[Contributions from the Chemical Laboratory of Cornell University.]

TETRAIODOPHENOLPHTHALEIN AND TETRAIODOPHENOLTETRACHLOROPHTHALEIN AND SOME OF THEIR DERIVATIVES.

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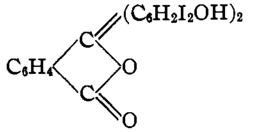
Historical.

Tetraiodophenolphthalein was first prepared by Classen and Löb.[1] Six g. of phenolphthalein was dissolved in 100 cc of water containing 8 g. of sodium hydroxide and to this was added at room temperature a solution containing 20 g. of iodine (8 atoms[2]) and 20 g. of potassium iodide in 100 cc. of water. The color of the solution gradually changed from red to blue and was a yellowish brown after all the iodine had been added. On acidification a porridge-like mass was precipitated which, after washing, was purified by again dissolving in caustic soda and precipitating with acid. The precipitate was then suspended in water and steam passed into the mixture. The product obtained in this way was an amorphous, almost white, powder which decomposed without melting at about 220°, giving off iodine. It dissolves easily in alkalies, with which it may be boiled without undergoing any change. It is insoluble in water and acids, difficultly soluble in alcohol, but somewhat more easily soluble in glacial acetic acid, chloroform and ether. Analysis confirmed the formula $C_{20}H_{10}O_4I_4$. As it is quite analogous in its conduct to Baeyer's tetrabromophenolphthalein[3] it was given the formula



The compound was obtained in the form of pale yellow granular crystals by dissolving the amorphous product in alcoholic sodium hydroxide solution and precipitating at the boiling point with alcoholic hydrochloric acid.

Just as Baeyer[4] found in the case of phenolphthalein that the red color of the sodium salt disappears on the addition of a large excess of alkali with a breaking of the anhydride condition, so the blue sodium salt of tetraiodophenolphthalein is converted into the colorless salt of the corresponding carbinolcarboxylic acid by treatment with alkali.

When a strong alkaline solution of tetraiodophenolphthalein was cooled

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[1] *Ber.*, **28**, 1603 (1895).

[2] This is 4.5% more than the calculated amount of iodine (8 atoms).

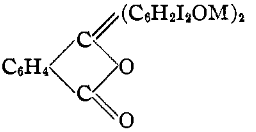
[3] *Ann.*, **202**, 68 (1880).

[4] *Loc. cit.*

to —5° and hydrochloric acid also cooled below 0° added, with continual cooling, a yellowish brown precipitate separated out. When dried on a porous plate, taken up in chloroform, precipitated with ligroin and then dried *in vacuo* at ordinary temperatures, analyses showed it to be the tetraiodophenolphthaleincarbinolcarboxylic acid differing from the phthalein only by one molecule of water. Most characteristic is the difference in solubility in chloroform and ether in which the acid dissolves very readily. It dissolves in caustic soda with a blue color and gives the above-described tetraiodophenolphthalein on precipitating it without cooling with acids. It may also be converted into the last named compound by heating it to about 100°.

Iodination of phenolphthalein was also carried out in solutions of ammonium hydroxide, barium hydroxide, alcohol, borax and by the electrolysis of an alkaline solution containing potassium iodide. The tetraiodo product resulted in all cases.

The authors state that the alkali salts of tetraiodophenolphthalein were obtained by evaporation of the neutral solutions of the phthalein in the alkalies. The sodium and potassium salts form pure blue prisms easily soluble in water and alcohol. They have the following structure:



The salts of various other metals were obtained by treating solutions of the sodium salt with solutions of metallic salts.

Patents were taken out by Classen covering the foregoing methods for the preparation of iodine derivatives of phenolphthalein.[1]

In the first patent[2] the method for iodinating in alkaline solution is modified by increasing the strength of alkali in which the phenolphthalein is dissolved from 2 *N* to 10 *N*. The amount of water in which the potassium iodide and iodine are dissolved is also changed so that the concentration of alkali in the reaction mixture is twice that used in the above method of preparation. The patent states that if the reaction mixture is kept below 20° and acidified, the carbinolcarboxylic acid is precipitated. It is purified by dissolving the undried product in chloroform and precipitating it with ligroin. If the reaction mixture is heated for some time on a steam bath and then acidified, tetraiodophenolphthalein is precipitated.

A patent was also taken out by Kalle & Company for the preparation

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[1] D. R. P. 85,930, Frdl., 4, 1090; D. R. P. 87,785, *Ibid.*, 4, 1091; D. R. P. 88,390, *Ibid.*, 4, 1093; D. R. P. 86,069, *Ibid.*, 4, 1094.

[2] D. R. P. 85,930, Frdl., 4, 1090.

of tetraiodophenolphthalein by the action of iodine chloride on phenolphthalein in hydrochloric acid solution or glacial acetic acid.[1]

This investigation was undertaken for the purpose of studying the effect on the chemical conduct and general properties of phenolphthalein and phenoltetrachlorophthalein of the introduction of iodine into the phenol part of the phthalein molecule, and to further study the relation of constitution to color in this class of compounds.

A review of the investigations carried out to determine the relationship between color and constitution of the phthaleins and their salts will be found in papers previously published from this laboratory.[2]

Experimental.

In this investigation the iodine determinations were made either by the lime method described by Delbridge[3] or by the permanganate oxidation method of Seeker and Mathewson.[4] Both methods were modified somewhat.

In the lime method some calcium iodate is formed[5] which must be reduced before adding the silver nitrate, while the temperature must be kept down during the acidification with nitric acid in order to prevent the loss of iodine by the oxidation of the hydriodic acid liberated. After heating the substance with lime in the usual way, the contents of the tube was emptied into a flask containing 100 cc. of water, 5 cc. of a saturated solution of sulfur dioxide was added and the flask shaken. The mixture was then cooled to about 15° and 6 N nitric acid added gradually in portions of 10 to 25 cc. The flask was shaken during the addition of the acid and cooled so that no rise in temperature occurred. About 125 cc. of the acid was required to dissolve the lime completely. When solution was complete an *excess* of 0.1 N silver nitrate was added, the carbon, insoluble material and silver iodide filtered off, and the silver nitrate in the filtrate titrated with ammonium thiocyanate, using ferric ammonium sulfate as indicator.

