CONDENSATION OF PHENOLS AND
AROMATIC AMINES WITH QUINOLINIC AND NICOTINIC ACID
TO FORM DYES ANALOGOUS TO THE PHTHALEINS

by

Julius Berger

Submitted in Partial Fulfilment of the Requirements
for the Degree
Master of Arts

McMaster University
1934
The author was desirous of investigating the properties of "quinilineins" as compared with those of corresponding phthaleins. As there was no quinolinic acid available in the laboratory, an attempt was made to prepare it. It was found that most methods gave very small yields, with the exception of one.

PART I - PREPARATION OF QUINOLINIC ACID

1. Beilstein, (4)122, prepared it from the oxidation of quinoline by potassium permanganate. The preparation is as follows:
   One oxidizes 25 gms. quinoline by means of 250 gms KMnO₄ dissolved in 5 litres of water, neutralizes the liquid almost with dilute sulfuric acid concentrates it by frequent removal of precipitating K₂SO₄ to a thin syrup, separates from this the quinolinic acid under ice-cooling by means of diluted sulfuric (1:1) and crystallizes it eventually from water by addition of animal charcoal. (Camps, Ar. 240, 352)

   Beilstein, (4)290, says of quinolinic acid:
   It is formed in very small amounts by the mixing of a solution of thirteen parts of quinoline with a boiling solution of thirty parts of KMnO₄. The steam treated alkaline fluid yields from alcohol the potassium salt, which one dissolves in diluted sulfuric acid and shakes out with ether. (Dewar, J.1880,949.) Needles m. 143°. Very difficultly soluble in water. Soluble in hot glycerine -- the solution fluoresces violet and at 180° gives off CO₂ and aniline.

DISCUSSION:

   Watt's Dictionary of Chemistry- Muir & Morley, Vol. 4, 380 gives:
   1. Quinoline and KMnO₄ in alkaline solution → pyridine dicarboxylic acid.
   2. Quinoline and KMnO₄ and conc. H₂SO₄ → quinolinic acid.
   3. Quinoline and KMnO₄ in dil. H₂SO₄ → quinoline B-3 carboxylic acid.

   In the preparation of quinolinic following Beilstein's directions, the solution was almost neutralized with dil. H₂SO₄ and allowed to stand to evaporate. After filtration and evaporation, about 10 g. of white crystalline solid was obtained which melted at 242 C with decomposition. A sample of product obtained from the same process in the previous year by a different man melted at 253° C (uncorr.) Since quinoline B-3 carboxylic acid melts at 248° C, I assume that it was this substance that was made and not quinolinic.

   A second trial was made of Beilstein's method, and the solution was not neutralized until after it had stood several days. After much difficulty of evaporation and recrystallization, quinolinic acid, m.p. 192° with decomp., was obtained. This was of a light brownish color, and still a bit contaminated with potassium sulphate, since on burning, a small white residue was left. The yield was small, 30-40%.
2. Chosh, India J. Chem. Soc. 115, 1102-5 (1919) prepared it by the oxidation of quinoline in aceton with the theoretical amount of 5% KMnO₄ at 10 °C. However, he does not report the yield obtained. The present author used this modification but obtained nothing better than the ordinary 30% yield.

3. O. Fischer & E. Renouf, Ber. 1884, 17, 755, prepared quinolinic acid from the oxidation with permanganate of ortho-quinoline sulfo acid, A. 40 gms. of A yielded 23 gms. of pure quinolinic. They also oxidized 40 gms. of ortho-hydroxy-quinoline with potassium permanganate to obtain a yield of 20 gms. quinolinic.

4. Lippman & Fleissner, M. 8, 312 (1887) prepared quinolinic acid from the oxidation of ortho-hydroxy-quinoline-carboxylic acid in alkaline solution with KMnO₄. The filtrate on separation from MnO₂ was converted to the lead salt with lead acetate; this was suspended in water, deprived of lead, and the solution evaporated after filtration from PbS. They go on to show that the decomposition point of quinolinic is at 140° C, and that at 160° C, the splitting off of CO₂ is complete.

5. E. Soucharda, Ber. 1925, 59, 1727, prepares quinolinic acid by the oxidation of 8-hydroxyquinoline with concentrated nitric acid as follows: 500 g. of 8-hydroxyquinoline are put in small pieces into a 10 l. flask provided with a long reflux tube and 50 g. of water poured over it. Then, with water-cooling, 1000 g. nitric acid (D. 1.52) are dropped in within 8 hours, and during the night it is left to itself.

The next day, the flask is warmed on the water-bath until violent evolution of the oxides of nitrogen ceases, and after the cooling, a new 1500 g. of HNO₃ are added. Then the solution is heated again and again treated with 2500 g. HNO₃ and kept 8 hours on the water-bath. The contents of the flask are put in a porcelain dish and evaporated down continually on a water-bath until the formation of crystals. After the cooling, the mass is pulverized in a mortar, filtered by a filter of Jena glass, washed at first with 30% HNO₃ and then with water. The residual quinolinic is obtained by evaporating the filtrate.

For purification, the crude quinolinic is pulverized, warmed with 1000 g. 40% acetic, and warmed on a water-bath; after cooling, filtering and washing with water, yield is 500-550 g.

DISCUSSION:

Only one-tenth quantities were used in this trial. 50 g. of powdered 8-OH-quinoline were placed in a 1 l. beaker and 5 g. of water added. Since this did not even appear to moisten the solid, 150 c.c. of water, sufficient to put part of the solid in solution, were added. Then 100 g. of nitric acid were added over a period of 8 hours. There was a violent evolution of nitric oxides when a little excess was dropped in suddenly, but otherwise the writer sees no reason for using a reflux. The solid appeared charred, but this subsequently dissolved completely in the further additions of conc. HNO₃.

