

tion the material was acetylated with acetic anhydride in the presence of a drop of pyridine. By 5 crystallizations from alcohol the melting point of this colorless acetyl derivative that crystallized in needles was elevated from $191-2^{\circ}$ to $197-200^{\circ}$.

Subs., 0.0667: CO_2 , 0.1444; H_2O , 0.0247.

Subs., 0.0921: AgI , 0.0466.

Calc. for $\text{C}_{16}\text{H}_8\text{O}_7(\text{COCH}_3)_4$: C, 59.5; H, 4.1; OCH_3 , 6.4. Found: C, 59.05; H, 4.15; OCH_3 , 6.7.

The pure acetyl derivative was hydrolyzed by boiling with 5% sulfuric acid in dilute alcohol and filtering after removing the alcohol on the steam bath. The recovered yellow substance separated from 95% alcohol in curved prisms and melted sharply at $314-315^{\circ}$ to a black oil.

Subs., 0.079: CO_2 , 0.1768; H_2O , 0.0288.

Calc. for $\text{C}_{16}\text{H}_{12}\text{O}_7$: C, 60.7; H, 3.8. Found: C, 61.05; H, 4.1.

This substance appears to be isorhamnetin, one of the monomethyl quercitins, and the purification through the acetyl derivative did not change the results of the combustion.

The *third lead precipitate* was decomposed with hydrogen sulfide and the filtrate from the lead sulfide was concentrated to a syrup but no crystals resulted. The syrup, when subjected to acid hydrolysis, yielded only calcium sulfate.

The writer is greatly indebted to Mr. Clayre Pomeroy for the analytical work.

KALAMAZOO, MICH.

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

PHTHALIC ACID DERIVATIVES; CONSTITUTION AND COLOR. XVI.¹ PHENOLTETRABROMO-PHTHALEIN AND SOME OF ITS DERIVATIVES.

BY DAVID S. PRATT, F. B. DOANE AND A. W. HARVEY.

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The preparation of various halogenated phenolphthaleins has been considered important from two standpoints, *i. e.*, to provide additional indicators of this excellent type for analytical work and to further our knowledge of the effect on absorption spectra brought about by the substitution of important atoms in phthalic acid derivatives. Since the corresponding chlorine and iodine derivatives of phenolphthalein have been prepared it was interesting to study the intermediary bromine analogues.

Phenoltetrabromo-phthalein with the halogen in the anhydride ring was probably obtained in an impure condition by Rupp,² but details are lacking

¹ THIS JOURNAL, 40, 1425 (1918).

² Arch. Pharm., 249, 56 (1911).

in his brief report. The phthalein and some of its more important derivatives have now been prepared in a condition of purity sufficient even for spectroscopic investigation. Unfortunately it is not possible to make this part of the contemplated study at the present time. For this reason the various probable effects due to introducing 4 bromine atoms possessing an acidity between chlorine and iodine and with characteristic activity on adjacent points of unsaturation will not be discussed until spectroscopic data are available.

The tetrabromo-phthalic anhydride used was prepared by the convenient method outlined in a previous article.¹

Phenoltetrabromo-phthalein.—464 g. of tetrabromo-phthalic anhydride was placed in a 2-liter, round-bottom flask provided with an air condenser and intimately mixed with 1390 g. of freshly distilled phenol. The temperature was raised to about 50° C. and 450 g. of fuming sulfuric acid (15% SO₃) added gradually as the reaction proceeded. Heat was then applied by means of an electrically heated air bath at 160° for 9 hours, during which the color of the mix changed nearly to black.

The hot reaction product was poured into a large volume of boiling water, washed several times by decantation and finally steamed thoroughly for several hours or until the odor of phenol had largely disappeared. The material was dissolved in dil. sodium hydroxide solution, precipitated hot with dil. hydrochloric acid, filtered, and washed free from chlorides. The phthalein in the dried product was extracted with alcohol in which unchanged anhydride and tetrabromo-fluoran are insoluble. The residue obtained by distilling off the alcohol contained some tar, and was therefore dissolved in glacial acetic acid and thoroughly treated with bone black. Faintly yellow crystals were deposited on concentration and cooling, giving a yield of 75% of the theoretical amount. Too rapid heating during condensation or prolonged time at high temperature causes excessive tar formation.

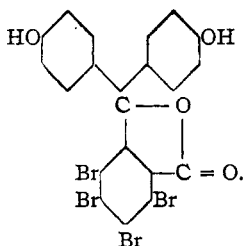
The phthalein was further purified by repeated alternate recrystallization from alcohol and glacial acetic acid until finally obtained in nearly colorless crystals. It is quite soluble, without color, in ordinary organic solvents, and very sensitive to alkali, giving deep purplish red solutions. Ammonia, however, either dry or moist, failed to give the corresponding salt when passed over the dry phthalein. Halogen in every case was determined by the modified lime combustion method.

Subs., (I) 0.3023; (II) 0.2912. Cc. 0.1 N AgNO₃: (I) 19.10; (II) 18.34.

Calc. for C₂₀H₁₀O₄Br₄: Br, 50.43. Found: (I) 50.50; (II) 50.34.

The structure of phenoltetrabromo-phthalein is undoubtedly represented correctly as

¹ THIS JOURNAL, 40, 1416 (1918).



Tetrabromo-fluoran.—The residue left after extracting the crude reaction product with alcohol consisted largely of unchanged anhydride and tetrabromo-fluoran. The former was removed by treating with warm dil. sodium hydroxide solution. The fluoran remaining was washed and purified by repeated recrystallization with bone black from glacial acid in which it is sparingly soluble, being finally obtained as well defined colorless crystals.