In the simultaneous determination of iodine and chlorine the same procedure was followed except that the carbon and insoluble material were filtered off before the addition of silver nitrate and the precipitated halides were collected on weighed Gooch crucibles and their weight determined after drying at 145°. From the weight of the silver halides and the volume of 0.1 N silver nitrate required to precipitate them,

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[1] D. R. P. 143,596, Frdl., **7**, 631.

[2] *Am. Chem. J.*, **42**, 183 (1909); THIS JOURNAL, **36**, 680 (1914); *Ibid.*, **37**, 1201 (1915).

[3] *Am. Chem. J.*, **41**, 397 (1909).

[4] *Chem. News*, **103**, 61 (1911).

[5] Meyer, "Analyse und Konstitutionsermittelung Organischer Verbindungen," 1909, p. 206.

the percentages of iodine and chlorine in the original compound can be calculated by means of the following formulas:[1]

Percentage of iodine $= 138.77B - 1.9892C/A$
Percentage of chlorine $= 0.9103C - 38.769B/A$
in which A = weight of substance taken.
B = weight of silver halides.
C = the volume in cc. of 0.1 N silver nitrate solution required to precipitate the silver halides.

As a check upon this indirect method of analysis, the silver halides were heated to just below the fusion point and treated with dry chlorine. This replaced all of the iodine in the silver iodide by chlorine. From the loss in weight and the weight of the silver halides, the halogen content of the original compound can be calculated from the formulas

Percentage of iodine $= 138.77D/A$.
Percentage of chlorine $= 24.738B - 63.511D/A$.
in which A = weight of substance taken.
B = weight of silver halides.
D = loss in weight of the silver halides on treatment with chlorine.

The permanganate oxidation method is especially applicable in the case of compounds containing iodine and chlorine or bromine, but it may be employed to advantage where only iodine is present, for it is fully as accurate and quite as rapid as the lime method where the acidification at a low temperature requires considerable time. If the permanganate oxidation method is modified by titrating the excess of silver nitrate instead of weighing the silver iodide, the time required is considerably shorter than in the lime method. The method of Seeker and Mathewson was followed except that an excess of 0.1 N silver nitrate was added and the silver iodide filtered off on a hardened filter and washed thoroughly with 1% nitric acid. The filtrate was treated with 10 cc. of conc. nitric acid, and the silver nitrate titrated as in the lime method.

That the two methods as modified give concordant results is shown by the following analyses:

		Substance. Gram.	0.1 N silver nitrate. Cc.	Iodine. %.
Lime	I	0.3675	17.68	61.06
Method	II	0.4026	19.42	61.22
Oxidation	III	0.4564	21.94	61.01
Method	IV	0.4096	19.70	61.04

Similar results were obtained throughout this investigation and good agreement with the theory was obtained by both methods when pure compounds were analyzed.

The results for iodine by the oxidation method were occasionally found to run a little higher when the silver iodide was weighed than when the excess of silver nitrate was titrated. This was found to be due to small

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[1] *Am. Chem. J.*, **41**, 380 (1909); THIS JOURNAL, **36**, 702 (1914).

amounts of suspended material in the solution after treatment with sulfur dioxide. By filtering the solution through a hardened filter before adding the silver nitrate, results were obtained which were in complete accord, consequently when the titrations were checked by weighing the silver iodide this additional modification was made in the oxidation method.

Tetraiodophenolphthalein.—This compound was prepared by treating phenolphthalein in alkaline solution with a little more than the calculated amount of iodine. It was found that the method described in the patent[1] gave small amounts of a tar-like material which colored the phthalein yellowish brown and rendered it exceedingly difficult to purify. This material was formed in much smaller amounts when the iodination was carried out in more dilute alkaline solution, hence the method described in the paper[2] of Classen and Löb was followed with some modifications.

The phenolphthalein used was a pure white product which darkened at 250° and melted at 254°. It dissolved completely in 2% alkali and hence was free from fluoran. The iodine used was the resublimed material.

The procedure in iodinating the phthalein was as follows: Thirty g. of phenolphthalein was dissolved in 500 cc. of 2 *N* sodium hydroxide. This solution was stirred mechanically and to it was added, in the course of half an hour, a solution containing 100 g. of iodine and 120 g. of potassium iodide in 500 cc. of water. The color darkened perceptibly and became a reddish blue after all of the iodine had been added. The reaction mixture was stirred for 8 hours. No apparent change in color took place in this time.

Acidification with strong hydrochloric acid as directed by Classen and Löb not only precipitates the phthalein but liberates some of the combined iodine in the inorganic salts, which gives the phthalein a deep brown color difficult to remove. To minimize this liberation of iodine, the reaction mixture was carefully neutralized with 2 *N* acetic acid while being mechanically stirred. A grayish white precipitate settled out which was readily filtered off with the aid of suction. The filtrate had a slight yellow color. It gave no precipitate with hydrochloric acid but darkened in color, due to the liberation of iodine. The precipitate was dissolved in 2% alkali and the solution acidified with acetic acid, an excess of the acid being avoided on account of the solubility of the phthalein in acetic acid. The precipitate when filtered off had a pale yellow color. The filtrate contained some free iodine. The phthalein was again dissolved in 2% alkali, the solution strongly acidified with hydrochloric acid and steam passed through it to coagulate the precipitate. The product thus obtained, when washed free from chlorides and air-dried had a slight tinge of yellow.

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[1] D. R. P. 85,930, Frdl., 4, 1090.

[2] *Ber.*, 28, 1603 (1895).

Yield, 87% of the theoretical calculated from the amount of phenolphthalein used.

The phthalein is difficultly soluble in methyl alcohol, ethyl alcohol, ether, chloroform, acetone, benzene, ethyl acetate and nitrobenzene, but readily soluble in pyridine. Acetone and a mixture of acetone and absolute ethyl alcohol were found to be the best solvents for use in purifying the phthalein although large volumes of these solvents had to be used on account of its slight solubility. By crystallization from acetone and then from acetone-ethyl alcohol, a perfectly colorless product was obtained in the form of microscopic needles. It decomposes at 270–272°[1] with the evolution of iodine and becomes brown. At 288–290° it becomes viscous, and changes to a brown liquid at 307–308°. The phthalein lost no weight in an electrically heated tube[2] at 150°. The air-dried sample was analyzed for iodine by the lime method.

