

**CORNELL UNIVERSITY,
DEPARTMENT OF CHEMISTRY; ON
THE
CONSTITUTION OF GALLEÏN AND
COERULEÏN; A DISSERTATION**

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CHARLES EDWARD BREWER

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CORNELL UNIVERSITY.

Department of Chemistry.

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and Coeruleïn. 111978

A DISSERTATION

Submitted to the University Faculty for the Degree of
Doctor of Philosophy.

BY

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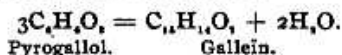
May, 1900.

HISTORICAL.

I. GALLEIN.

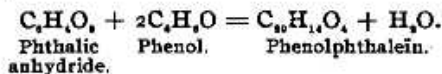
It was in 1871 that Adolph von Baeyer¹ discovered gallein. He made it by heating together phthalic anhydride and pyrogallol. The product was purified by dissolving in alcohol and precipitating with water. He described it as a solid, red by reflected light, blue by transmitted light. Later² he described it as a brown-red powder, or small metallic-green crystals. He found it to be soluble in alcohol with dark-red color, in potassium hydroxide with splendid blue color, which, however, it loses on continued exposure to air. In ammonium hydroxide it dissolves with purple color.

He regarded the compound as derived from pyrogallol by loss of water according to the reaction :



The results of his analysis of the new compound agreed with the above formula.

Later³ he tried the action of phthalic anhydride upon other hydroxyl derivatives of benzene, among them phenol and resorcin. He found that these reacted in a manner similar to that of pyrogallol, phenol giving phenolphthalein and resorcin giving fluorescein. From the analysis of phenolphthalein he was led to consider it as made up of one residue of phthalic anhydride and two residues of phenol, and represented the reaction thus :

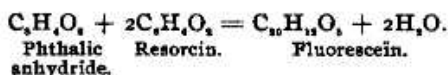


Fluorescein, from its similarity to phenolphthalein and also from the results of analysis, he regarded as derived from 1 molecule of phthalic anhydride and 2 of resorcin, thus :

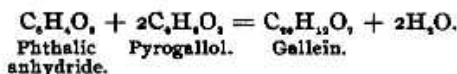
¹ Ber. d. chem. Ges., 4, 457.

² *Ibid.*, 4, 555.

³ *Ibid.*, 4, 658.



A study of these reactions led him to change his views of the reaction by which gallein was made.¹ He regarded it as made according to the following equation :



Thus it would be the phthalein of pyrogallol.

By reduction in alkaline solutions by zinc dust, Baeyer discovered that phthaleins lose color and are converted into closely related compounds which he called phthalins.

The structure of gallein is so closely related to that of the phthaleins in general that a summary of work done in establishing the structure of the latter is necessary for an intelligent study of the structure of the former.

Fluorescein was the first of the phthaleins to be investigated and have assigned to it a constitutional formula. The work was done by Baeyer and his assistants.² Fluorescein was made by heating together resorcin and phthalic anhydride. The purified product proved to be a yellow crystalline powder which dissolved in alkalis with a beautiful green fluorescence. Results of the analysis of the compound pointed to formula $\text{C}_{20}\text{H}_{12}\text{O}_5$ as representing its composition.

On the other hand, E. Fischer³ prepared *pure* fluorescein by first making its acetate, purifying it by recrystallization, and then saponifying it with alcoholic caustic potash. Fluorescein thus prepared was analyzed and the results pointed to $\text{C}_{20}\text{H}_{12}\text{O}_5$ as its formula.

Baeyer's next object was to determine the number of hydroxyl groups contained in fluorescein. This he did by making its acetyl and benzoyl derivatives in the usual way. He found that in each case two acid residues were introduced—that the compounds formed were the diacetate and the di-

¹ Ber. d. chem. Ges., 4, 663.

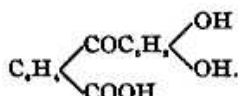
² Ann. Chem. (Liebig), 183, 2ff.

³ Ber. d. chem. Ges., 7, 1211.

benzoate of fluorescein. Further, he made what he termed the monoethyl and the diethyl ethers of fluorescein, and the dichloride. The fact that in all but one of the derivatives thus far mentioned two substituting atoms or groups replaced hydroxyls or the hydrogen atoms of these hydroxyl groups, pointed to the presence of two hydroxyl groups in fluorescein.