The next day 150 g. of conc. HNO₃ were again added, according to directions. This was allowed to stand for 2 weeks, since work was interrupted. The light brown viscous mass was heated on a water-bath
for 3 hours, during which dark fumes of nitric oxides came off. This was cooled, another 250 g. of HNO₃ added, and again heated for 8 hours on the water-bath. The mass was now a syrupy reddish orange liquid. This was poured into a porcelain dish and after 5 minutes' heating on the water-bath, it all solidified. It was further heated for 1 hour. After cooling, the solid was transferred to an ordinary funnel, and washed with 200 c.c. of 30% nitric (20 c.c. of nitric D 1.5 made up to 100 c.c. with water). This seemed to dissolve up not only impurities but almost all the solid. On washing what was left with 100 c.c. of distilled water, a yellowish-orange colored ppt. was formed. The beakers and funnel were then washed clean with 200 c.c. of water, and everything placed in a 5 l. evaporating dish. This was then allowed to evaporate on the steam-bath. On evaporation, the same colored sticky solid formed as previously. This was warmed with 200 c.c. of acetic (40% by vol.) cooled, and washed with 30 c.c. of water. The ppt. after drying was a fluffy fine powder of bright orange-brown color, weighing 21 g. A small sample of it burned with a luminous flame, odor of burning quinolinic, leaving a black carbon residue which could be burnt away completely.

A melting point was run on the solid. It melted at about 180°C. (uncorr) and then again at 228°C, showing it was quinolinic; that had been converted to nicotinic by heat.

The filtrate from the above solid was evaporated down to about 50 c.c. volume. After cooling, it solidified completely to a dark orange colored solid. Weight of the slightly moist solid was 45.2 g. The impurity in it was the nitric acid, which was yet to be washed out. However, since the purpose of the experiment was reached, namely, confirmation of at least a 50 g. yield of quinolinic, (but not much more) no effort was made to further purify the second half of the acid.

6. Eastman Kodak Co. R.P. Book 3, P.159, 3/15/26, prepared it from the oxidation of 8-hydroxyquinoline sulfate with permanganate. Yield was only 38%. Preparation was as follows:

1,370 g. of No. 1776 8-hydroxyquinoline sulfate was dissolved in 5 liters of water with the addition of 850 g. of potassium hydroxide. About one-fourth of the solution was added to 8 liters of water in a 17-gal. crock, and then with stirring solid potassium permanganate was added until the color of permanganate did not fade immediately. More of the hydroxyquinoline solution was then added, followed by permanganate, until all of the hydroxyquinoline had been added and the permanganate color faded only very slowly on standing. 5.5 kg. of permanganate was used. By the occasional addition of ice, the temperature was kept between 60-70°C throughout the oxidation. After standing for an hour at this temperature the permanganate color disappeared and the solution was filtered, washing the precipitate with hot water.

The filtrate was evaporated on a steam bath in 22-liter flasks to a volume of between 5 and 6 liters, meanwhile adding enough sulfuric acid (1:1) to neutralize most of the alkali, and leave the solution but slightly alkaline. The solution was cooled and the potassium sulfate filtered off. To the filtrate 250 c.c. of sulfuric acid diluted with 500 c.c. of water was added and the solution cooled to 0°C.
The crystals which formed were filtered off and washed with ice water. They were then dissolved in about 1 liter of 23% ammonia water and filtered with suction from undissolved potassium sulfate. The vacuum on the suction bottle removed part of the excess ammonia and the solution was then boiled until practically all excess ammonia was off. A little acetic acid was added to the boiling solution so that the reaction was slightly acid to litmus, but not enough to cause a precipitate to form. The solution was boiled with Norit decolorizing carbon, filtered, and poured with stirring into a solution of 200 g. of sulfuric acid in 2 liters of water. The solution was cooled to nearly 0°C to complete the precipitation. The crystals were filtered off and washed with ice water. MP 194-195° with decomposition. Yield: 450 g., or 32%.

7. Eastman Kodak Co. R.P. Book 8, p. 82, 3/26/34 prepared it from the oxidation of 8-hydroxyquinoline with potassium permanganate. Yield: 37% of theoretical. Preparation was as follows:

\[
\begin{align*}
\text{N} & \quad \text{COOH} \\
\text{HO} & \quad \text{COOH}
\end{align*}
\]

\[
\text{N} \quad \text{COOH} + 4 \text{O}_2 \rightarrow \text{N} \quad \text{COOH} + 4 \text{H}_2\text{O} + 2 \text{CO}_2
\]

**PROCEDURE:**

1,896 g. (11 moles) of P-794 8-hydroxyquinoline is stirred with 30 liters of water in a crock. 9320 g. (59 moles) of P-863 potassium permanganate is gradually added, using ice to keep the temperature from going above 75°C. The manganese dioxide is filtered off with suction and washed with water (Note 1). The filtrate is evaporated under vacuum until thick with precipitated salt (potassium carbonate). Concentrated hydrochloric acid is added as long as carbon dioxide is evolved, so as to completely convert the potassium carbonate to potassium chloride. The potassium chloride is filtered from the cooled solution, and the filtrate is made slightly acid to Congo paper with hydrochloric acid. The crude quinolinic acid is filtered from the cooled solution, washed with a little cold water, and recrystallized from water, using decolorizing carbon.

Yield: 675 g., or 37% of the theoretical amount of 1,837 g.

Molecular weights: 8-hydroxyquinoline 145
Quinolinic acid 167
Potassium Permanganate 158.

**Note 1.** The filtration and washing of the manganese dioxide precipitate goes slowly. It seems probable that if after the oxidation has been completed, the mixture were heated to boiling by injection of steam and the manganese filtered (or centrifuged) and thoroughly washed, the yield would be considerable increased.
Stix and Bulgatsch, Ber. 1932, 65, 11, describe a procedure for making quinolinic by oxidizing quinoline with hydrogen peroxide and copper sulphate, the latter acting as a double-role catalyst.

The procedure is:

24 g. of quinoline are warmed with a mixture of 2100 c.c. 3% hydrogen peroxide solution and 46 g. 25% sulfuric on the water-bath to 60°; to this solution is added 64 g. of crystalline copper sulphate dissolved in 160 c.c. of water. The solution begins to warm up with strong evolution of CO₂, so that one must take care by slight cooling that the temperature does not rise over 70°. After 8 hours heating, one adds another 200 c.c. of H₂O₂ solution and warms for another 3 hours at 70°C. In the course of the reaction, the copper quinolate separates out gradually in the form of a heavy green colored precipitate. Since the whole copper salt has not separated out of the strongly sulfuric acid solution, add Na₂CO₃ up to a weakly acid reaction to Congo Red. The solution is finally heated up to 90° and then left to cool overnight.