Subst., (I) 0.4414, (II) 0.4113; cc. 0.1 *N* $AgNO_3$, (I) 21.48, (II) 19.99.
Calc. for $C_{20}H_{10}I_4O_4$: I, 61.77. Found: (I) 61.76, (II) 61.69.

The phthalein dissolves in alkalies with a reddish blue color which rapidly fades on standing and finally the solution becomes colorless. This tendency is more marked than in the case of phenolphthalein. In thin layers the color of the alkaline solution is blue. The compound is stable in solid form but its acetone solution becomes colored yellow on long standing, probably due to the liberation of iodine. The alkaline solution is less sensitive to carbon dioxide than that of phenolphthalein.

An attempt was made to prepare the carbinolcarboxylic acid by the method described by Classen and Löb. Five g. of the pure tetraiodophenolphthalein was dissolved in 50 cc. of 6 *N* sodium hydroxide. The solution had a light yellowish green color. It was diluted to 1.5 *N* and cooled to —12°. It then had only a faint yellow color. This alkaline solution was added to an excess of 6 *N* hydrochloric acid cooled to —7°. The temperature of the reaction mixture was not allowed to go above —2°. A *white* flocculent precipitate came down which readily settled. The supernatant liquid was decanted off, water added, the precipitate allowed to settle and the supernatant liquid again poured off. The precipitate was washed in this way until the wash water gave no test for chlorides. The precipitate was then filtered off and dried to constant weight *in vacuo*. A portion was then further dried by heating.

Subst., 0.4546: loss at 110°, 0.0029; loss at 160°, 0.0033.
Calc. for $C_{20}H_{10}I_4O_4.H_2O$: H_2O, 2.14. Found: H_2O at 110°, 0.64; total loss at 160°, 0.73.

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[1] Melting points and decomposition temperatures are uncorrected and were made in an electrically heated Thiele apparatus.

[2] THIS JOURNAL, **32**, 635 (1910); *Am. Chem. J.*, 48, 477 (1912).

The sample dried at 160° was analyzed by the permanganate oxidation method.

Subst., (I) 0.2062, (II) 0.2366; cc. 0.1 *N* $AgNO_3$, (I) 10.02, (II) 11.48.
Calc. for $C_{20}H_{10}I_4O_4$: I, 61.77. Found: (I) 61.68, (II) 61.58.

These results show that the product precipitated at low temperatures is tetraiodophenolphthalein and not the carbinolcarboxylic acid as stated by Classen and Löb. It seems highly probable that their product was impure since they describe it as having a yellowish brown color while the product which we obtained starting with the pure phthalein is absolutely colorless.

Tetraiodophenolphthalein Diacetate.—Fifteen g. of the phthalein was boiled with 10 times its weight of redistilled acetic anhydride. The phthalein went into solution soon after the boiling began. The light yellow solution was boiled for one and a quarter hours, filtered, concentrated and allowed to cool when colorless rectangular plates separated out. These were filtered off, the filtrate further concentrated and a second crop of crystals obtained. Yield, 83%. The diacetate is quite soluble in benzene, ethyl acetate and chloroform, soluble in ether and somewhat soluble in methyl and in ethyl alcohol. The product crystallized from benzene melted at 245°. Recrystallization from benzene did not change the melting point. The product from benzene crystallized from ethyl acetate in needles melting at 246°. A sample dried at 150° gave the following results on analysis by the lime method:

Subst., (I) 0.4418, (II) 0.3695; cc. 0.1 *N* $AgNO_3$, (I) 19.62, (II) 16.32.
Calc. for $C_{20}H_8I_4O_4(COCH_3)_2$: I, 56.04. Found: (I) 56.36, (II) 56.06.

The diacetate is not changed by cold aqueous alkali but gives a blue color when warmed with it. When treated with an excess of alcoholic caustic potash in the cold and shaken for some time it dissolves completely, giving practically no color to the solution. Water and acid were added to the alcoholic alkaline solution and the precipitated phthalein filtered off, washed thoroughly, dried at 150°, and analyzed by the lime method.

Subst., 0.3325; cc. 0.1 *N* $AgNO_3$, 16.16.
Calc. for $C_{20}H_{10}I_4O_4$: I, 61.77. Found: 61.69.

Tetraiodophenolphthalein Dibenzoate.—Twenty g. of the phthalein was dissolved in 200 cc. of water containing 13.6 g. of potassium hydroxide. Twice the calculated amount of benzoyl chloride necessary to react with the phthalein was added and the mixture shaken in a 500 cc. wide-mouth glass-stoppered bottle. More alkali and benzoyl chloride were added from time to time until the alkaline solution no longer had a blue color. The reaction mixture had a faint odor of benzoyl chloride and was alkaline. The reddish powder which formed was shaken with soda solution, filtered and washed thoroughly. Yield, 72%. The dibenzoate is readily soluble in benzene, ethyl acetate and acetone, difficultly soluble in methyl and in ethyl alcohol and insoluble in ether. Crystallized from a mixture of ethyl alcohol and benzene it melted at 298°. When crystallized from benzene alone it was obtained in colorless rectangular plates melting at 298°. A portion of the dibenzoate dried at 160° was analyzed by the lime method.

Subst., (I) 0.2621, (II) 0.2904; cc. 0.1 *N* $AgNO_3$, (I) 10.20, (II) 11.21.
Calc. for $C_{20}H_8I_4O_4(COC_6H_5)_2$: I, 49.29. Found: (I) 49.39, (II) 48.99.

The dibenzoate is unaffected by aqueous alkalies but is quite readily saponified by boiling alcoholic alkalies.

