

dihydro-1,3,4-thiazine is 5-bromomethyl-2-ethoxy- Δ^4 -thiazoline is not substantiated by analyses of the compound in question.

3. Primary aliphatic alcohols react with dibromopropyl isothiocyanate with formation of 5-bromomethyl-2-hydroxy- Δ^4 -thiazoline.

4. Secondary aliphatic alcohols appear to react similarly.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF CORNELL UNIVERSITY]

PHENOLSULFONEPHTHALEIN AND SOME OF ITS DERIVATIVES

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Remsen¹ in 1884 was the first to note the formation of a substance analogous to fluorescein when resorcinol is heated with *o*-sulfobenzoic acid. In 1895 Remsen and Saunders² and in 1898 List and Stein³ stated that a compound analogous to phenolphthalein, and which they assumed to be phenolsulfonephthalein, was formed when the chlorides of *o*-sulfobenzoic acid were heated with phenol. Phenolsulfonephthalein was first prepared *pure* by Sohon⁴ by heating the anhydride of *o*-sulfobenzoic acid with phenol. These two methods are the ones always employed in making the compound.⁵

Most of the phenolsulfonephthalein used in this investigation was prepared by heating the chlorides of *o*-sulfobenzoic acid with an excess of phenol without the aid of a condensing agent.⁶ It was found that when the temperature of the bath did not exceed 100°, the diphenyl ester of *o*-sulfobenzoic acid was the main product of the reaction and very little of the sulfonephthalein was formed. At 135–140°, however, yields of 50% of the sulfonephthalein were obtained. The use of a condensing agent, such as zinc chloride, did not increase the yield, though it shortened the time of heating.

Purification of the Phenolsulfonephthalein.—Early in the course of this investigation, it was found that phenolsulfonephthalein purified by the usual method, by dissolving the crude product in a solution of sodium hydroxide, filtering the solution and precipitating the sulfonephthalein with acid, contained sometimes as much as 8% of a substance that was soluble in a solution of sodium hydroxide, but insoluble in the cold in

¹ Remsen, *Am. Chem. J.*, **6**, 180 (1884).

² Remsen and Saunders, *Am. Chem. J.*, **17**, 352 (1895).

³ List and Stein, *Ber.*, **31**, 1662 (1898).

⁴ Sohon, *Am. Chem. J.*, **20**, 257 (1898).

⁵ See White and Acree, *THIS JOURNAL*, **41**, 1190 (1919). Lubs and Clark, *J. Washington Acad. Sci.*, **5**, 609 (1915).

⁶ Most of the saccharin used in the preparation of the phenolsulfonephthalein was furnished gratis by the Monsanto Chemical Co. of St. Louis, Mo. It was a very pure product and contained only a trace of *p*-sulfaminobenzoic acid.

solutions of sodium or ammonium bicarbonate. Consequently, all the sulfonephthalein used in this investigation was purified by dissolving the crude product in the cold in a solution of sodium bicarbonate, filtering the solution and precipitating the sulfonephthalein from the boiling solution with dil. hydrochloric acid. The phenolsulfonephthalein purified in this way was crystalline and pure, as shown by the results of the analyses. The air-dried product always contains some water which it loses when heated at 120° to 140°: thus, 0.2221, 0.4588, 1.4843, 1.1043 and 1.3070 g. lost 0.0029, 0.0057, 0.0199, 0.0141, and 0.0175 g.; equivalent to 1.31%, 1.24%, 1.34%,⁷ 1.28%⁷ and 1.34%⁷ respectively, while the calculated percentage for $C_{19}H_{14}O_6S + \frac{1}{4} H_2O$ is 1.26.

The dried product absorbs water when exposed to the air.

Sulfur determinations on the above material dried at 120° to 140° gave the following results.

Subs., 0.6612, 0.5460, 0.5070, 0.5117: $BaSO_4$, 0.4278, 0.3635, 0.3331, 0.3347. Calc. for $C_{19}H_{14}O_6S$: S, 9.05. Found: S, 8.89, 9.14,⁷ 9.02,⁷ 8.98.⁷

Sulfur determinations on material made by using zinc chloride as a condensing agent and purified and dried as above gave,

Subs., 0.4427, 0.4755: $BaSO_4$, 0.2967, 0.3180. Found: S, 9.21, 9.19.

Some of the above material, made without the use of a condensing agent, was recrystallized⁸ from glacial acetic acid and after having been purified by the method given above, was dried at 120° to 140° and analyzed.

Subs., 0.4481: $BaSO_4$, 0.2973. Found: S, 9.11.

International atomic weights for 1922 were used in making the calculations recorded in this paper.

Substance Insoluble in Sodium Bicarbonate Solution.—This material is formed as a by-product in the preparation of phenolsulfonephthalein. An excess of phenol and prolonged heating or a temperature above 140° favor its formation. It dissolves in a 4% solution of sodium hydroxide with a brownish-red color very distinct from the bright purple color of solutions of phenolsulfonephthalein in sodium hydroxide. When this solution was heated to the boiling point and then acidified with hydrochloric acid, the substance was precipitated as a dark red, *amorphous* product. It was recrystallized from glacial acetic acid and analyzed. When dried at 120° it lost 6.37 to 6.55% of water and did not contain any acetic acid.

⁷ We are indebted to Mr. N. Fuchs for these determinations.

⁸ *Crystalline Form of Phenolsulfonephthalein.* Crystals of phenolsulfonephthalein from glacial acetic acid were examined by Professor A. C. Gill of the Department of Geology who reports as follows: "The substance appears to be pure and wholly crystalline. So little light is transmitted that not much can be definitely stated as to its optical behavior. The crystals show distinct parallel extinction. The habitus is tabular, the tablets being of elongated rectangular or approximately rectangular shape. These facts together with the (doubtful) appearance of an optical bisectrix normal to the larger faces, indicate but do not prove that the crystals are orthorhombic. The pleochroism is distinct but rather weak. The body color is red, somewhat modified in mass by the bronze-yellow surface color."

Analyses. Subs., 0.3959, 0.4626: BaSO₄, 0.1305, 0.1532. Found: S, 4.53, 4.55.

It will be seen from these analyses that the substance contains only half as much sulfur as phenolsulfonephthalein. Its formation seems to be due to the action of phenol on phenolsulfonephthalein (see action of aniline on phenolsulfonephthalein). When treated with aniline this substance dissolves with a reddish-brown color, which changes to a dark brown on heating, but no diphenylamine-sulfonephthalein is formed.