After the filtration, one obtains 32-34 g. copper quinolate of the formula C₇H₈O₄·Cu·2H₂O. The decomposition of the copper salt can be carried out with the aid of H₂S, whereby one continues to heat at 60° the water in which the copper salt is suspended, and one must take care to stir well besides. However, since the decomposition of the Cu salt through hydrogen sulphide goes very slowly on account of its insolubility, it is more suitable to carry out the decomposition by heating with a 10% sodium sulphide solution.

The solution containing the sodium quinolinate and Na₂S after filtering and washing of the copper sulphide precipitate is acidified with sulfuric acid, and then purified according to known methods. In this way one obtains the quinolinic acid in a yield of 19-20 g.

Note: The copper sulphate must be free from all iron impurities or the yield will be decreased.

DISCUSSION:

The first attempt to make quinolinic following Stix's method was unsuccessful because the temperature of the solution was accidentally allowed to rise to 80°C, and the whole solution charred up very badly.

However, a second trial was quite successful. This time the temperature was kept between 50-60°C; the yield of crude copper quinolate (fairly dry) was 48 g. Since this is so near theoretical yield, I assume that a good yield was obtained through lower temperature, or that the precipitate contained some basic copper salt, which was very probable. The copper salt was decomposed with the required amount of 10% sodium sulphide; after filtering and evaporating,
a dark brown solid was obtained which could not be purified very easily. It was quinolinic acid, m.p. 190°C even in the impure condition. Yield of crude quinolinic was about 70%. It was not purified.

CONCLUSION:

It appears that any process using potassium permanganate as the oxidant cannot hope to give more than 50% yield at best; nitric acid has been tried and gives a better yield; copper sulphate and hydrogen peroxide give the best yield yet known; it is possible, however, that oxidation by a dilute chromic acid solution or by a mercury catalyst in the vapour phase, under reduced pressure, such as is used in oxidizing naphthalene, might be more successful.
PART TWO

PREPARATION OF NICOTINIC ACID.

NICOTINIC ACID was prepared by oxidizing nicotine with concentrated HNO₃ acid, as described in Organic Syntheses 4, 49. Only 1/3 amounts were used. An excellent yield of the acid was obtained in fairly pure form, m.p. 210°. A sample of pure nicotinic from Eastman Kodak Co. melted at 221-2°C (uncorr). Melting point of nicotinic should be 231°C. (Bernthsen, 1930).

The nicotinic acid was used to make phenol condensation products, to be described later.

It is interesting to note that H. King J. Chem. Soc. 2,2763 (1932) reports 4-nitro 5-(3-pyridyl) pyrazole (1) or its tautomeric form (2) as a regular by-product in 5% yield in the preparation of nicotinic acid by oxidation of nicotine with HNO₃.

\[ \text{(1)} \quad \begin{array}{c}
\text{NO}_2 \quad \text{C} & \text{C} & \text{H} \\
\text{C} & \text{C} & \text{N} \\
\text{C} & \text{H} \\
\end{array} \]

\[ \text{(2)} \quad \begin{array}{c}
\text{NO}_2 \quad \text{C} & \text{C} & \text{H} \\
\text{C} & \text{C} & \text{N} \\
\text{C} & \text{H} \\
\end{array} \]

PART THREE

LITERATURE ON DICARBOXYLEINS.

A large number of dyestuffs have already been prepared from various dibasic acids. The general method of preparation has been the heating of the proper molecular proportions of the dibasic acid with an aromatic amine or phenol, with or without the use of a dehydrating agent. In almost every case, 2 molecules of the phenol react with one molecule of the acid to give a compound analogous in structure to that resulting from the union of phthalic acid and phenol. With the addition of a base such as NaOH, a quinoid structure may develop, leading to the formation of color, and an indicator or dye. The following are a few of those that have been reported. It was noted by the author that the names given to some of the dyes do not in some cases agree with the general method of nomenclature, which is the addition of the suffix "sin" to the acid from which the product is formed.
A. Succineins - Dutt & Thorpe, J.Chem.Soc. 125, 2524 (1924)
Dutt J.Chem.Soc. 1132-8 (1926)
Dutt J.Chem.Soc. 129, 1171 (1926)
P.GERM. 308, 335 (1918) - C.A. 13, 1621 (1919)

B. Camphoreins - Sircar & Dutt, J.Chem.Soc. 121, 1283 (1922)
Sircar & Singh, J.Chem.Soc. 121, 1421 (1922)

C. Itaconeins - Dhar & Dutt, Quart. J. Ind. Chem.Soc. 4, 247 (1927)

D. Citraconeins - Dhar & Dutt, Quart. J. Ind. Chem.Soc. 4, 253 (1927)

E. Sacchareins or Sulfampthaleins - P.Germ. 308, 335 (1918) or
C.A. 13, 1621 (1919)
Dutt - J.Chem. Soc. 121, 2389 (1922) or

E. Diglycolleins - Dey and Dutt, Quart. J. Indian Chem.Soc. 5, 639 (1923)
Read, J.A.C.S., 46, 1936 (1924); 48, 19, 528 (1926)

G. Naunthaleins -
G.F. Jaubert, Ber. 1895, 28, 991.
Terisse, Annalen 1885, 237, 1102.
Tanaka & Morikawa J.Chem.Soc. Japan 51, 121 (1930) or
C.A. 24, 3780 (1930)
Sen & Mukherji - J. Ind. Chem. Soc. 6, 557 (1929) or
C.A. 24, 1107 (1930)
Sen & Sarkar J.A.C.S. 47, 1079 (1925) or C.A. 19, 1567 (1925)

or C.A. 25, 2787 (1931)

The authors report heating resorcinol with acids of the formula \((CH_2)_n(COOH)_2\), where \(n\) is more than 2, in the presence of a condensing agent, e.g. \(ZnCl_2\). Ketonic acids and benzeins are obtained. In an example, resorcinol (2 mols) and adipic acid (1 mol) yield a benzein and a ketonic acid.

\[
\begin{align*}
\text{COOH} & \quad \text{(CH}_2\text{)}_4 \quad +
\text{COOH} \\
\text{(CH}_2\text{)}_4 & \quad \text{O} \\
\text{H} & \quad \text{O} \\
\text{OH} & \quad \text{OH} \\
\text{OH} & \quad \text{OH}
\end{align*}
\]

A. "Benzein"

\[
\begin{align*}
\text{COOH} & \quad \text{(CH}_2\text{)}_4 \\
\text{C=O} & \quad \\
\text{OH} & \quad \\
\text{OH} & \quad \\
\text{OH} & \quad \\
\text{OH}
\end{align*}
\]

"Ketonic Acid"
"A" is called a benzene but should not be, since it makes for confusion; as the compound is a derivative of adipic and not benzoic acid, it should properly be called an adipine. Another instance of this variation in nomenclature is observed in J. E. Gilpin's report in Amer. Chem. J. 1894, 16, 528. He reports that diorcinolsulphophthalein is obtained on heating together orcinol (2 mols) and orthosulphobenzoic acid (1 mol) at 180°. The product is a derivative of the benzoic acid molecule and should hence, strictly speaking, be called a "benzene", not a phthalein.

