zoate was prepared in a similar manner to that used for phenoltetrabromophthalein dibenzoate. The colorless crystals obtained after treating with bone black a benzene solution contained a molecule of solvent which was slowly driven off at 130°.

Subs., 0.9861. Loss in weight: 0.0580.
Calc. for $C_{34}H_{14}O_6Br_8.C_6H_6$: C_6H_6, 6.31. Found: 5.89.
Subs., (I) 0.2520; (II) 0.2763. Cc. 0.1 *N* $AgNO_3$: (I) 17.25; (II) 19.08.
Calc. for $C_{34}H_{14}O_6Br_8$: Br, 55.23. Found: (I) 54.70; (II) 55.19.

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

PHTHALIC ACID DERIVATIVES; CONSTITUTION AND COLOR. XVII.[1] TETRABROMO-FLUORESCEIN, TETRABROMO-EOSIN AND SOME OF THEIR DERIVATIVES.

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Received May 31, 1919.

The replacement of hydrogen in the anhydride ring of fluorescein by 4 iodine atoms has been found to alter the equilibrium between the benzenoid and quinoid structure.[2] Whereas fluorescein itself is stable in the latter, or highly colored, modification, the tetra-iodo molecule ordinarily assumes the former arrangement. The present paper deals with certain intermediate bromine derivatives.

Tetrabromo-fluorescein, prepared by condensing tetrabromo-phthalic anhydride with resorcin, shows an equilibrium that lies near the border between the two structural isomeric modifications. The intramolecular forces which determine stability for either form are probably resultants from proximity effects inherent in unsaturated centers residing in the phthalic residue. There is a close relationship throughout the series under investigation existing between these unsaturated centers and the stability of the anhydride ring structure. This structure is encountered only as part of a benzenoid arrangement. When the 4-carbon-1-oxygen ring opens the molecules may rearrange into a quinoid structure with a color change generally, although not necessarily, manifest to the eye. Under other circumstances the ring may open with the formation of a carbinol carboxylic acid but without the marked color change.

The stability of the anhydride ring and benzenoid structure necessarily influences chemical reactivity, as has been noted by various investigators. An example of this may be pointed out in the present instance of salt formation. Tetrabromo-fluorescein with dry ammonia gas gives a diammonium salt where tetrabromo-eosin or octabromo-fluorescein gives a tetrammonium salt. It is felt that a comparative study covering as many

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[1] THIS JOURNAL, 41, 1289 (1919).

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

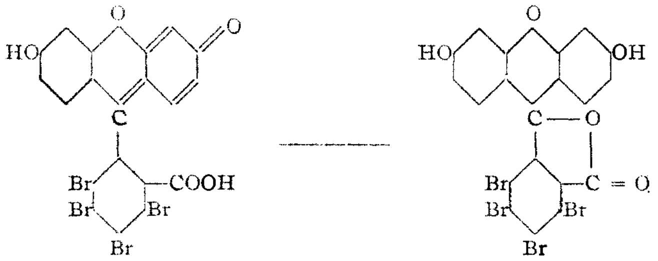
cases of these intramolecular resultant effects as possible and including spectrographic data will be of value.

Tetrabromo-fluorescein.—464 g. of tetrabromo-phthalic anhydride were well mixed with 216 g. of colorless resorcin and 216 g. of powdered, freshly fused zinc chloride. Fusion was carried out by gradually raising the temperature during half an hour to 200° with frequent stirring. The color darkened as the melt solidified. Heating was continued for two hours after which the cold fusion was powdered and washed with dil. hydrochloric acid until free from zinc. The crude fluorescein was then dissolved in a minimum of dil. sodium hydroxide solution and precipitated in tall cylinders with vigorous air stirring by adding 2% hydrochloric acid.

The yellow gelatinous hydrate resulting was washed free from chlorides by repeated decantation, filtered off and dried in a water oven. Yield, 90%. Purification was carried out most successfully through the diacetate as it crystallizes well and is readily prepared. Saponification was then carried out by filtering a hot saturated acetone solution of pure diacetate into 5% sodium hydroxide solution and after 72 hours' standing, acidifying with dilute acid. The product, after drying to constant weight in a water oven, was pure anhydrous tetrabromo-fluorescein. All analyses were made by the modified lime combustion method.