Tetraiodophenolphthaleinoxime.—In preparing this compound the method of Friedlander was used.[1] Four g. of pure tetraiodophenolphthalein was dissolved in 25 cc. of water containing 1.7 g. of potassium hydroxide. Eight-tenths g. of pure hydroxylamine hydrochloride was added to the hot alkaline phthalein solution and the mixture heated at 95° on a water bath for a quarter of an hour. The color changed from reddish violet to pale green. 2 *N* acetic acid was then added in excess to the hot solution, giving a yellow flocculent precipitate which was readily filtered off. The precipitate was washed with hot water and air dried, yield practically quantitative. Recrystallized from benzene, the oxime came down in almost colorless, diamond-shaped glistening plates which in the aggregate appeared light brown. These crystals decomposed (reddish color) at 135° and liquefied at 170.° Iodine determinations by the permanganate oxidation method on a sample of the oxime dried at 85° gave the following results:

Subst., (I) 0.1909, (II) 0.2564; cc. 0.1 *N* $AgNO_3$, (I) 9.14, (II) 12.31.
Calc. for $C_{20}H_{11}I_4O_4N$: I. 60.67. Found: (I) 60.77. (II) 60.94.

Nitrogen determinations were made on the oxime, dried at 85°, by the Kjeldahl method after reduction with zinc dust.

Subst., (I) 0.1537, (II) 0.1389; cc. 0.1 *N* HCl, (I) 1.73, (II) 1.76.
Calc. for $C_{20}H_{11}I_4O_4N$: N, 1.67. Found: (I) 1.58, (II) 1.78.

The oxime dissolved in alkalies with a yellow color. It is readily soluble in absolute ethyl alcohol, benzene, acetone and ether; quite soluble in methyl alcohol; insoluble in petroleum ether.

Action of Dry Ammonia on Tetraiodophenolphthalein.—Gaseous ammonia dried by passing it through soda lime and then through a tube containing sodium wire was allowed to act on a weighed amount of tetraiodophenolphthalein. The phthalein became bright blue in 15 minutes and a weighing showed it had taken up approximately 2 molecules of ammonia. The weight of the salt became constant in an hour and a quarter.

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[1] *Ber.*, 26, 173 (1893).

Subst., (I) 0.3794, (II) 0.2813; gain, (I) 0.0319, (II) 0.0235.
Calc. for $C_{20}H_{10}I_4O_4.4NH_3$: NH_3, 7.67. Found: (I) 7.76, (II) 7.71.

In a current of dry air at room temperature 2 molecules of the ammonia are lost in half an hour. The remaining two molecules are lost very slowly. Not all of the ammonia was lost in dry air at the end of 36 hours. It was all given up, however, if the salt was heated to 60° for 4 hours or allowed to stand in a desiccator over calcium chloride for several weeks.

Compound of Tetraiodophenolphthalein with Pyridine.—In attempting to find a suitable solvent from which to crystallize the phthalein, it was found that it is so excessively soluble in pyridine that it will not crystallize out. Four times its volume of absolute ethyl alcohol was added to the pyridine solution and the mixture allowed to stand for some time when a voluminous mass of hair-like needles separated out, which, when filtered off, had a faint yellow color. The crystals were washed thoroughly with absolute alcohol and allowed to dry in the air for half an hour. The material was then bottled and a sample analyzed by the permanganate oxidation method.

Subst., (I) 0.3667, (II) 0.4163; cc. 0.1 *N* $AgNO_3$, (I) 13.92, (II) 15.85.
Calc. for $C_{20}H_{10}I_4O_4.3C_5H_5N$: I, 47.94. Found: (I) 48.18, (II) 48.32.

After standing in a glass-stoppered bottle for two days a portion of the compound was dried to constant weight at 130–140°.

Subst., 0.2336; loss, 0.0413.
Calc. for $C_{20}H_{10}I_4O_4.3C_5H_5N$: C_5H_5N, 22.40.
Calc. for $C_{20}H_{10}I_4O_4.2C_5H_5N$: C_5H_5N, 16.14. Found: 17.68.

No further loss occurred when the sample was heated to 200°, but the sample took on a brownish color at 160°. Analysis of the sample dried at 130–140° showed it had lost all of the pyridine.

Subst., 0.1916; cc. 0.1 *N* $AgNO_3$, 9.29.
Calc. for $C_{20}H_{10}I_4O_4$: ·I, 61.77. Found: 61.54.

Monopotassium Salt of Tetraiodophenolphthaleincarbinolcarboxylic Acid.—To obtain this salt 5 g. of the pure phthalein was suspended in 100 cc of 95% alcohol. To this was added 1.5 g. of potassium acetate in 100 cc. of 95% alcohol. The mixture was boiled in a flask connected with a return condenser for one hour Not all of the material went into solution, so more alcohol was added from time to time and the boiling continued until solution was complete. The solution had a faint blue color. It was concentrated and allowed to stand when crystals with a very faint green tint separated out. These were filtered off and washed with 95% alcohol. When dry they were practically colorless. After standing in a glass-stoppered bottle for several months, samples of the salt were heated to constant weight at 160–170° in a current of dry air free from carbon dioxide. Water collected on the cool part of the tube, and the salt became green at 140–145°. As the temperature increased the color deepened. Heated above 170° the salt decomposed.

Subst., (I) 0.2806, (II) 0.1900; loss in weight, (I) 0.0077, (II) 0.0053.
Calc. for $C_{20}H_9I_4O_4K.1.5H_2O$: H_2O, 3.04. Found: (I) 2.74, (II) 2.79.

Samples of the undried salt were analyzed for iodine by the oxidation method.

Subst., (I) 0.2351, (II) 0.2127; cc. 0.1 *N* $AgNO_3$, (I) 10.56, (II) 9.53.
Calc. for $C_{20}H_9I_4O_4K.1.5H_2O$: I, 57.24. Found: (I) 57.01, (II) 56.87.

Potassium determinations were made on portions of the undried material by fuming down with sulfuric acid.

Subst., (I) 0.2148, (II) 0.2284; K_2SO_4, (I) 0.0207, (II) 0.0218.
Calc. for $C_{20}H_9I_4O_4K.1.5H_2O$: K, 4.40. Found: (I) 4.33, (II) 4.28.