   Underwood J. A. C. S. 51, 583 (1929).


L. Phthaleins - Sulphonphthaleins - etc.
   Clark & Lubs, J. Wash. Acad. Sci. 6, 483 (1916).

M. Benzeins, Glycerineins, Acroleins:
   Sen & Sarkar, J. A. C. S. 47, 1079 (1925); C.A. 19, 1567 (1925).
   Beil. 2, 1012 (Glycerineins).

N. Gallicins, Benzeins, Steareins, Pyromucains, Salicyleins, Coumareins,
   Isatineins and Furureins.
   Sen & Sirac, Quart. J. Ind. Chem. Soc. 1, 151-172 (1924) or
   C.A. 19, 2150 (1925).

O. Quinolineins:
   Ghosh, J. Chem. Soc. 115, 1102 (1919) or C.A. 14, 278 (1920)
   reported the following:

Dyes from quinolinic acid (A) analogous to the phthaleins were prepared: in comparison with the latter, the effect of the N. atom in the ring is to lighten the color and to diminish the fluorescence; in the dyes from A, the greater the power of an auxochromic group to deepen the color, the greater is its effect on fluorescence. A was prepared by the oxidation in acetone of quinoline with the theoretical amount of 5% MnO₄ at 10°C.
QUINOLINOL was formed on heating (A) and Ph NH$_2$; on cooling crystals separated m.248-51°C.

QUINOLINYL-PHENYLHYDRAZINE was prepared by heating (A) and PhNH$_2$; alcohol was added to the solution aftercooling and PhNH$_2$ was removed from the crystals by washing with ethyl alcohol; m.p.237-8°C (decompn).

RESORCINOL-QUINOLINEIN (B) is obtained on heating a mixture of A and resorcinol at 130-200°C for 2 hours; the cooled fusion was extracted with ethyl alcohol and the dye precipitated from the alcohol with water; it could not be crystallized and m.266-7°C (decompn). A Ag salt was prepared. (catechol -$^+$ note)

CATECHOL-QUINOLINEIN was prepared by heating (A) with phloroglucinol at 130-150°C for 10 minutes; recrystallized from water, a red compound was obtained which m.275-77°C (decompn) and is readily soluble in alcohol. The fusion mixture also contained a small amount of an unknown substance which does not melt 295°C.

PHLOROGLUCINOL-QUINOLINEIN was prepared by heating A and phloroglucinol at 150-150°C for about 10 minutes. On crystallization from water a red compound melting and decomposing at 275-7°C was obtained; very soluble in alcohol.

m-PHENYLENE-DIAMINE-QUINOLINEIN was prepared by heating A and m-C$_6$H$_4$(NH$_2$HCl)$_2$ at 210-220°C for 20-25 minutes. The fusion was extracted with ethyl alcohol and the dye precipitated by the addition of Et$_2$O; m.p. 232-5°C (decompn).

m-DIMETHYL-AMINOPHENOL-QUINOLINEIN was prepared by heating A and meta-H$_2$N-C$_6$H$_4$OH at 120-30°C for 15-20 minutes and raising the temperature slowly to 150°C; the dye was precipitated from the alcohol extract by addition of water; recrystallized from dilute alcohol; m.p. 148-51°C (decompn).

2,4-DIAMINOPHENOL-QUINOLINEIN was prepared by heating A and 2,4- (CLH$_2$H$_2$N) C$_6$H$_4$OH slowly to 180°C; the dye which could not be crystallized was precipitated from the alcohol extract with water; it does not m.290°C.

N.B. These condensations take place without the use of any condensing agent, by simply heating the two constituents together.

Further comment on this work is made later in this paper.

*Note: C.A. reported this, but it should obviously be catechol.
Nicotinylene 2,1 benzimidazole is formed from the condensation of quinolonic acid and o-phenylenediamine by heating equimolar quantities of each at 120-30°. Its formula is:

Noelting & Collins, Ber. 1884, 17, 258, mention phenolquinoline and resorcinoquinoline but few details are given. Phenol and quinolonic acid heated to 120° with sulphuric acid, give a product which dissolves in alkalies with a red color similar to phenolphthalein.

A. W. Dox, J. Am. C. S. 37, 1948 (1915) or C. A. 9, 2532 (1915) reports:

The similarity in behaviour of quinolonic acid and phthalic acid was pointed out by Bernthsen & Mettegang, Ber. 20, 1368 (1887) in 1887. They succeeded also in preparing a condensation product of quinolonic anhydride with resorcin, corresponding to fluorescein, which they named fluorseine. Like fluorescein it was strongly fluorescent and on treatment with bromine, it yielded an eosin-like dye. The writer thought it might be of interest to prepare the analog of phenolphthalein by condensing quinolonic anhydride with phenol and to ascertain whether the resulting product would have the properties of an indicator.

Quinolonic acid was converted into its anhydride by heating with acetic anhydride by means of carbon tetrachloride. Phillips (Ann., 288, 255 (1895) recommends heating one part of the acid with two parts of acetic anhydride at 120°, then gradually raising the temperature to 150°. The writer found that a quantitative yield of the anhydride was obtained by gently heating the mixture until solution was effected, then simply boiling for five minutes. On cooling, the anhydride separated out and after washing with CCl₄ it showed the correct m.p. of 134°C.

Ten grams of quinolonic anhydride, 20 g. phenol, and 8 g. of conc H₂SO₄ were heated in an oil bath at 120° for ten hours. The mixture was then poured into water and the solution boiled until the excess of phenol was expelled. A yellow granular precipitate formed which was collected on a filter, then dissolved in alcohol and purified by boiling with charcoal. A nearly colorless solution was obtained which on evaporating and diluting with water became milky and finally yielded a yellowish granular sediment. The product was analysed for nitrogen by the Kjeldahl-Dunning method.

