the filtrate residues. The product exhibits fluorescence in acid solution, and this is undoubtedly again due to the autocondensation of the meta-amino phenol, (B).

3. The next reaction tried was the treatment of meta-nitro sodium phenolate with meta-chloro aniline and meta-bromo aniline.

\[
(\text{NO}_2)_2\text{C}_6\text{H}_4-\text{O}-\left(\text{Na} + \text{Cl}\right)-\text{C}_6\text{H}_4-\text{NH}_2
\]

\[
\downarrow \text{NH}_2
\]

The meta-nitro sodium phenolate is a distinct compound so that auto-condensation in this case would be practically impossible. Various fusions were tried at different temperatures, and for different periods of time. It was found that no reaction occurred unless finely divided copper was used as a catalyst. The most satisfactory conditions for fusion, using the catalyst, seemed to be a temperature of 160° to 170° C., and fusion period of about four hours. The resulting fusion product was first extracted with water. Upon evaporating the water extract, sodium chloride crystals were observed. The mass was next extracted with 70 per cent alcohol and the product then reduced with hydrogen by the addition of dilute hydrochloric acid and zinc dust. After reducing it for six to eight hours a faint green fluorescence was observable in the filtered acid solution. The symmetrical meta-nitro amino phenyl ether does not show fluorescence, but this is to be expected from the "bathoflour"
action of nitro groups, i.e., nitro groups destroy the fluorescence of most compounds. The reaction in the above procedure does not take place very readily as was shown by the comparatively small amount of sodium chloride crystals and also by the very faint fluorescence obtained after the reduction of the nitro group. The fluorescence in the final acid solution would correspond to the previous conclusions, viz., that in this case fluorescence is due to the formation of \((\text{NH}_2\text{-C}_6\text{H}_4)_2 = 0\).

4. An attempt to unite meta-nitro sodium phenolate with meta-chloro nitro benzene was unsuccessful.

\[ \text{NO}_2 + \text{C}_6\text{H}_4 - 0 - (\text{Na} + \text{Cl}) - \text{C}_6\text{H}_4 - \text{NO}_2 \]

The nitro compounds are quite unstable at high temperatures. Several fusions tried at varied conditions all violently exploded at about 180°C. At a lower temperature no reaction takes place, even with longer periods of fusion and introduction of copper as a catalyst.

5. An alcoholic solution of meta-nitro sodium phenolate and meta-di chloro benzene was boiled for 20 hours on a steam bath, but no reaction occurred, though the following was considered possible.

\[ \text{C}_2\text{N} - \text{C}_6\text{H}_4 - 0 - (\text{Na} + \text{Cl}) - \text{C}_6\text{H}_4 - (\text{Cl} + \text{Na}) - 0 - \text{C}_6\text{H}_4 - \text{NO}_2 \]

A fusion in a sealed tube was tried, heating at 150°C. for five hours and using copper as a possible catalyst. As no sodium chloride crystals could be obtained from any of the extracts of the fusion mass it was assumed that no reaction as indicated above had taken place.
6. A fusion of meta-bromo toluene and meta-nitro sodium phenolate was tried, but no positive results were obtainable. The reaction thought possible would be as follows:

\[ \text{CH}_3\text{C}_6\text{H}_4-(\text{Br} + \text{Na})-\text{O-C}_6\text{H}_4-\text{NO}_2 \]

Upon reduction of the nitro group the amino compound might be expected to show fluorescence.

From the above mentioned methods it is evident that the halogen benzene compounds are not very reactive. A theoretical discussion of this observation will follow later.

The final attempt to obtain a synthetic meta-substituted diphenyl ether was made by starting with di-phenyl ether itself and introducing the substituted group. When a sulphonic acid group is introduced it would theoretically go into positions ortho and para to the oxygen linkage. If the subsequent fusion with potassium hydroxide follows the same rule as the fusion of benzene di-sulphonic acid into resorcinol, the meta-di-hydroxy di-phenyl ether would be expected to form. This compound should then compare with the products from resorcinol condensation in regard to its fluorescence.