***p*-Hydroxybenzoyl-benzene-*o*-sulfonic Acid.**—The aqueous filtrates from the crude phenolsulfonephthalein were concentrated and then boiled with an excess of pure barium carbonate.

After filtering the solution it was evaporated to crystallization. Some of the barium salt of *o*-sulfobenzoic acid always crystallized at this point. This was removed by filtration and the mother liquors evaporated to dryness on the water-bath. The dried material was extracted with methyl alcohol and more of the barium salt of *o*-sulfobenzoic acid separated by fractional crystallization. The dark red mother liquors were evaporated to dryness on the water-bath and the dried mass was extracted with absolute methyl alcohol until about $\frac{2}{3}$ of it had dissolved. This solution was evaporated to dryness on the water-bath, and the red residue was dried at 110° and weighed. It was then dissolved in water and the barium precipitated as sulfate.

Analysis. Subs., 7.0578: BaSO₄, 2.3279. Calc. for (C₁₃H₉O₆S)₂Ba: Ba, 19.86. Found: 19.41.

This result shows that the product is the barium salt of *p*-hydroxybenzoyl-benzene-*o*-sulfonic acid. When the filtrate was concentrated, some phenolsulfonephthalein crystallized out. This was removed by filtration. On the addition of conc. hydrochloric acid to the filtrate and evaporation of it to a small volume, dark red crystals of *p*-hydroxybenzoyl-benzene-*o*-sulfonic acid were obtained. When these crystals were heated to 110° they lost water and contained no hydrochloric acid.

Analyses. Subs., 0.5511, 0.4398; loss, 0.0659, 0.0523. Calc. for C₁₃H₉O₆S + 2 H₂O: H₂O, 12.16. Found: 11.96, 11.89.

Sulfur determinations on the dry residue gave the following results.

Analyses. Subs., 0.4852, 0.3875: BaSO₄, 0.4298, 0.3415. Calc. for C₁₃H₉O₆S: S, 12.32. Found: 12.17, 12.10.

These results show that the dried product is *p*-hydroxybenzoyl-benzene-*o*-sulfonic acid minus a molecule of water.

As *p*-hydroxybenzoyl-benzene-*o*-sulfonic acid is not known it was made by the method used by Remsen and Linn⁹ for the preparation of dihydroxybenzoyl-benzene-*o*-sulfonic acid. Ten g. of the acid ammonium salt of *o*-sulfobenzoic acid was heated with 7 g. of phenol. During the 15 hours' heating the temperature rose from 180° to 210°. The mixture was dissolved in water and the phenol distilled with steam. The solution was then boiled with an excess of barium carbonate until all the ammonia was expelled, filtered and evaporated to dryness on the water-bath. The residue was extracted with methyl alcohol and the extract evaporated to dryness. As barium determinations showed that the salt was not pure, it was treated with sufficient absolute ethyl alcohol to dissolve about $\frac{2}{3}$ of it, the solution filtered and evaporated to a sirup on the water-bath. On standing in a desiccator containing sulfuric acid, the barium salt solidified. When heated to 135°, it lost 3.34% in weight; barium determinations with the dry salt gave the following results.

Analyses. Subs., 0.4722, 0.4171: BaSO₄, 0.1583, 0.1402. Calc. for (C₁₃H₉O₆S)₂Ba: Ba, 19.86. Found: 19.73, 19.78.

⁹ Remsen and Linn, *Am. Chem. J.*, **11**, 73 (1889).

The barium salt was dissolved in water, the barium precipitated with a slight excess of sulfuric acid, the solution filtered and evaporated to a sirup. On standing for several days in a desiccator containing sulfuric acid, this solidified to a pink mass very soluble in water and soluble in the ordinary organic solvents except benzene and carbon tetrachloride. It crystallized in pink leaflets when its solution in conc. hydrochloric acid was concentrated to a small volume and allowed to stand. A product crystallized twice from hydrochloric acid was analyzed.

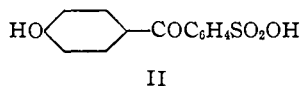
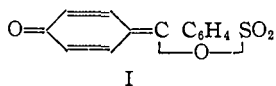
Analysis. Subs., 1.3191; loss at 110°, 0.1577. Calc. for C₁₃H₈O₄S + 2H₂O: H₂O, 12.16. Found: 11.96.

During the drying, even at 80°, the substance melted or dissolved in the water of crystallization, turned dark red and finally solidified to a hard, very hygroscopic red mass. It absorbed water so readily from the air that it was impossible to weigh out a sample for analysis. The dry substance was, therefore, dissolved in 100 cc. of water and 20cc. portions were taken for the sulfur determinations.

Analyses. Subs., 0.25816, 0.25816: BaSO₄, 0.2287, 0.2306. Calc. for C₁₃H₈O₄S: S, 12.32. Found: 12.17, 12.26.

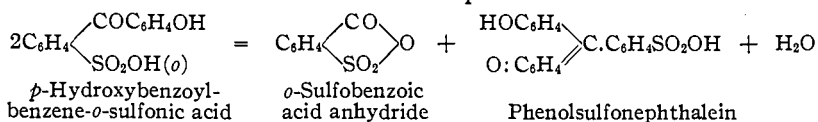
These results show that the red, dried product is *p*-hydroxy-benzoyl-benzene-*o*-sulfonic acid minus 1 molecule of water. This product dissolves in the same solvents that the unheated substance does. It dissolves in water with an amber color, which turns pink when alkali is added, showing that a small amount of phenolsulfonephthalein is formed during the heating to 110°.

From the results of the analyses and the color of the compound the red, dried product probably has the quinoid structure as represented in Formula I, while the pink crystallized form which differs from the dried, red product by 2 molecules of water is *p*-hydroxybenzoyl-benzene-*o*-sulfonic acid as shown in Formula II.



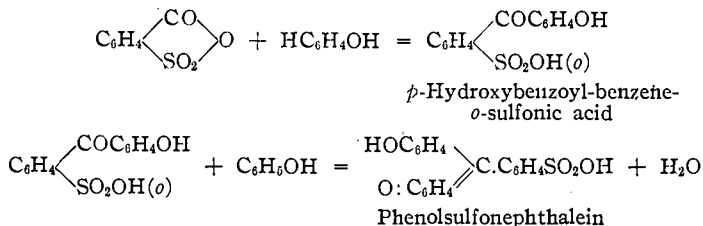
The second molecule of water is probably present as water of crystallization.