Like phenolphthalein, phenolquinoline n is a brilliant indicator, giving an intense pink color with alkalies which is immediately discharged on acidifying. On account of the basic nature of the pyridine nucleus, the end point might be expected to be somewhat different from that of phenolphthalein, but this was not determined. On account of the present cost of quinolonic acid, it is not probable that the indicator will find any extensive application in titrimetric work. The analogy, however, is considered of sufficient interest to warrant this brief paper.

Dox does not appear to have been aware of Noelting & Collins work or he might have referred to it.
Further work was reported on one of Ghosh's compounds in 1932 by P. Gupta & A.C. Sircar. J. Ind. Chem. Soc. 9, 145 (1932)--Reactions of Quinolinic anhydride and Phenylhydrazine--four types of reactions were reported as being possible of taking place, depending on the experimental conditions. However, quinolinic, as well as phthalic and naphthalic anhydrides on condensation with unsymmetrical methylphenylhydrazine, yield only compounds of type one. Ghosh's product was of type number one.

Since quinolinic acid evolves carbon dioxide and is converted to nicotinic, it is surmised that the same change took place under conditions of the experiment and the resulting nicotinic acid reacted with phenylhydrazine to form phenylhydrazinenicotinate.

0.5 g Quinolinic + 20 cc Phenylhydrazine $\xrightarrow{200-30^\circ}$ for 20 min

Yellow compound, from alcohol, m.p. 189°.

However, Ghosh's work was not criticized until 1926, by Tewari & Dutt--J. Ind. Chem. Soc. 3, 161 (1926) In the first of a series of three articles on the effect of N on color of dyes, they said;

"Ghosh concluded from his work that the effect of N in the ring was to lighten the color; but he did not measure the intensities of color in the two series. Quantitative experiments on absorption spectra, now in progress, tend to show the effect of the N atom in the ring is to intensify the color, instead of diminishing it. To obtain conclusive results, further dyes have been prepared by condensing B-phenylpyridinedicarboxylic acid with aromatic amino and hydroxy compounds, which are an alogous in constitution to the dipheneins except that they contain a N atom in the ring. These compounds are much more intense in color than the corresponding dipheneins.

Dyes derived from Imidazole--dicarboxylic acid A--to establish that the effect of a doubly linked N atom in a ring in a dye molecule is not to lighten the color, as Ghosh said, but on the contrary to intensify it. Quantitative measurements of absorption spectra tend to prove this. With this object in view, A was condensed with aromatic amino and hydroxy compounds & dyes obtained. The condensation as a rule, takes place without a condensing agent, but it is more suitable to use small quantities of conc. sulphuric acid or Sn Cl₂ to get better yields. The same applies to condensations in the article part 1. Also the phenols used were the same.
Phenol-imidazomaleeine

\[ C_3H_2N_2 \xrightarrow{\text{CO-O}} C(C_6H_4OH)_2 \]

Resorcinol-imidazomaleeine

\[ C_3H_2N_2 \xrightarrow{\text{CO-O}} C<\text{C}_6\text{H}_3\text{OH} \]

Part III. Tewari & Dutt J. Ind. Chem. Soc. 5, 59 (1928)
Dyes derived from 1:2:3: quinolinetrificarboxylic acid; 3 carboxy-acidic acid condensed with ar. amino & OH compounds.

\begin{center}
\includegraphics[width=0.5\textwidth]{dyeformula.png}
\end{center}

(With resorcinol, it yields an acridine.)

Beilstein IV (283) reports a dye formed by heating quinolinic acid anhydride & Hydroxyhydroquinone.

**Formula I** -- Acid C_{19}H_{13}O_{6}N_{4}

\[ C_5H_3(COOH)N \]

**Formula II** -- C_{19}H_{11}O_{7}N_{4}

\[ \text{O} \]

Beilstein calls it quinolinic acid -- dibydroxyflourescein--

C. Engler, Ber. 27, 1789 (1894) also prepared Ghosh's Quinolinanil. He called it Phenylquinolinic acid amide, NC\textsubscript{5}H\textsubscript{5}(CO)\textsubscript{2}N.C\textsubscript{6}H\textsubscript{5}. He obtained it by heating the imide with somewhat more than the calculated amount of aniline in a reflux condenser, until the original odour of NH\textsubscript{3} disappeared. After the excess aniline has been removed with a very little alcohol out of the residual crystalline mass, one crystallizes out of boiling alcohol and gets the anil thisway in the form of a silky, lustrous, felty needles of m. 228 (uncorr.) which are nearly insol. in water and difficultly sol. in alc.

**Cal.**

<table>
<thead>
<tr>
<th>C</th>
<th>69.64</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>3.57</td>
</tr>
<tr>
<td>N</td>
<td>12.5</td>
</tr>
</tbody>
</table>

**Found**

<table>
<thead>
<tr>
<th>C</th>
<th>69.85</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>3.48</td>
</tr>
<tr>
<td>N</td>
<td>12.83</td>
</tr>
</tbody>
</table>
Part FOUR: CONDENSATIONS WITH QUINOLINIC ACID, A.

A series of preliminary test fusions were run, using the following general method:

0.2 g. of acid were intimately mixed with 0.4 g. of the phenol, moistened with a drop or two of concentrated sulfuric acid, and heated varying lengths of time, usually 1-2 hours, on a glycerine bath at 140-150° C.

1. 0.2 g. A, 0.4 g. of *o*-cresol* and two drops conc. H₂SO₄ were heated one hour at 140°. After cooling, an alcohol extract of the fusion was tested with base (NaOH solution). It was a brilliant cherry purple color changing very sharply to an amber yellow in acid solution (addition of dilute HCl solution). Some of the alcohol extract with a few drops of conc. HNO₃ reacted violently— an orange red colored ppt. was formed. This solution on dilution gave an excellent yellow-colorless color change in base-acid. However, this is probably due to the formation of a substituted nitrophenol.

Note 1: An alc. sol. of *o*-cresol* alone with base gives only an amber colored darkening. With HCl acid, the sol. clears up and *o*-cresol* separates out as an oily liquid on top. No color reaction.