This colorless compound is therefore the salt of tetraiodophenolphthaleincarbinolcarboxylic acid. When heated it loses water and changes to the green monopotassium salt of the phthalein. It is difficultly soluble in water, but gradually goes into solution in boiling water with the production of a blue color. When a large amount of water is added and the solution boiled the salt is hydrolyzed and the free phthalein is precipitated.[1]

Disodium Salt of Tetraiodophenolphthaleincarbinolcarboxylic Acid.— In the preparation of this compound 0.4270 g. of sodium was dissolved in 100 cc. of absolute ethyl alcohol and 7.6281 g. of pure tetraiodophenolphthalein added. On warming the mixture the phthalein dissolved completely, giving the solution a reddish blue color in thick layers and a blue color in thin layers. The solution was concentrated to one-half its volume and allowed to stand. Large clusters of pale green crystals formed. These were filtered off and washed with absolute alcohol. When exposed to the air the crystals began to effloresce. Some of the crystals were ground in a mortar, the pulverized material transferred to a platinum boat, weighed and allowed to stand in a desiccator over calcium chloride and sodium hydroxide. On grinding the product became a white powder which immediately assumed a faint blue color. Standing in the desiccator for 12 hours, the salt lost weight and the color became more pronounced. On heating in a current of dry air free from carbon dioxide to 110°, further loss in weight occurred and the color became a deep blue. Moisture collected on the cool part of the tube and alcohol was given off as was shown by passing the escaping vapors into water, which gave a test for alcohol. The salt was dried to constant weight at 150–160°.

Subst., 0.2553; loss in weight, 0.0567.
Calc. for $C_{20}H_8I_4O_4Na_2.5C_2H_6O.H_2O$: 22.30. Found: 22.21.

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[1] THIS JOURNAL, **34**, 1424 (1912); *Ibid.*, **37**, 1222 (1915).

Sodium determinations were made on the dried product by fuming down with concentrated sulfuric acid.

Subst., (I) 0.2415, (II) 0.1403; Na_2SO_4, (I) 0.0394, (II) 0.0227.
Calc. for $C_{20}H_8I_4O_4Na_2$: Na, 5.31. Found: (I) 5.28, (II) 5.24.

A sample of the dried material was analyzed for iodine by the permanganate method.

Subst., 0.2907; cc. 0.1 *N* $AgNO_3$, 13.50.
Calc. for $C_{20}H_8I_4O_4Na_2$: I, 58.64. Found: 58.94.

A portion of the undried salt which had been ground to a powder, when exposed to the air for a short time, took on a deep blue color, which remained practically unchanged when this material was allowed to stand exposed to the air for several weeks.

The foregoing results show this compound to be the disodium salt of tetraiodophenolphthaleincarbinolcarboxylic acid which, when heated or allowed to stand exposed to the air, loses water and alcohol and forms the blue disodium salt of tetraiodophenolphthalein. Both salts dissolve in water with a blue color.

Tetraiodophenoltetrachlorophthalein.—This compound was prepared by iodinating phenoltetrachlorophthalein in alkaline solution. The phenoltetrachlorophthalein used for this purpose was made by the method of Orndorff and Black.[1] The tetrachlorophthalic acid used in the preparation of the latter compound was the commercial product purified by the method described by Delbridge.[2] The purity of the acid was checked by molecular-weight determinations made by titrating samples with standard sodium hydroxide.[3]

Subst., (I) 0.4252, (II) 0.3296; cc. 0.1 *N* NaOH, (I) 27.19, (II) 21.06.
Calc. for $C_6Cl_4(COOH)_2.0.5H_2O$: M. W., 312.9. Found: (I) 312.8, (II) 313.0.

The acid[4] was condensed with redistilled phenol which boiled at 180° and the phenoltetrachlorophthalein thus obtained, when purified and air-dried, gave the following results on analysis by the lime method:

Subst., (I) 0.2374, (II) 0.2806; cc. 0.1 *N* $AgNO_3$, (I) 20.70, (II) 24.53.
Calc. for $C_{20}H_{10}Cl_4O_4$: Cl, 31.10. Found: (I) 30.92, (II) 31.00.

The procedure in iodinating the phthalein was as follows: Twenty-five g. of the pure phenoltetrachlorophthalein was dissolved in 300 cc. of 2 *N* sodium hydroxide solution. This solution was mechanically stirred and to it was added, in the course of 20 minutes, an iodine solution containing 58.2 g. of iodine and 75 g. of potassium iodide in 300 cc. of water. The color changed rapidly from red to blue when all of the iodine had been added and the solution remained clear. The reaction

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[1] *Am. Chem. J.*, **41**, 349 (1909).

[2] *Ibid.*, **41**, 414 (1909).

[3] *Ibid.*, **41**, 399 (1909).

[4] THIS JOURNAL, **38**, 2486 (1916).

mixture was stirred for 9 hours at room temperature. 2 *N* acetic acid was then added to neutral reaction to litmus when a deep blue precipitate, a sodium salt of tetraiodophenoltetrachlorophthalein, separated out which was readily filtered off by the aid of suction. The filtrate had a yellowish brown color and gave no precipitate on being strongly acidified, but darkened, due to the liberation of iodine. The precipitate dissolved in water with a blue color. It was dissolved in water and 2% alkali, the solution stirred and 2 *N* acetic acid added to acid reaction. The phthalein came down as a yellowish green precipitate and was filtered off. The filtrate contained some free iodine. The precipitate was again dissolved in 2% alkali and this time acidified with conc. hydrochloric acid and steam passed through the mixture. The phthalein came out as a light brown material which became white as the mixture warmed up. It was washed by decantation, filtered off and air-dried. Yield, 85%.

Unlike tetraiodophenolphthalein, the tetraiodophenoltetrachlorophthalein is excessively soluble in acetone and absolute ethyl alcohol; readily soluble in benzene, ethyl acetate, methyl alcohol and chloroform and quite soluble in glacial acetic acid. Ethyl acetate proved the most suitable solvent for purifying the phthalein. On crystallization from this solvent 2 products were obtained, one as a crystalline powder which analysis showed to be a mixture of lower iodination products and the other in well-formed crystals which when recrystallized and analyzed proved to be the pure tetraiodophenoltetrachlorophthalein. It came out of ethyl acetate in thick diamond-shaped crystals. When heated in a melting-point tube it becomes blue at 202° due to reaction with the alkali of the glass, decomposes at 240–44° with the evolution of iodine and melts to a dark brown liquid at 250–55°. The crystals contain ethyl acetate which they lose on standing or when heated to 170°.