When heated to 135–140° *p*-hydroxybenzoyl-benzene-*o*-sulfonic acid lost water and formed phenolsulfonephthalein and the anhydride of *o*-sulfobenzoic acid. The anhydride sublimed in the form of colorless needles, which melted at 128° and absorbed moisture from the air forming a sirup of *o*-sulfobenzoic acid. The reaction is represented as follows.



The phenolsulfonephthalein formed in this way dissolves *completely* in a solution of sodium bicarbonate. When heated with phenol to 135°, *p*-hydroxybenzoyl-benzene-*o*-sulfonic acid also give phenolsulfonephthalein which, however, contains some material insoluble in sodium bi-

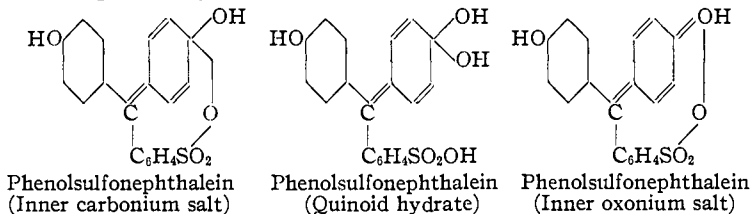
carbonate solution. As *p*-hydroxybenzoyl-benzene-*o*-sulfonic acid combines so readily with phenol to form phenolsulfonephthalein and has been isolated from the filtrate from the crude phenolsulfonephthalein, it is highly probable that it is an intermediate product in the formation of phenolsulfonephthalein. The equations may be written as follows.



As phenolsulfonephthalein is a colored compound it is represented by the above quinoid formula. Because it is the sulfonic acid derivative of

benzaurin (phenolbenzein), $\text{O: C}_6\text{H}_4 : \text{C} \begin{array}{l} \diagup \text{C}_6\text{H}_4\text{OH} \\ \diagdown \text{C}_6\text{H}_5 \end{array}$, which Baeyer¹⁰ has

shown has *basic* properties and forms a *crystalline sulfate*, it is highly probable that dry phenolsulfonephthalein should be represented as an inner oxonium or carbonium salt. The crystallized, air-dried product always contains about 1.26% of water, which would indicate that it is a solid solution of 75% of the quinoid, inner oxonium or carbonium salt and 25% of the quinoid hydrate.



Action of Ammonia on Phenolsulfonephthalein.—When pure *dry* phenolsulfonephthalein is exposed to the action of *dry* ammonia it quickly turns dark red and absorbs somewhat more than 2 molecules of ammonia.

Analyses. Subs., 0.2606, 1.9470: gain, 0.0332, 0.2087. Calc. for $\text{C}_{19}\text{H}_{14}\text{O}_6\text{S} + 2\text{NH}_3$: gain, 9.62. Found: 12.74, 10.72.

This diammonium salt was unstable and slowly lost ammonia, becoming lighter colored when placed in a desiccator containing sulfuric acid. It required a week or more to come to constant weight.

Analyses. Subs., (a) 0.2606, (b) 1.9470: gain, after standing over H_2SO_4 , 0.0119, 0.0787. Calc. for $\text{C}_{19}\text{H}_{14}\text{O}_6\text{S} + \text{NH}_3$: gain, 4.81. Found: 4.57, 4.04.¹¹

This mono-ammonium salt is brownish-red and it dissolves in water with an orange-red color, quite different from the purple of solutions of the diammonium salt.

¹⁰ Baeyer, *Ber.*, **36**, 2791 (1903).

¹¹ Sample a stood for 1 week and Sample b for 5 weeks over conc. sulfuric acid.

Monosodium Salt of Phenolsulfonephthalein.—This was prepared by adding the calculated amount of sodium hydroxide solution to pure phenolsulfonephthalein and filtering off the small amount of the undissolved sulfonephthalein. The filtrate was evaporated to dryness on the water-bath and the residue was dried at 120° and dissolved in absolute alcohol. The solution was diluted with dry ether, and after a few hours was poured off from a dark red sirup and diluted with a large excess of dry ether. The monosodium salt separated as a dark red very viscous liquid. This was dissolved in water and the solution evaporated to dryness on the water-bath. The dark red mass was dried at 120° and analyzed.

Analysis. Subs., 1.0128; loss, 0.0966. Calc. for $C_{19}H_{13}O_6SNa + 2H_2O$: H_2O , 8.74. Found: 9.54.

Sodium determinations on the dry substance gave the following results.

Analyses. Subs., 0.4811, 0.4327; Na_2SO_4 , 0.0881, 0.0802. Calc. for $C_{19}H_{13}O_6SNa$: Na, 6.11. Found: 5.93, 6.00.

This salt is very deliquescent, becoming a red, viscous liquid when exposed to an atmosphere saturated with water vapor. Its aqueous solution has an orange-red color similar to that of the mono-ammonium salt.

Disodium Salt of Phenolsulfonephthalein.—This was made by heating to boiling 3 g. of pure sulfonephthalein with 25 cc. of absolute alcohol in which 0.4 g. of sodium had been dissolved. The salt was precipitated with dry ether. In the mother liquor the salt has a copper color, but after drying it in a desiccator it turned purple with a green surface color. It is very deliquescent, and after it has absorbed moisture the surface color is more intense. Analyses of the salt dried at 110° gave the following results.

Analyses. Subs., 0.6835, 0.6307, 0.7518. Na_2SO_4 , 0.2413, 0.2274, 0.2760. Calc. for $C_{19}H_{12}O_6SNa_2$: Na, 11.55. Found: 11.43, 11.67, 11.89.

Phenolsulfonephthalein Diacetate.—This was made by boiling 3 g. of the pure sulfonephthalein with 35 cc. of acetic anhydride for half an hour and then distilling most of the acetic anhydride. The residue was evaporated to a thick sirup in an evaporating dish in a water-oven. When cold, this solidified to a yellow mass, which was crystallized twice from absolute methyl alcohol. The *colorless*, needle-shaped crystals melted at 165° and turned pink on exposure to the air. The substance lost no weight when heated to 120° and gave the following results on analysis.

