3. Alcohol acting on the hydrate converts it into the pale yellow carbinol-carboxylic acid.

4. Acetone on the anhydrous material gives a lemon yellow acetonate which loses acetone to give benzenoid tetraiodofluorescein.

5. Benzenoid tetraiodofluorescein rapidly rearranges into the red quinoid form at 180°.

6. The monopotassium salt was prepared in reddish orange crystals.

7. Dry ammonia on tetraiodofluorescein gives a deep red salt with gain in weight corresponding to a diammonium salt.

8. The red silver salt and monomethyl ether are characteristic of the quinoid form, while the yellow diacetate and dibenzoate, the yellow tetraiodofluorescein and carbinol acid characterize the benzenoid type.

9. Absorption spectra of the entire series will be reported in a later paper.

PITTSBURGH, PA.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF PITTSBURGH.]

PHTHALIC ACID DERIVATIVES; CONSTITUTION AND COLOR, IX.[1] TETRAIODOEOSIN AND SOME OF ITS DERIVATIVES.

BY DAVID S. PRATT AND ARTHUR B. COLEMAN.

Received October 17, 1917.

Tetraiodofluorescein[2] in the anhydrous condition readily takes up four atoms of bromine, replacing hydrogen in the two resorcin residues. For this purpose 10 g. were suspended in 500 cc. of glacial acetic acid containing 10 cc. of bromine and the mixture boiled gently for an hour. The reddish brown tetraiodofluorescein gradually changed to a yellow crystalline substance. After cooling this was filtered off and washed with 40% alcohol until the filtrate gave no test for halogen. The product was heated to constant weight at 105° and found to be pure tetraiodoeosin. Yield, theoretical.

The material was analyzed by the lime combustion method, filtering off all acid-insoluble material before adding silver nitrate. Titration values and weight of combined silver halides gave the necessary data:

Subst. (I) 0.3946, (II) 0.4656; cc. 0.1 *N* $AgNO_3$, (I) 26.86, (II) 29.10. Weight AgI + AgBr, (I) 0.5674, (II) 0.6468.

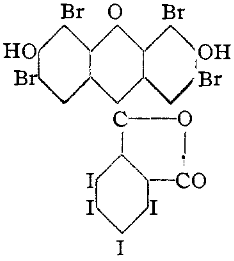
Calc. for $C_{20}H_4O_5Br_4I_4$: Br, 27.76; I, 44.09. Found: (I) Br, 27.19, I, 43.19, (II) Br, 27.63; I, 43.88.

Tetraiodoeosin forms canary-yellow crystals which show no tendency whatever to go over into the highly colored quinoid form. It should be represented, therefore, by the structure

---

[1] THIS JOURNAL, **40**, 198 (1918).

[2] *Ibid.*, **40**, 236 (1918).



Tetraiodoeosin (yellow).

The yellow color represents the effect due to four iodine atoms in the phthalic anhydride residue, the tetraiodo anhydride itself being canary-yellow.

Tetraiodoeosin is slightly soluble in acetone, ethyl acetate and benzol, practically insoluble in alcohol. Alcohol does not cause a rearrangement into the carbinol carboxylic acid as in the case of tetraiodofluorescein. It decomposes upon heating to about 200° with loss of iodine, and is very sensitive to alkalies, giving a deep red solution with faint greenish fluorescence. It should therefore be valuable as an indicator.

Tetraiodoeosin Hydrate.—A dilute alkaline solution of tetraiodoeosin was acidified by adding a slight excess of 2% hydrochloric acid, giving an abundant precipitation of pink amorphous hydrate which was allowed to settle. It was washed as free from chlorides as possible, filtered, and air-dried to constant weight. Attempts to crystallize it always gave yellow anhydrous tetraiodoeosin.

The air-dried hydrate lost weight on heating at 140° as follows:

Subst. 7.2552 g., loss in weight, 0.0372 g.

Calc. for $C_{20}H_4O_5Br_4I_4.H_2O$: H_2O, 1.54. Found: 0.51.

This would indicate one-third of a molecule of water, but the hydrate is so unstable it probably lost water during air-drying. In fact it was noticed that boiling a suspension of hydrate in water caused a lessening of the pink color, although it never became the clear yellow of anhydrous tetraiodoeosin.

Diammonium Salt.—A weighed sample of tetraiodoeosin was placed in a porcelain boat and subjected to the action of dry ammonia gas. The color slowly changed from yellow to brilliant red and the crystalline structure was destroyed. Constant weight was obtained after 24 hours.