Twenty grams of phenyl ether were added to about twice this weight of concentrated sulphuric acid, and the mixture heated on a steam bath for about 36 hours. The resulting homogeneous solution was poured into about a liter of water, and then neutralized with excess calcium carbonate. The solution was heated to boiling and filtered. The filtrate was carefully treated with sodium carbonate to precipitate the calcium, avoiding an excess. After concentrating the solution on a steam bath the very soluble sodium salt
finally precipitated from a cooled solution. This was collected on a Witt plate and washed with a small amount of cold water. The mother liquid was further concentrated and more of the sodium sulphonie acid derivative was collected. Twenty-four grams of the dried salt was next placed in an iron crucible, and then dissolved in a small quantity of hot water. About 25 grams of solid potassium hydroxide was added and the mixture stirred till a thick paste resulted. Heating was slowly continued, with stirring to avoid spattering. The mass could finally be collected in a soft ball. When it assumed a dark brown color the heating was stopped, the product dissolved in water, and the solution neutralized with hydrochloric acid. Much sulphur dioxide was liberated, showing the presence of a sulphite and thereby proving that a sulphonie acid derivative had been formed in the original phenyl ether-sulphuric acid reaction. When no more sulphur dioxide was given off the acid solution was heated to expel the gas remaining in solution. A tarry mass floated on the surface of the hot solution which was easily removed with a stirring rod. The odor of phenol was very pronounced, indicating that considerable decomposition of the phenyl ether had also taken place during the alkali fusion. When the tar was placed in an ether solution part of it dissolved imparting greenish fluorescence to the solution, while another part was insoluble. The fluorescence observed was similar to that of the resorcinol fusion product although the later is not soluble in ether. On standing the ether solution darkens and fluorescence is no longer observable. Alcohol and dilute alkali solutions are very dark in color so that if a faint fluorescence does exist here, it is not observable.
CONCLUSIONS

I. Theoretical Consideration of Results

It is of interest to note that the theory of J. Stieglits (22) in regard to the electronic charges of the benzene ring, can be applied to practically every result obtained in this investigation. According to this author the carbon atoms of the benzene ring are assumed to be alternately 4/4 and 1/4 negatively charged; the alternate carbon atoms (meta positions) being identical in their electronic condition.

![Diagram of benzene ring]

According to this theory, in the case of a halogen, amino or hydroxyl substitution group, the negative charge on these groups is the most stable condition, but in certain instances, where rearrangements are not possible, these groups may be positively charged. On the other hand, certain groups such as the nitro group (HO-NO₂) are considered as being always positive. Thus we may represent the electronic condition of meta-amino phenol and meta-nitro phenol as follows:

![Diagram of meta-amino phenol and meta-nitro phenol]
The autocondensation of meta-amino phenol is theoretically possible because the reaction \((\text{H} + \text{HO})\) is possible, as the \(\text{H}\) is + and the \(\text{HO}\) is -. This was verified by experimental results. On the other hand, the condensation of meta-nitro phenol would involve a change of electrons for the combination \((\text{H} + \text{HO})\) is not possible, both the \(\text{H}\) and the \(\text{HO}\) being +. Experimental work indicated that the meta-nitro phenol did not condense. The difference in the character of the hydroxyl groups of the two compounds was clearly shown by their salt formation. The meta-nitro sodium phenolate forms a beautiful colored crystalline substance, while the meta-amino phenol partly undergoes autocondensation and forms only a sticky, sirupy mass.

In the case of the benzene halide compounds we would have:

As shown by the above illustration the halogen in meta-chloro aniline only would be capable of uniting with the sodium of phenolate compounds. However, the treatment of meta-chloro aniline and meta-bromo aniline with meta-amino phenol was of little value as far as positive results are concerned, for meta-amino phenol readily undergoes autocondensation. The treatment of the chloro aniline with meta-nitro sodium phenolate gave indications of a reaction, and after reducing the nitro group to the amino group, a faint fluorescence was observed. The conditions here would theoretically be as follows:
According to Stieglitz' theory the charges on phenyl ether would be

\[
\begin{align*}
\text{NH}_2 & \quad (\text{Cl}_4 \text{Na})\overset{+}{\text{O}} \quad \text{NO}_2 \\
\overset{\text{H}_2}{\text{NH}_2} & \quad \overset{\text{O}}{\text{O}} \quad \overset{\text{OH}}{\text{H}_2}
\end{align*}
\]

In sulphonating phenyl ether the positive sulphonyl group would therefore be expected to go into positions ortho and para to the negative oxygen linkage. This is known to be so in the sulphonation of phenol, in which case a mixture of the ortho and para products are obtained. It is known also that the fusion of ortho- and para-benzene disulphonyl acid with alkali always yields the meta-hydroxy compound, which is resorcinol. If on fusion of diphenyl ether sulphonyl acid with alkali a like rearrangement occurs, the resulting hydroxy group should go in the position meta to the ether linkage, and we should obtain the fluorescent meta-dihydroxy di-phenyl ether with the structural formula

\[
\begin{align*}
\text{HO} & \quad \overset{\text{O}}{\text{O}} \quad \overset{\text{OH}}{\text{H}}
\end{align*}
\]
Fluorescence was observed, although only as a faint qualitative result.

While this work was undertaken without the purpose of either proving or disproving the electronic theory as applied to organic compounds, it is evident that the theory forms a basis on which this research work may be developed. Moreover, it gives the only satisfactory explanation as to why certain reactions took place while others did not.