Analyses. Subs., 0.4829, 0.5300; $BaSO_4$, 0.2597, 0.2762. Calc. for $C_{19}H_{12}O_6S(COCH_3)_2$: S, 7.31. Found: 7.39, 7.16.

Phenolsulfonephthalein diacetate is very soluble in benzene, soluble in methyl and in ethyl alcohols and in ether. It is insoluble in ligroin. It is very easily saponified by alkaline solutions and is slowly hydrolyzed by water alone. When the dry substance is kept in a well-stoppered bottle, it slowly turns red, due to partial saponification by the alkali of the glass.

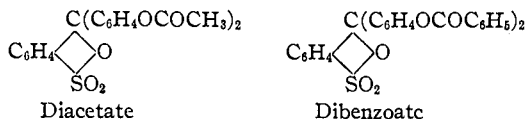
Phenolsulfonephthalein Dibenzoate.—Five g. of pure sulfonephthalein was warmed with 30 cc. of benzoyl chloride until solution was complete. The excess of benzoyl chloride was evaporated in a water-oven and the highly colored crystalline mass crystallized first from absolute methyl alcohol and then from a mixture of ligroin and benzene. The *colorless* needles melted at 185–186° with decomposition and lost no weight at 120°.

Analyses. Subs., 0.7920, 0.5356, 0.6605; $BaSO_4$, 0.3405, 0.2273, 0.2727. Calc. for $C_{19}H_{12}O_6S(COC_6H_5)_2$: S, 5.70. Found: 5.90, 5.83, 5.67.

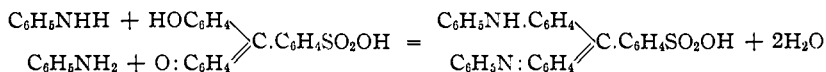
The dibenzoate is very soluble in benzene, less soluble in ether and in methyl and ethyl alcohols, and insoluble in ligroin. It is very slowly saponified by a cold aqueous solution of sodium bicarbonate, but is more rapidly saponified by a cold aqueous solution

of sodium hydroxide. Alcoholic solutions of the alkalis saponify it very rapidly. It has not become colored after standing in a glass bottle for 6 years.

Phenolsulfonephthalein reacts as a tautomeric substance like all the other phthaleins investigated and gives rise to both colorless *lactoid* and colored, *quinoid* derivatives. The diacetate and dibenzoate are colorless lactoid derivatives.



Action of Aniline on Phenolsulfonephthalein. Diphenylamine-sulfonephthalein.—Five g. of pure phenolsulfonephthalein was heated with 50 cc. of aniline at 140–150° for 2 hours. A well-crystallized green product separated during the heating. This was filtered off, boiled with alcohol and well washed with alcohol and then with ether. It was further purified by crystallization from glacial acetic acid. In one preparation 1.87 g. of pure, dry sulfonephthalein gave 2.67 g. of the crude product. The calculated yield according to the equation¹² given below is 2.66 g. The reaction takes place according to the equation.



The substance lost no weight when heated to 120°.

Subs., 0.3414, 0.2750, 0.2822: N, 16.7 cc. (30°, 751.84 mm.), 14.6 cc. (30°, 751.84 mm.), 15.4 cc. (30°, 755.4 mm.). Subs., 0.2702, 0.1588: BaSO₄, 0.1273, 0.0739. Calc. for C₁₉H₁₃O₃S(C₆H₅NH)(:NC₆H₅): N, 5.55; S, 6.36. Found: N, 5.22, 5.67, 5.86; S, 6.47, 6.39.

From these analyses it will be seen that the product is diphenylamine-sulfonephthalein.¹³ The formation of this substance is so characteristic that it may be used as a test for phenolsulfonephthalein. It does not melt even when heated to 315°. It is only slightly soluble in boiling glacial acetic acid and in boiling ethyl alcohol with a blue-green color and is insoluble in water, ether, acetone, benzene, chloroform or ethyl acetate. When suspended in aqueous sodium hydroxide solution it dissolves to a slight extent with a faint red color. On boiling the solution, a little more dissolves and the solution becomes darker red. When this solution is neutralized with acid, the diphenylamine-sulfonephthalein is precipitated in such finely divided form that it remains suspended in the liquid and gives it the appearance of a blue-green solution. The precipitate can, however, be removed by filtration through ordinary filter paper. Alcoholic sodium hydroxide solution dissolves it with a cherry-red color, from which solution

¹² We are indebted to Mr. A. C. Wintringham for this determination.

¹³ Unlike diphenylamine-phthalein, which is colorless, it is a highly-colored compound.

it is precipitated unchanged by acids. Conc. hydrochloric acid dissolves it with a brown color. Water precipitates the green compound from this solution. Phenolsulfonephthalein when boiled with dimethylaniline dissolves with a red color, but no formation of diphenylamine-sulfonephthalein takes place. The presence of the 2 amino-hydrogen atoms is necessary to bring about the reaction (see equation above). Diphenylamine-sulfonephthalein does not combine with dry ammonia and hence does not contain a *free* sulfonic acid group. It is probably an inner ammonium salt. Diphenylamine-sulfonephthalein is also formed by heating the mono-methyl or mono-ethyl ether of phenolsulfonephthalein with aniline.¹⁴

Phenolsulfonephthalin, Dihydroxy-triphenylmethane Sulfonic Acid, $(\text{HOC}_6\text{H}_4)_2\text{CH.C}_6\text{H}_4\text{SO}_2\text{OH}$.—When pure phenolsulfonephthalein suspended in water is boiled with zinc dust, all of it goes into solution and the solution becomes *colorless* after 2 hours. When allowed to cool in the air this solution becomes colored again.

The colorless solution was concentrated to a small volume by distillation in carbon dioxide, filtered from the excess of zinc dust and evaporated to dryness in a vacuum on the water-bath. The zinc salt of the sulfonephthalin remained as a glassy, pale pink mass. It was soluble in alcohol and in acetone, but insoluble in benzene and in ether. All attempts to obtain it in a crystalline form failed. Zinc was determined in the vacuum-dried salt by dissolving it in water and precipitating the zinc with hydrogen sulfide.

Analysis. Subs., 4.65: ZnS, 0.5849. Calc. for $(\text{C}_{19}\text{H}_{16}\text{O}_5\text{S})_2\text{Zn}$: Zn, 8.43. Found: 8.44.