2. 0.2 g. A, 0.4 g. *m*-cresol* and two drops conc. H₂SO₄ heated at 150° the resulting fusion was completely soluble in alcohol, but no color change was observed on addition of acid or base. In acid, a white emulsion is formed.

Note 2: An alc. sol. of *m*-cresol* and a few drops conc. HNO₃ form a dark red color. Made basic with KOH sol., color becomes a beautiful green.

3. 0.2 g. A, 0.4 g. *p*-cresol* and two drops conc. sulfuric acid were heated one hour at 150°. Not all the quinolinic was used up in the reaction since there was a white alcohol insoluble solid left in the reaction tube. Alcohol extract made basic gave a white emulsion. No color change observed with acid-base. No fusion apparently took place.

4. 0.2 g. A, 0.4 g. *o*-nitrophenol* and conc. sulfuric acid heated at 150° for an hour gave a black solid char. On testing, no fusion seemed to have occurred.

Note 3: *o*-nitrophenol* alone is an excellent yellow-colorless indicator.

5. 0.2 g. A, 0.4 g. *p*-cinnol* and conc. sulfuric acid heated at 140° for an hour—a cherry red fusion resulted; alc. extract was dark orange color in base, light yellow in acid. After standing, a deep green fluorescence was observed in the alkaline solution of the original alcohol extract.
6. 0.2 g. A, 0.4 g. "m-nitrotoluol" and conc. sulfuric acid—no reaction took place.

7. 0.2 g. A, 0.4 g. "p-xylenol" and conc. sulfuric acid—an alcohol extract of the fusion gave no color change with acid base. A water extract made basic gave a beautiful light blue color, colorless in acid.

8. 0.2 g. A, 0.4 g. "m-xylenol" and conc. sulfuric acid—cherry red viscous fusion—alcohol extract is yellow in base and colorless in acid. However, the change is very slow and poor.

9. 0.2 g. A, 0.4 g. "p-xylenol" and conc. sulfuric acid at 150°. Dark orange solid fusion. Alcohol extract tends towards a greenish color. No color change with acid base. The fusion was probably not heated long enough. Water extract might have been made, because a dye should have formed here.

10. 0.2 g. A, 0.4 g. "2,4 dinitrophenol" and conc. sulfuric acid for one hour—black solid char—no fusion.

11. 0.2 g. A, 0.4 g. "a-naphthol" and conc. sulfuric acid heated at 150° for one hour—formed a black-brown solid char. No color change was observed on addition of acid-base to an alcohol extract.

12. 0.2 g. A, 0.4 g. "a-naphthol" and conc. sulfuric acid at 150°. No fusion took place.

13. 0.2 g. A, 0.4 g. "thymol" and sulfuric acid—heated only a few minutes at 140°. On cooling, it was seen that fusion was incomplete since separate layers appeared. Another trial of longer time was made and the whole mass charred badly.

14. 0.2 g. A, 0.4 g. "o-nitrotoluol" and sulfuric acid—incomplete fusion—no color change when alc. extract treated with alkali-acid.

15. 0.2 g. A, 0.4 g. "phenol" and conc. sulfuric acid heated at 150° results in a cherry-colored fusion, viscous mass, which is soluble in alcohol. An alcohol extract gives a pink color in base and colorless in acid—sharp change was observed. This confirms A.W. Dox's phenolquinolone in prepared from quinolinic anhydride and phenol.
16. 0.2 g. A, 0.4 g. "resorcinol" and conc. sulfuric acid heated at 150° for an hour-fusion was incomplete--no color change observed--probably not heated long enough nor high enough temperature.

17. 0.2 g. A, 0.4 g. "hydroquinone" and conc. sulfuric acid--fusion appeared incomplete--no color change with alkali-acid.

18. 0.2 g. A, 0.4 g. "p-nitrotoluol" and conc. sulfuric acid--no fusion.

19. 0.2 g. A, 0.4 g. "trinitroresorcinol" and conc. sulfuric acid. No fusion.

20. 0.2 g. A, 0.4 g. "1-8 dihydroxy-naphthalene 3,6, disulfonic acid" & a few drops of conc. sulfuric acid heated one hour at 150°--no fusion.

21. 0.2 g. A, 0.4 g. "m-phenylene-diamine" and conc. sulfuric acid at 150°. Alkaline alcohol extract was orange in color with a very pronounced green fluorescence. m-phenylene-diamine alone in alcohol does not fluoresce. However a similar test was made with nicotinic acid and the same amine. It gave a similarly colored fusion, the alcohol extract having a very green fluorescence on being made basic. It may thus be the dye of nicotinic acid which was responsible for the fluorescence in the first case also. Ghosh does not mention anything about nicotinelines or suggest that his phenols might have reacted with the nicotinic from his decomposed quinolinic acid. Although quinolinic does not melt till 190°, it begins to give off carbon dioxide at 140° and may be completely decomposed at 160°. [Lippman & Fleissner, M.8, 312 (1887).]

22. 0.2 g. A, 0.4 g. "diphenylamine" and conc. sulfuric acid, heated at 150°. Black char resulted. Alcohol extract was colored blue. No color change with acid base, and hence probably no fusion.

23. 2 g. "quinolinic acid" 4.0 g. C- cresol" were heated alone at 180° for two hours the same way that Ghosh conducted his fusions. After cooling, water was added to the fusion extract, as well as the water extract, gave no color change with acid-base. It appeared that conc. sulfuric acid or some sort of condensing agent was necessary for the two to react.
24. 2 g. A, 4 g. "o-cresol" and 2 c.c. conc. sulfuric acid were heated in a T.T. for two hours on a glycerine bath. (Quinolinic was Eastman Kodak's.) As it was heated up past 160°C, the quinolinic began to dissolve, a gas being given off. At 170-180°C all the solid had gone into solution. After cooling, a solid dark red sticky mass was formed. This was first extracted with alcohol, and then the dye was precipitated by the addition of dilute HCl solution and water. It was filtered off by suction pump. The weight of this reddish solid fairly dry was one gram. It was dissolved in acetone and allowed to crystallize. The filtrate was evaporated down over the bunsen flame; this was equivalent to distillation with steam; i.e. excess o-cresol should have been eliminated. On cooling, it solidified totally, forming a very sticky resinous deep red solid. This was found to be soluble in acetone and alcohol. It was dissolved up in acetone and allowed to crystallize. After filtering off the last bit of acetone, the crystals were washed with alcohol and ether, in which they were only slightly soluble.