Subs., (I) 0.3175; (II) 0.3356. Cc. 0.1 *N* AgNO₃: (I) 20.55; (II) 21.83.

Calc. for C₂₀H₈O₃Br₄: Br, 51.91. Found: (I) 51.74; (II) 51.98.

Phenoltetrabromo-phthalein Diacetate.—The diacetate was prepared by boiling for one hour a mixture of 15 g. of the pure phthalein, 9 g. of fused sodium acetate, and 45 cc. of acetic anhydride. The impure acetate was dissolved in benzene containing acetic anhydride, boiled with bone black for many hours, and finally recrystallized from benzene and alcohol. A yield of pure colorless, well formed crystals corresponding to 65%, was obtained.

Subs., (I) 0.2716; (II) 0.4026. Cc. 0.1 *N* AgNO₃: (I) 15.13; (II) 22.48.

Calc. for C₂₄H₁₄O₅Br₄: Br, 44.53. Found: (I) 44.42; (II) 44.62.

Phenoltetrabromo-phthalein Dibenzoate.—The dibenzoate was prepared by dissolving the pure phthalein in 2% sodium hydroxide solution and shaking with successive portions of benzoyl chloride until the red color disappeared. The product was washed with dilute alkali and 50% alcohol, and recrystallized several times from alcohol. A yield representing 80% was obtained as fine, colorless needles readily soluble in benzene, less so in alcohol.

Subs., (I) 0.2726; (II) 0.2244. Cc. 0.1 *N* AgNO₃: (I) 12.84; (II) 10.58.

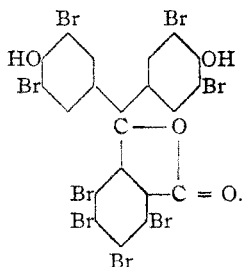
Calc. for C₂₈H₁₈O₆Br₄: Br, 37.97. Found: (I) 37.81; (II) 37.69.

Phenoltetrabromo-phthalein Dimethyl Ether.—15 g. of the pure phthalein was dissolved in 5% sodium hydroxide solution and shaken with successive small portions of dimethyl sulfate. The purple color gradually disappeared and the crude ether precipitated in a yellow amorphous condition. This was purified from alcohol and obtained as colorless crystals which tended to become pale salmon color on drying.

Subs., (I) 0.3217; (II) 0.3026. Cc. 0.1 *N* AgNO₃: (I) 19.44; (II) 18.18.

Calc. for C₂₂H₁₄O₄Br₄: Br, 48.30. Found: (I) 48.12; (II) 48.01.

Tetrabromophenol-tetrabromophthalein.—A solution of 10 g. of bromine in 25 cc. of alcohol was added through a reflux condenser to a boiling solution containing 10 g. of pure phenoltetrabromo-phthalein in 75 cc. of alcohol. Yellow crystals separated at once, the reaction being complete by the time all the bromine was added. A theoretical yield was obtained. The crude product was purified by recrystallization from acetone, giving very pale yellow crystals very slightly soluble in alcohol, easily in acetone. Aqueous alkali dissolves the phthalein with a brilliant clear blue color. Spectroscopic analysis will probably show that the yellow color is due to shifting the limit of visible general absorption toward the longer wave lengths sufficiently to make it evident to the eye. It is exactly these progressive shiftings in the absorption bands that will be investigated when the essential apparatus becomes available. There are no facts, however, opposed to the usual benzenoid structure which should therefore be represented as



Subs., (I) 0.2575; (II) 0.2291. Cc. 0.1 *N* AgNO₃: (I) 21.63; (II) 19.29.
Calc. for C₂₀H₆O₄Br₈: Br, 67.34. Found: (I) 67.14; (II) 67.25.

Diammonium Salt.—Exposure of a weighed quantity of the phthalein to dry ammonia caused the color to become turquoise blue with a gain in weight corresponding to two molecules of ammonia. The salt is not very stable even at ordinary temperatures, and loses its ammonia quantitatively at 100°.

Subs., 0.8047: (I) gain in weight, 0.0283; (II) loss in weight, 0.0282.
Calc. for C₂₀H₆O₄Br₈·2NH₃: NH₃, 3.46. Found: (I) 3.43; (II) 3.40.

Tetrabromophenol-tetrabromophthalein Diacetate.—10 g. of pure phthalein was boiled for one hour in 35 cc. of acetic anhydride containing 8 g. of fused sodium acetate. The hot solution was poured on ice and the crude acetate washed thoroughly with water. It was purified from benzene containing acetic anhydride. The colorless crystals so obtained contained a molecule of benzene removable by heating at 175°.

Subs., 0.6269. Loss in weight, 0.0472.
Calc. for C₂₄H₁₀O₆Br₈·C₆H₆: C₆H₆, 7.02. Found: 7.52.
Subs., (I) 0.2352; (II) 0.2515. Cc. 0.1 *N* AgNO₃: (I) 18.14; (II) 19.44.
Calc. for C₂₄H₁₀O₆Br₈: Br, 61.86. Found: (I) 61.64; (II) 61.79.

Tetrabromophenol-tetrabromophthalein Dibenzoate.—The diben-

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 $C_{24}H_{14}O_6Br_8 \cdot C_6H_6$: C_6H_6 , 6.31. Found: 5.89.

Subs., (I) 0.2520; (II) 0.2763. Cc. 0.1 *N* AgNO₃: (I) 17.25; (II) 19.08.

Calc. for $C_{24}H_{14}O_6Br_8$: 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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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

¹ THIS JOURNAL, 41, 1289 (1919).

² *Ibid.*, 40, 236 (1918).