The filtrate containing the free sulfonephthalin was evaporated to dryness in a vacuum on a water-bath. The amorphous pink residue was soluble in acetone and in alcohol, but insoluble in benzene and in ether. It was not obtained crystalline. Sulfur determinations on the material dried in a vacuum gave the following results.

Analyses. Subs., 0.5055, 0.5000: BaSO_4 , 0.3005, 0.2995. Calc. for $\text{C}_{19}\text{H}_{16}\text{O}_5\text{S}$: S, 9.00. Found: 8.16, 8.23.

The low results are due to the fact that it was impossible to dry the substance completely without oxidizing it. The sodium salt of phenolsulfonephthalin is very readily formed when a solution of the sulfonephthalein in caustic soda solution is boiled with zinc dust until it is completely decolorized. All attempts to isolate this salt failed on account of its great solubility in water and in alcohol and because it so readily undergoes oxidation in the air to the sodium salt of phenolsulfonephthalcin.

Colorless Monomethyl Ether of Phenolsulfonephthalein.—As phenol-sulfonephthalein is a strong acid, decomposing carbonates and forming salts, it was thought that it would form esters by the catalytic method of esterification with methyl and ethyl alcohols. Instead, colorless mono-methyl and mono-ethyl ethers were obtained.

Five g. of the pure sulfonephthalein was boiled with 250 cc. of absolute methyl alcohol containing 3% hydrochloric acid until it all went into solution, which required about 4 hours. The orange-red solution was poured into 1.5 liters of cold, dil. sodium

¹⁴ See Baeyer and Villiger, *Ber.*, **35**, 3013 (1902), and **38**, 569 (1905), for the analogous formation of triphenylpararosaniline.

carbonate solution and the ether was precipitated from this solution by the addition of a slight excess of hydrochloric acid. The pink precipitate was crystallized first from methyl alcohol and then from ether and was finally obtained as *colorless* needles which rapidly turned flesh-colored when drained and exposed to the air. It melted at 178° and lost no weight when heated to 120°.

Analyses. Subs., 0.5211, 0.5015: BaSO₄, 0.3240, 0.3132. Calc. for C₁₉H₁₃O₄-SOCH₃: S, 8.71. Found: 8.54, 8.58.⁷

The monomethyl ether of phenolsulfonephthalein resembles the monomethyl ether of phenolphthalein¹⁵ very closely in its properties and chemical conduct. It is soluble in methyl or ethyl alcohol, acetone, benzene, glacial acetic acid, chloroform or ethyl acetate. It is difficultly soluble in ether, and is insoluble in petroleum ether. It dissolves in cold water to a limited extent and the solution has a yellow color. When the solution is boiled the color deepens, but not much more of the substance dissolves. When the hot, saturated aqueous solution is concentrated the color becomes red. When the volume of the solution becomes small by evaporation at room temperature, globules of a red oil separate and on allowing this mixture to evaporate to dryness in the air the residue consists of a mixture of this red material and colorless crystals. This mixture dissolves readily in water with an orange-red color which becomes yellow when the solution is made alkaline, showing that the monomethyl ether is not hydrolyzed by boiling with water. Caustic soda solution dissolves a small amount of the ether with a yellow color which becomes red when the solution is boiled. This red color is quite different from the purple-red of solutions of phenolsulfonephthalein in alkalis. When the hot, saturated alkaline solution cools the color fades to pink, and after a time colorless prisms

of the disodium salt of the carbinol sulfonic acid,

$$\begin{array}{c} \text{H}_3\text{COC}_6\text{H}_4 \\ \text{NaOC}_6\text{H}_4 \quad \text{C} \quad \begin{array}{l} \text{OH} \\ \text{C}_6\text{H}_4\text{SO}_2\text{ONa} \end{array} \end{array}$$

crystallize. The monomethyl ether is not saponified even by long, continued boiling with solutions of the alkalis. When boiled for some time with dil. hydrochloric acid, however, it is partially hydrolyzed and crystals of phenolsulfonephthalein are deposited when the solution cools. The ether dissolves in conc. sulfuric acid with red color and is precipitated unchanged from this solution by water. Cold aniline dissolves the ether with a red color. When this solution is boiled the color gradually changes to blue and then to green, and green crystals of diphenylamine-sulfonephthalein separate. Dimethylaniline dissolves the ether in the cold with a yellow color which deepens somewhat when the solution is boiled, but no other change takes place. Pyridine also dissolves the ether with a yellow color, but does not react with it even when boiled.

Colored Monomethyl Ether of Phenolsulfonephthalein.—When heated for half an hour in a current of dry air to 170° the colorless monomethyl ether melts to a dark red liquid, but 0.5419 g. lost only 0.0013 g. When the substance is heated for less than half an hour, the conversion into the colored modification is not complete, while when heated longer, even at a lower temperature, it slowly loses weight due to decomposition.

When exposed to dry ammonia gas the colorless ether *does not gain* in weight, but the red modification, obtained by heating, absorbs about 2 molecules of ammonia. After standing in a desiccator containing sulfuric acid until it has come to constant weight it contains 1 molecule of ammonia as shown by the following results.

Analyses. Subs., 0.5185: gain, 0.0496; gain after standing over H₂SO₄, 0.0243. Calc. for C₁₉H₁₃O₅SCH₃ + NH₃, 4.63. Calc. for C₁₉H₁₃O₅SCH₃ + 2NH₃, 9.25. Found: 9.57; over H₂SO₄, 4.69.

¹⁵ See R. Meyer and Spengler, *Ber.*, **38**, 1321 (1905).

The change of the colorless to the colored ether is represented as follows.



It was found impossible to prepare an acetate or benzoate of the mono-ethyl ether.

Colorless Mono-ethyl Ether of Phenolsulfonephthalein.—This ether was made in the same way as the monomethyl ether.

It crystallizes in colorless needles which become pale pink on exposure to the air and melt at 171°. The air-dried material lost no weight when heated to 110°.

Analyses. Subs., 0.6769, 0.7355: BaSO₄, 0.4114, 0.4423. Calc. for C₁₉H₁₃O₄S·OC₂H₅: S, 8.39. Found: 8.35, 8.26.

This ether has practically the same solubilities as has the monomethyl ether. It dissolves in water to a slight extent and the solution has a pale yellow color. Like the colorless monomethyl ether, the colorless mono-ethyl ether does not gain in weight in an atmosphere of ammonia or of dry hydrogen chloride. When heated to 170° for half an hour it melts to a dark red liquid practically without loss in weight; thus, 0.9285 g. lost only 0.0009 g.