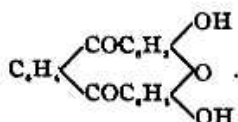
Quite a series of substitution-products in which two or more hydrogen atoms were replaced, gave information of other characteristics of fluorescein. Thus, dinitro and tetranitro fluorescein; mono-, di-, and tetrabrom fluorescein (eosin); salts of eosin; erythrin (ethyl ester of eosin); diethyl ether of eosin—all followed in rapid succession.

By fusing fluorescein with potassium hydroxide Baeyer found that decomposition follows in two stages. First, he obtained what he called monoresorcin phthalein, to which he gave the formula:

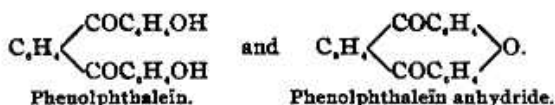


When heated further this compound yielded, besides resorcin, benzoic acid and carbon dioxide. The last two compounds came from the phthalic acid residue.

As the result of his investigation, he concluded that without doubt fluorescein was a diketone and should be given the formula:

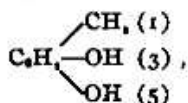


The formation of the anhydride between the hydroxyl groups in the resorcin residues was, he said, in harmony with an observation made by him in the preparation of phenolphthalein. Two compounds were in reality formed in the synthesis of phenolphthalein—one a phthalein proper, the other a phthalein anhydride. The relation of the two is expressed in the formulas:

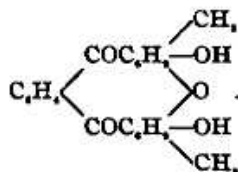


Fluorescein would, therefore, be a dihydroxyl derivative of the above anhydride form,

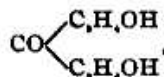
E. Fischer¹ made the phthalein of orcin,



and found it to resemble fluorescein very closely. He made a series of derivatives similar to those made from fluorescein by Baeyer. As a result of his study of this new phthalein he gave it a formula in harmony with that of Baeyer for fluorescein, as follows :



Baeyer's view of the structure of fluorescein, (and of the phthaleins in general), was modified in some essential points as a result of his further study of phenolphthalein.² A difficulty arose in explaining by the accepted diketone formula the action of melted alkalis on phenolphthalein. Such action resulted in the formation of dioxybenzophenone,

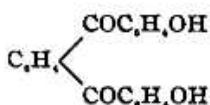
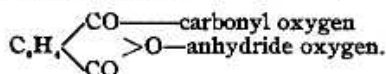


and benzoic acid. According to the diketone formula, this would require a shifting of one of the C₆H₄OH groups. It occurred to him that this decomposition could easily be explained by assuming that it is one of the carbonyl oxygen atoms and

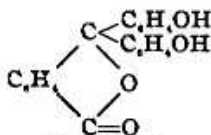
¹ Ann. Chem (Liebig), 183, 63.

² *Ibid.*, 202, 36.

not the anhydride oxygen of the phthalic anhydride that is replaced by two phenol residues. The difference is seen in the following structural formulas :

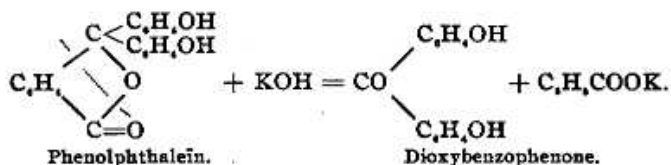


Diketone formula.

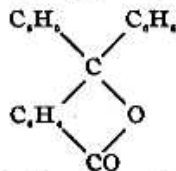


New formula.

The explanation of the formation of dioxybenzophenone is very difficult by the diketone formula, while it is quite simple by the new one, as will appear from the following scheme :



Baeyer found further evidence for the new formula in the synthesis of phenolphthaleïn by a method which can leave no doubt as to its structure and genetic relations. He treated benzene with phthalic anhydride in presence of aluminium chloride and obtained diphenylphthalid :



This, on reduction with zinc dust, gave triphenylmethane carbonic acid :