II. Relation of Experimental Results to the Theories of Fluorescence as Related to Structure

From the experimental work of this research it has been established that the fluorescent substance in the autocondensation of resorcinol is a meta-dihydroxy phenyl ether compound. Our conclusion is based on a comparison of the various methods for condensing the resorcinol and the synthesis of similar, if not identical, fluorescent substances by three different methods. It is then, safe to conclude that the meta-di-hydroxy diphenyl ether has fluorescent properties. Whether or not the larger molecules of condensed resorcinol, consisting of three or four benzene rings, are fluorescent cannot be positively determined. The meta-di-hydroxy diphenyl ether has the following structure:

\[
\text{HO} \quad \text{O} \quad \text{OH}
\]
In trying to apply to this compound the various theories relating fluorescence to structure we find that they are quite unsatisfactory. Meyer's theory is inadequate in that no "fluorophore" group can exist in the above formula which has no para substitutions. This also applies to Kaufmann's theory which requires the Dewar arrangement of valence bonds in one of the benzene rings.

The tautomerization of a labile hydrogen, according to Hewitt's theory, is quite impossible in this compound. A simple tautomerization due to changes of valence bonds is difficult to visualize when there is no apparent reason for such changes. If this was the cause of fluorescence, many other simple meta-substituted benzene derivatives would be expected to show fluorescence.

According to the recent work of Moir, (16) two benzene rings should be joined in two places by groups of almost any sort if the compound is to show fluorescence. In the resorcinol condensation product this necessitates the structure:

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{O} \\
\end{array}
\]

That this is not the case is pointed out by the fluorescence of di-amino di-phenyl ether, \((\text{NH}_2\text{-C}_6\text{H}_4)_2\text{O}\), and also by the fact that salts of the hydroxy phenyl ether compounds can be formed. Moir claims that where only one ring is present the meta position gives a faint fluorescence where one of the groups is an auxochrome. If we assume the fluorescence of the above compound to be due to each of the two rings individually, we would have this condition with the
hydroxyl groups as auxochromes and the oxygen linkage in a meta-position. However, the fluorescence of the above compound is very pronounced, although, according to this author it should be rather faint.

The similarity of the fluorescence of the prepared resorcinol ether and that of fluorescein is very striking. This would lead us to the supposition that the phenomenon is due to similar groupings in the two compounds. A comparison of their respective structural formulas reveals this similarity:

![Structural formulas of fluorescein, di-hydroxy-diphenyl ether, and phenolphthalein (non-fluorescent)](image)

From the above formulas it is easily seen that the only similarity in structure exists in the meta-hydroxy phenyl ether linkage, and the conclusion follows that the fluorescence of each of the above compounds must be due to this arrangement. This is further supported by the structure of phenolphthalein which lacks the ether linkage and shows no fluorescence. Our conclusion may be summed up by the statement that phenyl ether derivatives show fluorescence when auxochromes (NH₂, OH) are substituted in the positions meta to the ether linkage. Additional substitutions would undoubtedly influence fluorescence according to the nature of the group introduced.

A few compounds having the meta-ether linkage will be mentioned here to show their similarity. While many other compounds
which cannot be connected with this classification show fluorescence, it is worthy of note that this classification can be applied to many that are fluorescent. The only exceptions are cases in which groups or elements (iodine) "overshadow" the fluorescence or where the nature of the substituted group destroys fluorescence, ("nathofluors").

Fluorescein (green fluorescence)  Eosine (green fluorescence)  Erythrosine (not fluorescent)

Phloxine (greenish-yellow fluorescence)  Eosine BN (faint green fluorescence)

Rhodamine B (Strong fluorescence in alcohol which disappears on heating, but returns on cooling)  Pyronine G (yellowish fluorescence)
Finally it should be mentioned that the fluorescence of many condensation products which involve resorcinol, may be due to an autocondensation of some of the resorcinol. Sen and Sircar\(^{(23)}\) recently condensed resorcinol with many other organic compounds and report that nearly all of these products exhibit fluorescence. The methods used were favorable for autocondensation of resorcinol, and this would naturally impart fluorescence to the products. Another investigator\(^{(24)}\) has reported that the fusion of diphenic anhydride with resorcinol yields a fluorescent substance. Here again the conditions are such that the fluorescence of the product is very probably due to the formation of resorcinol ether.

The heating of phthalic anhydride with resorcinol and concentrated sulphuric acid is frequently given as a method for preparing small amounts of fluorescein, followed by the statement that the fluorescence of an alkaline solution of the product proves that this reaction has taken place.\(^{(25)}\) This investigation has proved conclusively that a similar fluorescent product is obtained by condensing resorcinol without the presence of phthalic anhydride. The fluorescence of the fusion product is, therefore, no positive indication of fluorescein.
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