The one gram of solid which was dissolved in acetone would not crystallize from it. It was dissolved in water and the acetone boiled off; a black-charred solid resulted. In an attempt to pursue a different method of isolation, solutions were all mixed again and made basic with conc. NaOH solution. The color became deep red, and a white precipitate appeared. This was filtered off, and later proved to be NaCl. The filtrate was evaporated to dryness in the air. It left a pinkish colored solid, an alcohol solution of which gave a pink colorless change with base-acid. The solid was not very soluble in water nor alcohol. It could not be melted up to 260°C. It burned with a luminous flame, leaving a tiny bit of white residue, proving it to be impure.

25. 2.0 g. A, (as prepared by author) 6.0 g. or α-4 diaminophenol hydrochloride were slowly heated without any condensing agents up to 180°C and kept at this point for a few minutes. No dye could be extracted from half the mass with alcohol, although Ghosh reported he got one.

To the other half, 1 c.c. of conc. sulfuric acid was added. The solid turned blue at the point of contact. The reaction tube was reheated at 210°C for half an hour. No fusion appeared to take place. No dye could be extracted.

Note 4: Diaminophenol alone in alcohol solution on addition of base goes from red, green to dark greenish blue color.

26. 0.2 g. A, 0.4 g. 8-OH quinoline and conc. sulfuric were heated together. On testing the resulting fusion, no change in properties was apparent.
27. 2.0 g of 4.0 g of Phloroglucinol alone were heated at 130-150° for ten minutes, according to Ghosh's directions. No melting or change of any sort took place. It was heated at the same temperature for half an hour and still no reaction was observed.

The mixture was then slowly heated up to 180°, below the m.p. of phloroglucinol which is 200-209°. Here a melting occurred, the mixture turning red. When the heat was removed, the melting stopped. Accordingly, the contents were heated for thirty five minutes at 170-180°.

After cooling, water was added to the melt. A dark red solution resulted, leaving considerable brown ppt that did not dissolve. On evaporation from the water solution, a light brown compound melting at 121-125° was obtained weighing approximately 4.0 g when dry.

Ghosh reported m.p. 275-7° Some of this was dissolved in two drops of conc. NaOH solution. A deep red color resulted. With the addition of 2-3 drops of conc HCl, a yellow color with a heavy white ppt. was formed. The color change was not particularly sharp.

The residue from the water solution was dissolved in alcohol and allowed to stand in the air to crystallize out. On evaporation, a light brown colored solid was left. Yield of dry solid was 0.6 to 0.8 g. A m.p. was run. It melted with excess charring and decomposition at 215-23°. whereas the solid of the water extract on melting turned a cherry red color.

The solid of the alcohol extract was insoluble in water when tested, but soluble in conc. NaOH solution giving a deep cherry-red color. With addition of conc HCl, a heavy white ppt. was thrown down.

28. 0.5 g. quinolin and 2 c.c. aniline were heated in a test tube by means of a glycerine bath at 170-180°. After two or three minutes the acid all went into solution. On cooling, crystals separated out.

With the addition of 35 c.c. alcohol, most of the crystals redissolved. A melting point was run on the first crop — it was 330° C. (Engler reported 226°). The crystals which appeared from the evaporation of the alcohol solution melted at 155-90° with charring and decomposition.

29. 0.5 g. A, (quinolin) were heated with 2 c.c. phenylhydrazine for one hour and a half at 170-90°. On testing the resulting fusion, no reaction seemed to have taken place.

30. 2.0 g. Quinolin, 4.0 g. resorcinol were heated without a condensing agent at 180° for 2 hours. On cooling, the fusion was extracted with alcohol, from which it crystallized in clusters of long needles. A rough m.p. ran 150-70°, well above that of resorcinol m.p. 116°. An alc. solution of the solid with addition of base gave an orange green fluorescence. Ghosh reported the m.p. as 226-7°.

Note: Resorcinol alone - alcoholic solution made basic is orange, and there is a sharp change to colorless on acidifying. It is also soluble in basic acetone with a very green fluorescence, and an orange-brown color, at first bright yellow which quickly darkens.
CONCLUSIONS.

Experiments have been run to confirm other workers' results and to establish new ones. Some, such as phenol-quinolinein, m-phenylene-diamine-quinolinein, phlorogluconol-quinolinein, quinolinanil, have been positively confirmed, while a few, as already pointed out, are doubted. Of the new dyes investigated, ordinol-quinolinein and o-cresolquinolinein show the best promise.
PART FIVE: CONDENSATIONS WITH NICOTINIC ACID B.

The same procedure for the fusions was followed here as in Part four, namely:

0.2 g. of acid were intimately mixed with 0.4 g. of the phenol, moistened with 2-3 drops of concentrated sulfuric acid, and heated 1-2 hours in a large test tube on a glycerine bath at 140-150°.

31. 0.2 g. B were heated with 0.4 g. orcinol and sulfuric acid. The fusion on cooling was extracted with alcohol. The alcohol extract made basic gave a beautiful dark red color, which changed very sharply to yellow on acidifying.

32. 0.2 g. B, 0.4 g. dinitrophenol were heated with sulfuric. No reaction appeared to have occurred.

33. 0.2 g. B, 0.4 g. alpha-naphthol and sulfuric were heated together at 150°. On cooling, the melt was a black solid char. No dye could be extracted.

34. 0.2 g. B, 0.4 g. o-cresol, and sulfuric acid were heated at 150° for only a few minutes. An alcohol extract with 5% KOH solution gave a beautiful green color, which changed suddenly and sharply to pink on acidification. The color change was observed clearly in very diluted solutions.

35. 0.2 g. B, 0.4 g. beta-naphthol and sulfuric acid were heated. Black solid char. Some of the water extract with base gives dark brownish yellow color, changing to light green in acid. A better change was observed with the alcohol extract.

36. 0.2 g. B, 0.4 g. o-cresol and sulfuric. Confirmed previous fusion number 34.

37. 0.2 g. B, 0.4 g. beta-naphthol -- same results as in trial 35. No definite sharp colors however with acid-base.