Subst., (I) 1.1819, (II) 0.5569, (III) 0.2438, (IV) 0.3255; loss in weight, (I) 0.0949, (II) 0.0437, (III) 0.0179, (IV) 0.0095.

Calc. for $C_{20}H_6I_4Cl_4O_4.C_4H_8O_2$: $C_4H_8O_2$, 8.41. Found: (I) 8.03, (II) 7.85, (III) 7.34, (IV) 2.92.

Determinations I and II were made on crystals which had been air-dried and then pulverized; Determination III was made on the same sample after standing for a month in a glass-stoppered bottle, and IV after standing 7 months.

In the analysis of compounds containing both chlorine and iodine by the permanganate oxidation method, the samples were treated a second time with 5 cc. of permanganate solution and 5 cc. of nitric acid and evaporated to dryness in order to insure the complete elimination of the chlorine. The following results were thus obtained on samples of the tetraiodophenoltetrachlorophthalein dried to constant weight at 170°:

Subst., (I) 0.2496, (II) 0.2382; cc. 0.1 *N* $AgNO_3$, (I) 10.39, (II) 9.93.
Calc. for $C_{20}H_6I_4Cl_4O_4$: I, 52.90. Found: (I) 52.84, (II) 52.91.

To check the titration on these samples, the silver iodide was collected on weighed Gooch crucibles and dried to constant weight at 145°.

Subst., (I) 0.2496, (II) 0.2382; AgI, (I) 0.2440, (II) 0.2329.
Calc. for $C_{20}H_6I_4Cl_4O_4$: I, 52.90. Found: (I) 52.84, (II) 52.85.

Samples similarly dried were analyzed by the lime method.

	Substance. Gram.	Silver halides. Gram.	0.1 *N* silver nitrate. Cc.	% chlorine.	% iodine.
I..........	0.1872	0.2961	15.69	14.96	52.78
II..........	0.2435	0.3848	20.39	14.95	52.73
		Calc. for $C_{20}H_6I_4Cl_4O_4$:		14.78	52.90

The silver halides were treated with dry chlorine and the following results obtained:

	Substance. Gram.	Silver halides. Gram.	Decrease. Gram.	% chlorine.	% iodine.
I..........	0.1872	0.2961	0.0713	14.90	52.85
II..........	0.2435	0.3848	0.0930	14.84	53.00
		Calc. for $C_{20}H_6I_4Cl_4O_4$:		14.78	52.90

The phthalein dissolves in dilute alkalies with an almost pure blue color which does not fade appreciably on standing for several days. Strong alkalies precipitate the phthalein in the form of a blue-colored salt. The alkaline solution of tetraiodophenoltetrachlorophthalein is less sensitive to carbon dioxide than a similar solution of tetraiodophenolphthalein. The phthalein is stable in the solid form but its ethyl acetate solution turns brown on standing probably due to the liberation of some iodine.

Diacetate of Tetraiodophenoltetrachlorophthalein.—To prepare the diacetate 12 g. of the phthalein was boiled with 120 g. of acetic anhydried. The phthalein went into solution in 15 minutes after boiling began. The boiling was continued for one hour and after cooling the solution somewhat 108 g. of absolute ethyl alcohol was added. Fine needle-like crystals began to separate out which increased in quantity when the solution was allowed to stand. These were filtered off and the solution concentrated when more crystals came out. The diacetate was recrystallized from benzene from which it was obtained in the form of needles, which melted sharply at 262°. The product crystallized from benzene contains benzene of crystallization which it losses when dried at 200°.

Subst., (I) 0.4773, (II) 0.4610; loss in weight, (I) 0.0318, (II) 0.0382.
Calc. for $C_{20}H_4I_4Cl_4O_4(COCH_3)_2.C_6H_6$: C_6H_6, 6.96. Found: (I) 6.66, (II) 8.29.

Both samples were air-dried for one-half hour. Sample I had stood for 3 days in a glass-stoppered bottle.

Samples of the diacetates were analyzed by adding 5 cc. of 95% alcohol and 5 cc. of 10% sodium hydroxide solution and evaporating to dryness on the water bath, then adding 10 cc. of water and concentrating the solution to 5 cc. Iodine determinations were then made by the permanganate oxidation method.

Subst., (I) 0.2160, (II) 0.2275; cc. 0.1 *N* $AgNO_3$, (I) 8.26, (II) 8.74.
Calc. for $C_{20}H_4I_4Cl_4O_4(COCH_3)_2$: I, 48.64. Found: (I) 48.54, (II) 48.76.

The diacetate is unaffected by cold 2 *N* aqueous alkali but saponifies when boiled with this reagent. It is soluble in acetone, benzene and ethyl acetate, difficultly soluble in absolute ethyl alcohol.

Dibenzoate of Tetraiodophenoltetrachlorophthalein.—An attempt was made to prepare this compound by boiling 10 g. of the phthalein with 100 g. of benzoyl chloride. The phthalein went into solution quite readily, but when the solution began to boil iodine was liberated, showing that the phthalein was being decomposed. The Baumann-Schotten method was therefore used in preparing the dibenzoate.

Six g. of tetraiodophenoltetrachlorophthalein was dissolved in 240 cc. of $^1/_3$ *N* sodium hydroxide and 4 g. of benzoyl chloride added. The mixture was stirred and alkali and benzoyl chloride added from time to time until the color of the solution became somewhat lighter. The dibenzoate settled to the bottom of the container as yellow granular particles. It was filtered off, triturated with sodium carbonate solution, and again filtered off, washed, and air-dried. Yield, 82%.