When this red ethyl ether is ground in a mortar and exposed to dry ammonia it absorbs between 1 and 2 molecules. After standing in a desiccator over sulfuric acid until it comes to constant weight, it has gained an amount which corresponds to a little less than 1 molecule of ammonia.

Analyses. Subs., 0.9236: gain, 0.0742; gain after standing over H₂SO₄, 0.0341. Calc. for C₁₉H₁₃O₄S·OC₂H₅ + NH₃, 4.46. Calc. for C₁₉H₁₃O₄S·O·C₂H₅ + 2NH₃, 8.91. Found: 8.03; over H₂SO₄, 3.78.

The colorless mono-ethyl ether gives substantially the same colors and reactions as the colorless monomethyl ether when boiled with caustic soda solution, aniline, dimethylaniline or with pyridine. It seems to be less stable than the methyl ether, for it is partially hydrolyzed to phenolsulfonephthalein when its aqueous solution is boiled for some time.

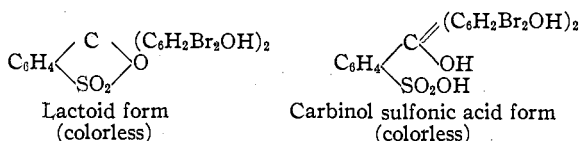
Tetrabromo-phenolsulfonephthalein.—In preparing this compound, the methods of Lubs and Clark and of White and Acree were used. As usually obtained it has an orange or brown tinge (possibly due to the presence of some hydrate) but a practically colorless product can be obtained by recrystallizing the substance from glacial acetic acid and drying it over solid sodium hydroxide in an evacuated desiccator or by heating the red hydrate (see below) to 115° to 120° for 1/2 to 3/4 of an hour. When perfectly pure, the tetrabromo compound crystallizes in colorless prisms, which have an elongated hexagonal outline. It is soluble in water (at least 0.4 g. in 100 cc.), more soluble in methyl and ethyl alcohols, in benzene and glacial acetic acid and can be crystallized from the two latter solvents.

As the percentage of bromine in the published analysis of this tetrabromo-phenolsulfonephthalein and in our first analyses did not agree with the calculated amount in either the lactoid or carbinol sulfonic acid forms of this compound, but was intermediate between them, it became necessary to purify the substance with all possible care and

analyze it for bromine and sulfur. To do this, a commercial sample,¹⁶ the melting point of which was 275–276° (corr.), was carefully crystallized from benzene and then from glacial acetic acid and dried in a vacuum desiccator containing solid sodium hydroxide. The melting point rose to 279° (corr.), with decomposition and evolution of gas, after crystallization from benzene and did not change after recrystallization from glacial acetic acid. This product was practically colorless and lost no weight when heated to 120°.

Analyses. Subs., 0.2582, 0.2741: 0.1 N AgNO₃, 15.43 cc., 16.36 cc. Subs., 0.3638, 0.3772: BaSO₄, 0.1261, 0.1340. Calc. for (lactoid) C₁₉H₁₀O₆Br₄S: Br, 47.72; S, 4.79. Calc. for (carbinol sulfonic acid) C₁₉H₁₂O₆Br₄S: Br, 46.47; S, 4.66. Found: Br, 47.75, 47.70; S, 4.76, 4.88.

From these results it will be seen that tetrabromo-phenolsulfonephthalein is the lactoid modification and not the carbinol sulfonic acid.



It is interesting to note that while phenolsulfonephthalein is known only in the colored, quinoid form, its tetrabromo derivative is colorless and has the lactoid structure. A colored modification of the tetrabromo derivative has also been obtained (see below). Unlike phenolsulfonephthalein, tetrabromo-phenolsulfonephthalein does not form a compound analogous to diphenylamine-sulfonephthalein when boiled with aniline. It is quite soluble in aniline with a deep red color.

Hydrate of Tetrabromo-phenolsulfonephthalein.—This compound was made by dissolving 2 g. of the tetrabromo-phenolsulfonephthalein in 500 cc. of water and adding 150 to 200 cc. of conc. hydrochloric acid. On standing overnight, the amorphous, orange-colored precipitate, which is first formed, goes over to a dark red hydrate and settles to the bottom of the flask. When insufficient acid is added the orange-colored precipitate does not change color or settle on standing, but remains suspended for several weeks. From 1.5 g. of the tetrabromo compound 1.4 g. of the hydrate was obtained. On standing in dry air for several days, the dark red hydrate gradually loses water and becomes lighter colored, but it re-absorbs the water lost and returns to its original color when placed in air saturated with water vapor. It loses most of its water when kept in a vacuum desiccator over sulfuric acid for 3 to 4 days. This dried product has a *light brown color* and contains less than 0.2% of water, which may be driven off at 120°. During the heating the substance becomes practically colorless as the *quinoid*, colored form of the tetrabromo-phenolsulfonephthalein is converted into the *lactoid*, colorless form. Several different samples of the air-dried hydrate gave the following results when dried to constant weight in a vacuum desiccator over sulfuric acid.

Analyses. Subs., 0.3611, 0.8950, 0.7711: loss (over H₂SO₄) 0.0351, 0.0877, 0.0769. Subs., 0.6301, 0.2110, 0.5127: loss (at 120°), 0.0613, 0.0207, 0.0521. Calc. for C₁₉H₁₀O₆Br₄S + 4H₂O: H₂O, 9.71. Found: (over H₂SO₄) 9.72, 9.80, 9.97; (at 120°) 9.73, 9.81, 10.16.

Bromine was determined in the colorless material resulting from drying the hydrate at 120°.

¹⁶ Kindly sent us by Mr. H. A. B. Dunning.

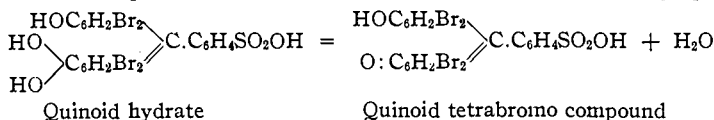
Analysis. Subs., 0.2240: 0.1 *N* AgNO₃, 13.34 cc. Calc. for C₁₉H₁₀O₆Br₄S: Br, 47.72. Found: 47.60.