Subs., (I) 0.3239; (II) 0.2827. Cc. 0.1 *N* $AgNO_3$: (I) 19.87; (II) 17.30.
Calc. for $C_{20}H_8O_5Br_4$: Br, 49.34. Found: (I) 49.03; (II) 48.91.

The fluorescein so obtained is a brick-red amorphous powder. It changes rapidly to bright yellow when moistened with acetone or ethyl acetate without permanent alteration in weight, behaving in this respect analogously to tetraiodo-fluorescein.[1] This ready transformation from the unstable red quinoid to the stable yellow benzenoid form probably takes place through partial solution of an intermediate loose addition product. The yellow color of benzenoid tetraiodo-fluorescein was attributed to the similar color of tetraiodo-phthalic anhydride from which it is derived, but in this case the parent anhydride is colorless. Heating for a short time at high temperatures reverses the equilibrium with formation of the red form. These changes are represented as



Red. Yellow.

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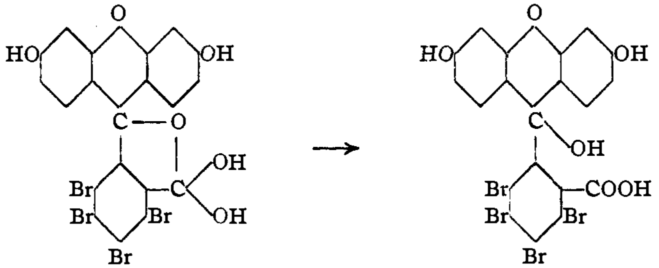
[1] *Ibid.*

The yellow hydrate obtained upon precipitation from alkaline solution was air dried to constant weight at room temperature without visible change in color. Heating at 110° caused a loss in weight corresponding to approximately one molecule of water of constitution, and a partial conversion into the red quinoid form.

Subs., 1.2921. Loss in weight, 0.0318.
Calc. for $C_{20}H_8O_5Br_4.H_2O$: H_2O, 2.70. Found: 2.46.

Alkaline solutions of tetrabromo-fluorescein are deeply colored and highly fluorescent, resembling closely the unhalogenated parent substance. Silk is dyed directly a vivid purplish red similar to that produced by fluorescein. Visual examination, therefore, indicates that the vibrational alterations brought about by the introduction of bromine probably lie chiefly, if not entirely, in the ultraviolet region of the spectrum.

Tetrabromo-fluorescein Carbinol Carboxylic Acid.—When tetrabromo-fluorescein hydrate is treated with absolute alcohol the color changes rapidly to a very much lighter yellow corresponding to the arrangement of the molecule represented by



Hydrous tetrabromo-fluorescein.

Tetrabromo-fluorescein carbinol carboxylic acid.

The resulting carboxylic acid deposits from an alcohol solution in a nearly colorless, amorphous form. Heating at 110° causes a loss in weight corresponding to a molecule of water and a reversion to the yellow benzenoid fluorescein.

Subs., 0.7375. Loss in weight, 0.0173.
Calc. for $C_{20}H_{10}O_6Br_4.H_2O$: H_2O, 2.70. Found: 2.33.

Diammonium Salt.—The salt was formed by exposing a weighed sample of pure anhydrous fluorescein for 18 hours to a current of dry ammonia. When constant weight was attained, the color was bright red. Heating at 100° reconverts the salt into the original fluorescein.

Subs., 0.2520: (I) gain in weight, 0.0123; (II) loss in weight at 100°, 0.0119.
Calc. for $C_{20}H_8O_5Br_4.2NH_3$: NH_3, 4.99. Found: (I) 4.88; (II) 4.72.

Tetrabromo-fluorescein Diacetate.—370 g. of crude tetrabromo-fluorescein was added to 800 cc. of acetic anhydride containing 35 g. of fused sodium acetate. The suspension was heated in a water bath for 30 minutes and finally boiled gently for 20 minutes. The material in suspension gradually lightened until it became nearly colorless. After standing two days, the mixture was poured into water, filtered, washed and dried. The crude diacetate was dissolved in acetone and boiled for several days with successive small portions of bone black. Concentration of the light amber solution gave colorless crystals.