The dibenzoate is not affected by cold aqueous sodium hydroxide but is slowly saponified when heated with it. It is quite readily saponified by hot alcoholic caustic soda. It is readily soluble in benzene, ethyl acetate, ether and chloroform, somewhat soluble in methyl and in ethyl alcohol and insoluble in petroleum ether. When recrystallized from methyl alcohol the dibenzoate was obtained in the form of white flakes containing no methyl alcohol of crystallization and melting to a colorless liquid at 205°. In the analysis by the permanganate oxidation method, samples of the dibenzoate were saponified by adding 5 cc. of 10% sodium hydroxide solution and 5 cc. of 95% alcohol and evaporating to dryness on the water bath. The residue was treated twice with 5 cc. of 95% alcohol and taken to dryness, 5 cc. of water then added, potassium permanganate added to the hot aqueous solution and the analysis carried out as usual. The following results were thus obtained:

Subst., (I) 0.2979, (II) 0.2128; cc. 0.1 *N* $AgNO_3$, (I) 10.20, (II) 7.32.
Calc. for $C_{20}H_4I_4Cl_4O_4(COC_6H_5)_2$: I, 43.47. Found: (I) 43.46, (II) 43.66.

Action of Dry Ammonia on Tetraiodophenoltetrachlorophthalein.—When a sample of the pure tetraiodophenoltetrachlorophthalein was placed in dry ammonia it assumed a blue-green color almost immediately. A weighing in 15 minutes showed that the sample had taken up 3 molecules of ammonia. Several hours in contact with ammonia were required, however, for the substance to come to constant weight when a total of 4 molecules of ammonia had been taken up.

Subst., 0.3121; gain in weight, 0.0208.
Calc. for $C_{20}H_6I_4Cl_4O_4.4NH_3$: NH_3, 6.63. Found: 6.25.

The salt loses 2 molecules of ammonia in half an hour in a desiccator over calcium chloride. The remaining 2 molecules are not entirely given up on standing in the desiccator for 10 days, but are lost when the salt is heated to 60° for 3 hours in a current of dry air. The material becomes colorless when all the ammonia is lost.

The Visible and Ultra-Violet Absorption Spectra of Phenolphthalein and Some of Its Halogen Derivatives.

The compounds whose spectra were determined are phenolphthalein, phenoltetrachlorophthalein and the derivatives of these 2 compounds obtained by substituting 4 bromine or iodine atoms for hydrogen in the phenol residues. The compounds used had been purified and were shown to be pure by analysis. Since the alkaline solutions are more or less sensitive to carbon dioxide, precautions were taken to exclude this gas from the solutions used.

The spectral determinations were made and the curves plotted by Drs. H. E. Howe and K. S. Gibson of the Physics Department of Cornell University and the results published in the *Physical Review, N. S.*, **10**, 767 (1917). From a study of the curves and tables the following summarized statement of facts may be made:

Neutral alcoholic solutions of the phthaleins studied have absorption spectra of the same type.

The type of absorption changes when the solution becomes alkaline. In some cases the change in type can be followed through a transition stage.

The absorption of the aqueous alkaline solutions is of the same type as that of the alcoholic. The characteristic spectrum of the alkaline solutions consists of 3 absorption bands, one in the visible in the region 1600–1800, the other two in the ultra-violet, one in the region 2500–2700, the second in the region 3200–3600.

The magnitude of the absorption in the visible band and in the band near 2600 varies greatly with the phthalein, and is considerably greater in the aqueous than in the alcoholic solutions; the magnitude of the absorption in the band near 3200 is practically the same for all solutions, both aqueous and alcoholic.

Band centers have lower frequencies for alcoholic than for aqueous solutions.

Bromine and iodine in the phenol residues shift all bands toward lower frequencies.

Chlorine in the phthalic acid residue shifts the visible band in the same direction, but shifts the two ultra-violet bands in the opposite direction.

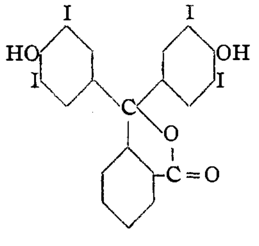
Chlorine adds a shoulder to the band in the visible on the side toward higher frequency. In the case of the neutral solutions, it adds a shoulder on the side toward lower frequency.

The shifts of the band in the visible are less in alcohol than in water.

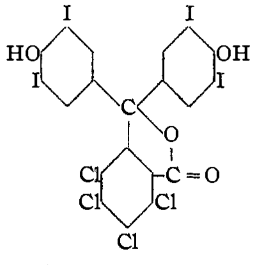
The shift increases with the mass of the substituent.

Theoretical.

Classen and Löb represent the 4 iodine atoms in tetraiodophenolphthalein as replacing 2 hydrogen atoms in each of the phenol residues. Since halogens substitute in the ortho and para positions in phenol it seems probable that, as the para positions are occupied, the iodine atoms take up the ortho positions with reference to the hydroxyl groups. In tetraiodophenoltetrachlorophthalein the iodine atoms must be in combination with the phenol residues as the hydrogen atoms of the phthalic acid residue are all replaced by chlorine. Here, too, the iodine probably takes up the ortho positions with reference to the hydroxyl groups. The two compounds are both colorless and may be represented by the following formulas:



Tetraiodophenol-
phthalein.



Tetraiodophenol-
tetrachlorophthalein.

Rupp[1] designates the compound obtained by the condensation of tetraiodophthalic acid and phenol as tetraiodophenolphthalein. The name phenoltetraiodophthalein for this compound would be more in harmony with the accepted nomenclature for the phthaleins.

It is interesting to note that although tetraiodophenolphthalein and tetraiodophenoltetrachlorophthalein contain 61.77% and 67.68% of halogens, respectively, they conduct themselves chemically like phthaleins and form derivatives similar to those of phenolphthalein.

Contrary to the statement of Classen and Löb, tetraiodophenolphthalein does not form a carbinolcarboxylic acid. The monopotassium and disodium salts of such an acid have, however, been obtained. These salts are colorless and may be represented by the following formulas:

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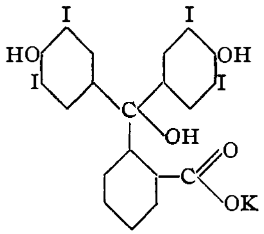
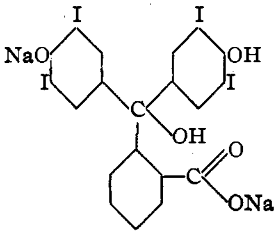
[1] *Chem. Zentr.*, 15, 1058 (1911).