When the light brown, vacuum-dried material was placed over water in a desiccator and allowed to come to constant weight (4 days) and then kept in air overnight, it was found to have become dark red and to have re-absorbed all the water that it had lost on drying; thus, 0.5090 g. gained 0.0537 g., equivalent to 9.54% of water absorbed on the basis of the final product.

The material that had been heated to 120°, however, on exposure to moist air did not absorb moisture readily and seemed to form a dark red substance and a lighter colored one.

Analysis. Subs., 0.2252: gain, 0.0029. Calc. for C₁₉H₁₀O₆Br₄S + 1/2 H₂O: H₂O, 1.33. Found: 1.27.

Tetrabromo-phenolsulfonephthalein hydrate when heated in a melting-point tube becomes light orange colored at about 95°, turns darker and has a greenish tinge at about 195°, becomes almost colorless at about 265° and melts at 278–279° (corr.), with decomposition and evolution of gas. The conversion of the colored hydrate into the colored form of tetrabromo-phenolsulfonephthalein is represented by the following equation.



Action of Ammonia on Tetrabromo-sulfonephthalein.—When pure, dry tetrabromo-phenolsulfonephthalein is exposed to the action of dry ammonia it absorbs slightly more than 4 molecules of ammonia and becomes deep purple-blue with a bronzy surface color. The exposure was for 24 hours, after which the salt was allowed to stand for several weeks in a desiccator over sulfuric acid until constant weight was reached. The material then contained 2 molecules of ammonia and had a dark blue color.

Analyses. Subs., 0.9829: gain, 0.1046; gain after standing over H₂SO₄, 0.0460. Calc. for C₁₉H₁₀O₆Br₄S + 4NH₃: NH₃, 10.18. Found: 10.64. Calc. for C₁₉H₁₀O₆Br₄S + 2NH₃: NH₃, 5.09. Found: 4.68.

Monosodium Salt of Tetrabromo-phenolsulfonephthalein.—This salt was prepared by dissolving pure tetrabromo-phenolsulfonephthalein in slightly more than the calculated amount of sodium hydroxide in absolute alcohol. On concentrating the solution and cooling, a scarlet salt separated. As it was deliquescent it was dried in a desiccator over calcium chloride. When it is heated to 110° it becomes dark red. It dissolves in water with an orange-red color which becomes blue when the solution is diluted sufficiently. The salt was dried at 110°.

Analyses. Subs., 0.3216, 0.3125: Na₂SO₄, 0.0330, 0.0320. Calc. for C₁₉H₉O-Br₄SNa: Na, 3.32. Found: 3.32, 3.32.

Disodium Salt of Tetrabromo-phenolsulfonephthalein.—This salt was made by the method used in making the disodium salt of phenolsulfonephthalein. It is purple-blue with a bronzy surface color and is very deliquescent. Either its aqueous or alcoholic solution in thin layers is purple, but in bulk both are blue. The salt was dried at 130°.

Analyses. Subs., 0.3664, 0.3618: Na₂SO₄, 0.0715, 0.0695. Calc. for C₁₉H₈O-Br₄SNa₂: Na, 6.44. Found: 6.32, 6.22.

Tetrabromo-phenolsulfonephthalein Diacetate.—This was made by the method used in preparing phenolsulfonephthalein diacetate. It crystallizes from absolute methyl alcohol in colorless prisms which melt at 234°. It is much more stable than phenolsulfonephthalein diacetate and is only slowly saponified by aqueous alkalis.

Some of the dry material has been kept for 6 years in a cork-stoppered bottle without becoming colored, except that the layer in contact with the glass has a faintly bluish tinge. It is readily saponified by alcoholic caustic soda. It is soluble in benzene, or methyl or ethyl alcohol, but is insoluble in ether or acetone. The substance was dried at 110°.

Analyses. Subs., 0.2859, 0.3326, 0.5153: 0.1 N AgNO₃, 15.15 cc., 17.55 cc. Subs., 0.5153: BaSO₄, 0.1570. Calc. for C₁₉H₈O₆Br₄S(COCH₃)₂: Br, 42.40; S, 4.25. Found: Br, 42.36, 42.17; S, 4.18.

Tetrabromo-phenolsulfonephthalein Dibenzoate.—This was prepared by the method used in making phenolsulfonephthalein dibenzoate. After extraction with hot methyl alcohol it was crystallized from a mixture of benzene and methyl alcohol. The colorless product lost no weight when heated to 120°. It decomposes at 270° without melting.

Analyses. Subs., 0.2614, 0.2477: 0.1 N AgNO₃, 11.92, 11.28 cc. Subs., 0.4136: BaSO₄, 0.1074. Calc. for C₁₉H₈O₆Br₄S(COC₆H₅)₂: Br, 36.41; S, 3.65. Found: Br, 36.45, 36.40; S, 3.57.

The dibenzoate is very soluble in benzene, but only slightly soluble in methyl or ethyl alcohol. It is much more stable than the diacetate. A specimen that has been kept in a cork stoppered bottle for 6 years has not changed. It is saponified very slowly even by boiling aqueous sodium hydroxide. Boiling alcoholic sodium hydroxide solution saponifies it more readily.

Monomethyl Ether of Tetrabromo-phenolsulfonephthalein.—This substance could not be made by boiling tetrabromo-phenolsulfonephthalein with absolute methyl alcohol containing either 3% hydrochloric acid or 5% sulfuric acid. It was prepared by dissolving tetrabromo-phenolsulfonephthalein in absolute methyl alcohol containing sufficient sodium methylate to form the disodium salt, adding an excess of methyl iodide and boiling the solution for 4 days. Whenever the solution lost its purple color more sodium methylate and methyl iodide were added. The reaction goes on more rapidly when the mixture is heated to 115° in an autoclave. The purple solution which contained a blue precipitate (probably the sodium salt) was acidified with an excess of hydrochloric acid. The solution became orange-colored and the blue precipitate became yellow. This was filtered off and extracted with boiling benzene, in order to remove any unchanged tetrabromo-phenolsulfonephthalein that might be present. This extraction changed the color of the substance, first to a red-brown and then to a green. This green product turned very dark colored when heated in a melting point to tube 100°, became red-brown at 285° and melted at 299°. The yellow unextracted product turned green when exposed to the air for several days. When heated in a melting point tube, it undergoes the same color changes as the green product obtained by extraction with benzene, but it melted at 295–296°. The green product obtained by extraction with benzene, dissolved in absolute methyl alcohol with a deep red color. This solution was made acid by passing dry hydrogen chloride into it, filtered and evaporated to a small volume. The product which separated was yellow at first, but became bright red when dried in the air. When dried at 140° this substance became dark red in color and lost 9.57% in weight; this loss seemed to be due to methyl alcohol.