Subst. 0.3948 g.. gain in weight, 0.0119 g.

Calc. for $C_{20}H_4O_5Br_4I_4.2NH_3$: NH_3, 2.87. Found: 2.92.

The diammonium salt is sparingly soluble in cold water, readily on heating, giving a deep red solution with slight greenish fluorescence.

When the dry salt is heated at 120° it loses two molecules of ammonia, giving amorphous yellow tetraiodoeosin.

Subst. 0.4067, loss in weight, 0.0102.

Calc. for $C_{20}H_4O_5Br_4I_4.2NH_3$: NH_3, 2.87. Found: 2.52.

The brilliant red color of the diammonium salt is evidence of its quinoid structure.

Tetraiodoeosin Diacetate.—The diacetate was prepared by gently boiling for 5 hours a suspension of 10 g. pure tetraiodoeosin in 30 cc. acetic anhydride containing 10 g. freshly fused sodium acetate. Red sodium salt at first formed around the suspended particles but these gradually reacted. The crude acetate was purified by repeated crystallization from acetone, using boneblack. The acetate forms light yellow crystals which darken with evolution of iodine at 270–280°. It is quite soluble in acetone, ethyl acetate, chloroform and benzol. The best solvent, however, appears to be a mixture of equal parts of acetone and alcohol. Yield, 92%.

The formation of diacetate does not take place as readily as in the case of tetraiodofluorescein, but once formed it is quite stable. Cold dilute alkali does not produce a trace of color, but heating with 10% sodium hydroxide causes saponification.

Subst. (I) 0.2401, (II) 0.2224; cc. 0.1 *N* $AgNO_3$, (I) 15.51, (II) 14.39.

Weight of AgI + AgBr: (I) 0.3275, (II) 0.3032.

Calc. for $C_{24}H_8O_7Br_4I_4$: Br, 25.87; I, 41.09. Found: (I) Br, 25.74; I, 40.97, (II) Br, 25.71; I, 40.83.

Tetraiodoeosin Dibenzoate.—The Baumann-Schotten method was found convenient for making the benzoate. Benzoyl chloride was added with vigorous shaking to a solution of tetraiodoeosin in dilute sodium hydroxide. The crude product separated in a sticky mass that was first thoroughly washed and dried, then dissolved in hot chloroform, and alcohol slowly added until the solution became faintly turbid. Upon cooling the benzoate separated in brownish crystals. This procedure was twice repeated. Several recrystallizations from acetone finally gave pale yellow crystals of pure benzoate which softened about 261° but gave no sharp melting point, as iodine is readily split off. The dibenzoate is readily soluble in chloroform, acetone, methyl alcohol and ethyl acetate. Yield, 40%. It is interesting to note the unusually high formula weight of 1360.

Subst. (I) 0.1593, (II) 0.2295; cc. 0.1 *N* $AgNO_3$. (I) 7.06, (II) 12.61.

Weight AgI + AgBr: (I) 0.1880, (II) 0.2679.

Calc. for $C_{34}H_{12}O_7Br_4I_4$: Br, 23.51; I, 37.34. Found: (I) Br, 22.32; I, 35.45, (II) Br, 22.20; I, 35.26.

Tetraiodoeosin Monomethyl Ether.—An alkaline solution of tetraiodoeosin was vigorously shaken with successive small portions of dimethyl sulfate, taking care to maintain alkalinity at all times. The ether so formed precipitated out as a brilliant red amorphous powder that was treated with strong potassium hydroxide solution to remove unchanged tetraiodoeosin and to saponify any methyl ester which migh thave been formed, washed with water, and finally purified from acetone and methyl alcohol.

The ether is fairly soluble in ethyl ether, ethyl acetate, methyl alcohol and acetone, sparingly so in chloroform. The unusually brilliant red color shows that the quinoid structure should be given this product.

Subst. (I) 0.3954; cc. 0.1 *N* $AgNO_3$. 26.39. Weight of AgI + AgBr, 0.5616.
Calc. for $C_{21}H_6O_7Br_4I_4$: Br, 27.43; I, 43.56. Found: Br, 26.86; I, 42.66.

A methoxyl determination by the Zeissel method was made to establish beyond doubt the presence of but one methoxyl radical.

Subst. (I) 0.3147, (II) 0.0880. Weight AgI, (I) 0.0786, (II) 0.0225.
Calc. for $C_{21}H_6O_5Br_4I_4$: CH_3O, 2.75. Found: (I) 3.30, (II) 3.38.