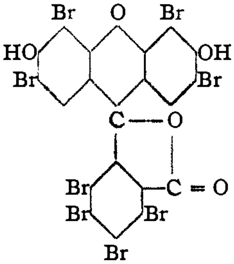
Subs., (I) 0.3964; (II) 0.3156. Cc. 0.1 *N* $AgNO_3$: (I) 21.56; (II) 17.10.
Calc. for $C_{24}H_{12}O_7Br_4$: Br, 43.68. Found: (I) 43.47; (II) 43.30.

The crystalline diacetate is attacked rather slowly by aqueous alkali. The method of saponification indicated above is preferable as the acetone solution gives flocculent material readily acted upon.

Tetrabromo-eosin.—Anhydrous tetrabromo-fluorescein reacts easily with bromine to give tetrabromo-eosin or octabromo-fluorescein. The replacement of 4 additional hydrogen atoms was carried out by suspending 200 g. of pure tetrabromo-fluorescein in 400 cc. of glacial acetic acid containing 80 cc. of bromine. The mixture was boiled gently for an hour, during which the color lightened to a faint pink. The crystalline material was washed with alcohol and further purified from acetone. A yield representing 80% of pure product was obtained.

Subs., (I) 0.2834; (II) 0.2124. Cc. 0.1 *N* $AgNO_3$: (I) 23.48; (II) 17.65.
Calc. for $C_{20}H_4O_5Br_8$: Br, 66.36. Found: (I) 66.21; (II) 66.43.

Tetrabromo-eosin shows only a very slight tendency to rearrange into the quinoid or colored form except in the presence of alkali. Its structure should, therefore, be represented as



It is extremely sensitive toward alkali, and is therefore generally obtained faintly tinged with pink. This color is intensified upon heating to 150° but all efforts to shift the equilibrium further towards the red form failed. Tetrabromo-eosin is practically insoluble in alcohol, slightly so in acetone. It dissolves readily in aqueous alkali with a deep red color and slight fluorescence. Such a solution dyes silk an attractive pink.

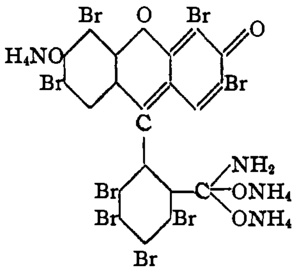
The addition of acid to a dilute alkaline solution precipitated a voluminous pink hydrate which was carefully washed and air dried to constant weight without change in color. Further heating at 110° drove off approximately one molecule of water of constitution.

Subs., 1.3013. Loss in weight, 0.0187.
Calc. for $C_{20}H_4O_5Br_8.H_2O$: H_2O, 1.83. Found: 1.44.

Tetrammonium Salt.—Dry ammonia gas was passed over a weighed quantity of tetrabromo-eosin until constant weight was obtained. The color changed to purple immediately, followed by the formation of a very brilliant deep bronze. The addition corresponded to 4 molecules of ammonia whereas tetrabromo-fluorescein did not react further than the diammonium salt. The ammonia is driven off readily by heating.

Subs., 0.6802. (I) gain in weight, 0.0473; (II) loss in weight at 120°, 0.0468.
Calc. for $C_{20}H_4O_5Br_8.4NH_3$: NH_3, 6.60. Found: (I) 6.50; (II) 6.44.

The addition of 4 molecules of ammonia is probably best accounted for by a rearrangement into the quinoid structure and subsequent direct addition of 2 NH_3 to the carboxyl group. This would give the salt the structure represented by



Tetrabromo-eosin Diacetate.—20 g. of pure tetrabromo-eosin was suspended in 75 cc. of acetic anhydride containing 20 g. of fused sodium acetate. Some of the bright red sodium salt formed at first but upon boiling gently for 30 minutes this largely disappeared. The lumps were then crushed and boiling continued for 15 minutes to insure complete reaction. A theoretical yield of crude product was obtained. The material was recrystallized from benzene until obtained pure as colorless crystals. These contained a molecule of solvent of crystallization as shown by the loss in weight or heating at 130°.

Subs., 1.5622. Loss in weight, 0.0885.
Calc. for $C_{24}H_8O_7Br_8.C_6H_6$: C_6H_6, 6.93. Found: 5.66.
Subs., (I) 0.2520; (II) 0.2500. Cc. 0.1 *N* $AgNO_3$: (I) 19.17; (II) 18.16.
Calc. for $C_{24}H_8O_7Br_8$: Br, 61.06. Found: (I) 60.79; (II) 61.33.

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