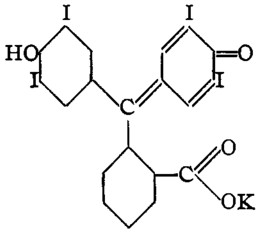


Monopotassium salt
of the carbinol acid.

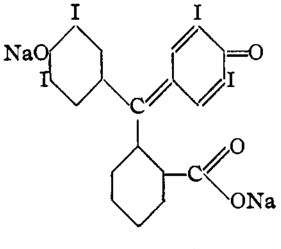


Disodium salt
of the carbinol acid.

The monopotassium salt, when heated, loses water forming the green monopotassium salt of tetraiodophenolphthalein.



The disodium salt crystallized from alcohol loses both alcohol and water when heated, forming the blue disodium salt of tetraiodophenolphthalein. Classen and Löb represent this latter compound as being formed by the replacement of the phenolic hydrogen atoms by the metal. Since the salt is colored it is best represented as having a quinoid structure.



This blue salt is quite stable in air, showing tetraiodophenolphthalein to be a stronger acid than phenolphthalein.

Both the phthaleins react with gaseous ammonia forming colored ammonium salts. While a maximum of 4 molecules of ammonia are taken up 2 of these are given up very readily and the remaining 2 more slowly. Even the diammonium salts are unstable, however, for all of the ammonia is lost on standing and the colorless phthalein results. The successive steps in the formation of polyammonia salts are given by Orndorff and Hitch.[1] The tetraammonia salts may be represented as follows:

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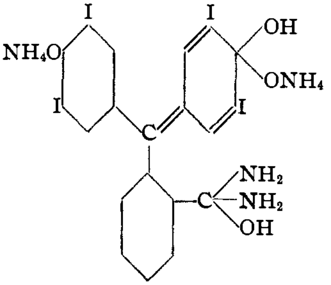
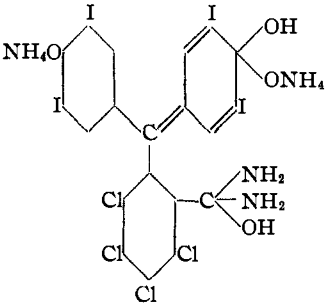
[1] This Journal, 36, 717, 722 (1914).

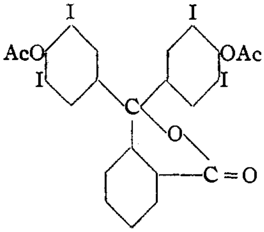


Tetraammonia salt of
tetraiodophenol-
phthalein.

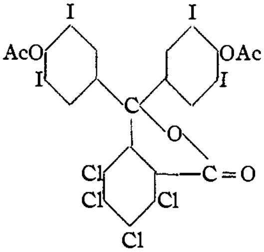


Tetraammonia salt of
tetraiodophenol-
tetrachlorophthalein.

The diacetates and dibenzoates of tetraiodophenolphthalein and tetraiodophenoltetrachlorophthalein are colorless compounds and hence have lactoid structures.



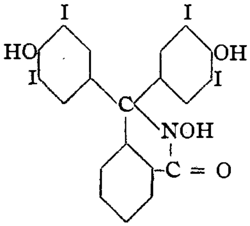
Diacetate and dibenzoate
of tetraiodophenol·
phthalein.



Diacetate and dibenzoate
of tetraiodophenol·
tetrachlorophthalein.

Tetraiodophenolphthalein reacts with hydroxylamine to give an oxime which is colored.

The oxime would therefore have the following formula:[1]



The results of the spectral determinations confirm the work of Meyer and Marx and Meyer and Fischer on phenolphthalein and tetrabromophenolphthalein and show an additional band in the ultra-violet which those investigators did not detect.

The neutral alcoholic solutions of all 6 phthaleins show the same type

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[1] This Journal, 39, 689 (1917).

of absorption in the ultra-violet indicating that these compounds have similar structures.

In the alkaline solutions, both alcoholic and aqueous, the type of absorption in the ultra-violet is different from that of the neutral solutions showing that the phthaleins have undergone a change in constitution. The alkaline solutions, with the exception of tetraiodo- and tetrabromophenolphthaleins, have decided color and in these two cases the apparent absence of color is probably due to the thinness of layer and dilution of the solution necessary to allow the transmission of the ultra-violet light.

The absorption of the alkaline solutions, in the visible region is of the same type for all solutions indicating a similarity in constitution of the salts in solution. As was found in the cases of fluorescein and its halogen derivatives[1] and of the orcinolphthaleins and their halogen derivatives,[2] the introduction of halogens into the molecule shifts the absorption bands toward the red end of the spectrum and the shift is approximately proportional to the number of the halogen atoms introduced rather than to the molecular weight of the substituents.

Summary.

The results of this investigation may be briefly stated as follows:

1. Pure tetraiodophenolphthalein has been prepared and studied. It has been shown not to form a carbinolcarboxylic acid, but colorless salts of such an acid have been obtained. When these salts are heated they lose water or water and alcohol and give the colored salts of the phthalein.
2. A colorless diacetate and dibenzoate and a colored oxime have been made.
3. Tetraiodophenoltetrachlorophthalein has been made and studied. This compound is colorless and yields a colorless diacetate and dibenzoate.
4. The action of ammonia on these 2 phthaleins has been investigated.
5. The absorption spectra of phenolphthalein and some of its halogen derivatives have been studied and the absorption curves plotted.

[CONTRIBUTIONS FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY, No. 310.]

A STUDY OF THE GLUCOSAZONE REACTION.

BY IRA D. GARARD AND H. C. SHERMAN.

Received February 4, 1918.

Introduction.

Since Fischer[3] first carried out the osazone reaction in 1884, it has been applied to analytical problems by numerous workers, among whom may be

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[1] THIS JOURNAL, 36, 680 (1914).

[2] *Ibid.*, 37, 1201 (1915).

[3] Fischer, *Ber.*, 17, 579 (1884). See also *Ibid.*, 20, 821 (1887).