Silver Salt.—An ammoniacal solution was prepared by dissolving 5 g. of tetraiodoeosin in 10 cc. concentrated ammonium hydroxide and diluting to about 400 cc. A slight excess of 10% silver nitrate solution was added and the solution boiled until free from ammonia. The silver salt separated gradually as a bright crimson sticky precipitate very difficult to wash or handle. On drying to constant weight at 120° it changed to a beautiful red-violet color. The dry salt was boiled several hours with absolute alcohol to free it, if possible, from adsorbed silver, but this was not entirely successful.

Subst. (I) 0.2011, (II) 0.3138; cc. 0.1 *N* NH_4SCN, (I) 2.12, (II) 3.25.
Calc. for $C_{20}H_8O_5Br_4I_4Ag$: Ag, 8.57. Found: (I) 11.37. (II) 11.17.

The analyses were made by adding an excess of six normal nitric acid and letting it stand at room temperature overnight, then diluting with water and titrating the silver nitrate with standard ammonium thiocyanate solution using ferric alum as indicator.

The silver salt is insoluble in ordinary solvents, but dissolves in ammonium hydroxide, giving a deep red solution with slight greenish fluorescence.

It was noted during the above analyses that the action of dilute nitric acid on the purple-silver salt always left a brick-red precipitate. This may have contained more or less quinoid tetraiodoeosin, but the amount available was so small it was not investigated further.

Summary.

1. Tetraiodoesin has been prepared. It exists in the benzenoid modification as canary-yellow crystals.

2. The diacetate and dibenzoate are also benzenoid.

3. The hydrate is pink, losing water very readily to give the yellow tetraiodoeosin.

4. The diammonium salt is red, and the monosilver salt a red-purple. The former loses ammonia on heating, regenerating the yellow tetraiodoeosin.

5. Tetraiodoeosin monomethyl ether has been prepared. It shows vivid red color indicating quinoid structure.

6. The absorption spectra of this series will be reported upon in a later paper.

PITTSBURGH, PA.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF PITTSBURGH.]

PHTHALIC ACID DERIVATIVES; CONSTITUTION AND COLOR, X.[1] TETRAIODOERYTHROSIN (OCTOIODOFLUORESCEIN) AND SOME OF ITS DERIVATIVES.

BY DAVID S. PRATT AND ARTHUR B. COLEMAN.

Received October 17, 1917.

Tetraiodoerythrosin or octoiodofluorescein is a new dye derived from fluorescein by substituting four iodine atoms for hydrogen in the phthalic acid residue and two in each of the resorcin residues of the molecule. Somewhat similar derivatives of ordinary fluorescein but without any iodine in the phthalic residue have been made commercially by methods of electrolysis, carrying on the reaction until the desired color has been obtained. Such compounds have varying percentages of iodine and are, *per se*, mixtures. A variety of ways were tried to obtain the definite fluorescein mentioned above with eight atoms of iodine in the molecule. An alkaline solution of tetraiodofluorescein was treated with iodine in potassium iodide solution. The mixture gradually lost its brilliant fluorescence and became light red in color, but the purified dye contained considerably less iodine than the desired tetraiodoerythrosin.

Subst. 0.3993; cc. 0.1 N $AgNO_3$, 20.91.

Calc. for $C_{20}H_4O_5I_8$: I, 75.80. Found: 66.46.

A second more successful method was to suspend tetraiodofluorescein in glacial acetic acid containing iodine and finely powdered potassium iodate, the latter being added to remove hydriodic acid as fast as formed. The mixture was heated in a water bath for 5 hours, during which time its color changed from dark red to orange-yellow. Longer heating or a higher temperature did not improve the yield. This method gave some of the desired product but the greater part of the material appeared to contain approximately six atoms of iodine.

The most satisfactory method found consisted in suspending 20 g. of pure tetraiodofluorescein in 200 cc. of absolute alcohol and adding to this 13 g. of iodine and 0.2 g. of iodic acid. The mixture was heated with reflux condenser for 12 hours, then diluted with water and acidified. A brown material settled out which was filtered off and heated 2 hours at 100° with glacial acetic acid containing 0.5 g. of potassium iodate, as this was found to improve the yield considerably. The material was finally filtered off and washed with dilute potassium iodide solution to remove

---

[1] THIS JOURNAL, **40**, 198 (1918).