38. 0.2 g. B, 0.4 g. m-phenylene-diamine and sulfuric heated at 150° for an hour. Color of alcohol extract was reddish orange, with a very deep and pronounced green fluorescence.

39. 0.2 g. B, 0.4 g. diphenylamine and sulfuric. Fusion on cooling was a greenish black viscous liquid. A circle of blue was observed around the top of the T.T. No color change with addition of acid-base to the alcohol extract.
CONCLUSION:

Nicotinic acid forms two interesting dyes with o-cresol and m-phenylene-diamine which the author has not had time to isolate and describe fully. The o-cresol derivative is especially interesting since it gives such a good color change with acid-base.

PART SIX. OTHER DICARBOXYLIC ACID FUSIONS.

General procedure of the fusions was the same as in Parts Four and Five.

40. 0.2 g. Benzoic, 0.4 g. Phenol and 2-3 drops conc. sulfuric were heated at 150° for one hour. The fusion on cooling separated into two layers, the upper one solid, of a dark orange color. The alcohol extract, colored dark cherry red, gave with base-acid a very sharp color change of cherry purple to colorless. (odor of benzophenone in the fusion). After a few minutes standing, the dark cherry colored basic solution turned almost colorless; with the addition of acid, it became milky orange, which was cleared up by addition of base to a faint pink color.

About 2 weeks later, some of the same alcohol extract, on testing with base-acid, gave a sharp pink to yellow colorless change.

41. 0.2 g. 3-nitrophthalic anhydride, 0.4 g. o-cresol and 2-3 drops sulfuric. Melt is a very viscous liquid. An alcohol extract made very dilute gave with base-acid an excellent, sharp pink-colorless color change.

42. 2.0 g. Oxalic, 4.0 g. Phenol and 2.0 g. granular ZnCl₂ intimately mixed, were heated up to 150°. Within ten minutes, the mass melted and the color changed from white to bright orange; kept at 140-50° the mixture continued to boil gently. After half an hour of heating, the fusion was poured while still hot into 25 c.c. of distilled water. The orange colored liquid was decanted from the ZnCl₂ and allowed to evaporate. The whole melt was then extracted with alcohol. On crystallization from alcohol, a reddish orange solid, possibly a phenoxazolein was obtained, m.p. 105-10°C (uncorr) which with base-acid gave a sharp intense red-yellow color change. The solid was easily soluble in water and alcohol.
The experiment was repeated, 2.0 g. of anhydrous oxalic acid being heated with 4.0 g. phenol. After 20 minutes, no color change appeared, so some granular ZnCl₂ was added. An orange color immediately appeared, and the liquid began to boil strongly.

After cooling, the mixture was filtered and the filtrate allowed to evaporate. A very dark red solid with a bright green fluorescence was formed. It dissolved readily in alcohol with a yellow color. With base the color turned intense red, with acid it turned yellow very sharply. The acetone solution is also yellow.

43. 2.0 g. Oxalic, 4.0 g. Resorcinol and 2 g. anhydrous AlCl₃ were heated up to 150°C for 1 1/2 hour. There was no reaction or melting, so the temperature was raised gradually to 200°C where the solid mass turned pinkish color.

On testing the cooled fusion, it seemed that no fusion had taken place.

44. 2.0 g. Oxalic, 4.0 g. Catechol, and 2 g. granular ZnCl₂ were heated in a glycerine bath at 120-40°C for an hour. The color of the melt turned intense red. After cooling, an alcohol extract with a base-acid gave a beautiful blue-red color change.

However, catechol and ZnCl₂ were heated alone at 150°C and a red colored melt developed; an alcohol extract of which gave the same color changes with base-acid.

Oxalic acid and ZnCl₂ heated alone give no color change.

45. 2.0 g. Oxalic, 4.0 g. Orceinol and 2.0 g. ZnCl₂ were heated at 120-50°C for 1 hour. The cooled melt was extracted with alcohol. Alc. sol. was reddish orange in color; with base it became dark red, with intense green fluorescence; with acid, color remains lighter red, but fluorescence disappears. Results seem to indicate an orceinol-oxalate.

46. 2.0 g. Oxalic, 4.0 g. Pyrogallic acid and 2.0 g. ZnCl₂ heated at 120-50°C for two hours. Color of massat first turned purple, and later seemed to char a little. The cooled viscous liquid was extracted with alcohol. Alc. sol. has a very green fluorescence. Not any particular color change with base-acid however. (purple-yellow if any
47. 1.0 g. crystalline Oxalic \( (\text{H}_2\text{C}_2\text{O}_4) \), 2.0 g. \( \text{O}-\text{aminophenol} \) were heated at 180° for \( \frac{1}{2} \) an hour, according to the directions of C.A. 23, 2430 (1929). The color of the mixture did not turn red, as reported above, nor did the mixture fuse at any time for the next \( \frac{1}{2} \) hour. The trial was repeated with the same observations.

48. 1.0 g. Oxalic, 2.0 g. \( \text{O}-\text{aminophenol} \), and 1.0 g. \( \text{ZnCl}_2 \) heated at 180° for 1 hour. Color of the cooled solid melt was purplish black. An alcohol solution was red with slight green fluorescence. With acid-base, the alcohol extract turned color slowly from purplish to amber.

49. 1.0 g. Saccharin, 2.0 g. Orcinol and 3-4 drops of sulfuric acid were heated for 1 hour at 140° according to the method of Dutt, J.Chem. Soc. 121, 2 389 (1922). The melt turned a blood red color. On cooling, the whole mass solidified. An alcohol solution was orange-red in color with a slight green fluorescence. Addition of alkali produced an intense green fluorescence. This is a positive confirmation (i.e. from general observations) of an "orcinol-saccharin".

50. 2.0 g. Succinio anhydride, 4.0 g. Catechol, and 2 drops of conc. sulfuric acid were heated. At 150°, the whole mass had melted to a red color. It was further heated for an hour at 140°. An alcohol solution had an intense green fluorescence; the alkali solution was a green color also, turning to a pink color very sharply in acid.

However, catechol alone gives a very similar reaction.

51. 2.0 g. Citric acid, 4.0 g. 2,4-diamino-phenol HCl and a few drops sulfuric were heated for \( \frac{1}{2} \) hour at 140°, then up to 180°. An alcohol solution of the cooled mass had a very intense blue fluorescence.