Analyses. Subs., 0.2235, 0.2173: 0.1 N AgNO₃, 12.75 cc., 12.67 cc. Subs., 0.4429, 0.3828: BaSO₄, 0.1542, 0.1321. Calc. for C₁₉H₈O₆Br₄SCH₃: Br, 46.74; S, 4.69. Found: Br, 46.66, 46.60; S, 4.78, 4.74.

This red methyl ether dissolves in water with a deep red color which gradually becomes blue on dilution. Alkalies turn this red solution blue. It is soluble with a red color in methyl or ethyl alcohol, acetone or ethyl acetate, but could not be obtained

crystalline from these solvents. It is insoluble in ether, benzene or chloroform. It dissolves in aniline with a deep red color. When this solution is boiled, the aniline does not react with the methyl ether to form a compound analogous to diphenylamine-sulfonephthalein. In this respect this colored ether resembles its parent substance, tetrabromo-phenolsulfonephthalein, and differs from the monomethyl ether of phenolsulfonephthalein. The colored methyl ether is not saponified by long continued boiling with solutions of the caustic alkalis. The blue solution gradually becomes almost colorless when boiled and when cold is colorless. This is due to the formation of the di-

sodium salt of the carbinol sulfonic acid,

$$\begin{array}{c} \text{H}_3\text{COC}_6\text{H}_2\text{Br}_2 \\ \text{NaOC}_6\text{H}_2\text{Br}_2 \end{array} \text{C} \begin{array}{l} \text{OH} \\ \text{C}_6\text{H}_4\text{SO}_2\text{ONa} \end{array}$$

When hydrochloric acid is gradually added to this colorless solution it turns blue, as the excess of alkali is neutralized and when the acid is added in excess a yellow precipitate of the hydrochloride of the methyl ether is precipitated.

Action of Hydrochloric Acid on the Colored Methyl Ether.—When exposed to dry hydrogen chloride this red monomethyl ether becomes yellow and forms an unstable hydrochloride as is shown by the following results.

Analyses. Subs., 0.4664: gain, 0.0276; gain after standing over solid NaOH for 2 days, 0.0015. Calc. for $\text{C}_{19}\text{H}_9\text{O}_6\text{Br}_4\text{SCH}_3 + \text{HCl}$: HCl, 5.33. Found: 5.92; over NaOH, 0.32.

Action of Ammonia on the Colored Methyl Ether.—When exposed to dry ammonia the dry methyl ether absorbed 3 molecules, but lost 2 of them very readily when kept in a desiccator containing sulfuric acid. The product was dark blue with an intense bronze surface color.

Analyses. Subs., 0.7845: gain, 0.0572; gain after 3 days over H_2SO_4 , 0.0204. Calc. for $\text{C}_{19}\text{H}_9\text{O}_6\text{Br}_4\text{SCH}_3 + 3\text{NH}_3$: gain in NH_3 , 7.47. Found: 7.33. Calc. for $\text{C}_{19}\text{H}_9\text{O}_6\text{Br}_4\text{SCH}_3 + \text{NH}_3$: gain in NH_3 , 2.49. Found: over H_2SO_4 , 2.60.

It will be seen from the above results that while phenolsulfonephthalein gives a colorless monomethyl ether, which does not combine with either hydrogen chloride or with ammonia, tetrabromo-phenolsulfonephthalein gives a colored monomethyl ether which combines with both hydrogen chloride and ammonia. The formula of this colored methyl ether is analogous to that of the colored monomethyl ether of phenolsulfonephthalein obtained by heating the colorless ether. It will be recalled that this colored ether forms an ammonium salt with dry ammonia.

Summary

1. Pure crystallized phenolsulfonephthalein has been made and analyzed and its reactions have been carefully studied. The pure anhydrous substance probably has an inner oxonium or inner carbonium salt structure, while the crystallized, air-dried product seems to be a solid solution of this inner salt and the quinoid hydrate.

2. Some material which is insoluble in sodium bicarbonate solution is always formed in the preparation of phenolsulfonephthalein. It contains half as much sulfur as phenolsulfonephthalein and results from the action of phenol on phenolsulfonephthalein.

3. It has been shown that *p*-hydroxybenzoyl-benzene-*o*-sulfonic acid is formed as an intermediate product in the formation of phenolsulfonephthalein. *p*-Hydroxybenzoyl-benzene-*o*-sulfonic acid has been isolated from the filtrates from the crude sulfonephthalein and it has also been pre-

pared pure from the acid ammonium salt of *o*-sulfobenzoic acid and phenol. When heated alone or with phenol it gives phenolsulfonephthalein.

4. Phenolsulfonephthalein, like the other phthaleins, acts as a tautomeric substance and yields *colorless* derivatives of the *lactoid* modification and *colored* derivatives having a quinoid structure. Phenolsulfonephthalein, its salts, the *colored* monomethyl and mono-ethyl ethers, and diphenylamine-sulfonephthalein are colored and have the quinoid structure. The diacetate and dibenzoate, the *colorless* monomethyl and mono-ethyl ethers and *pure* tetrabromo-phenolsulfonephthalein are colorless and are derivatives of the lactoid modification.

5. The *colorless* monomethyl and mono-ethyl ethers are converted into the *colored* quinoid ethers, without loss of weight, by heating them to 170° for half an hour. The colorless ethers do not combine with ammonia. The colored ones form stable mono-ammonium salts, showing that they contain a *free* sulfonic acid group or are inner carbonium or oxonium salts.

6. Phenolsulfonephthalein and its ethers when heated with aniline react with it with the elimination of 2 molecules of water or one of water and one of alcohol to form diphenylamine-sulfonephthalin. This substance unlike the colorless diphenylamine-phthalein is *colored* and hence has a *quinoid* structure.

7. When phenolsulfonephthalein suspended in water is boiled with zinc dust it all goes into solution forming the colorless zinc salt of the sulfonephthalin. Dihydroxy-triphenylmethane sulfonic acid has been made from this zinc salt by decomposing it in aqueous solution with hydrogen sulfide. It is extremely readily oxidized by the air to the sulfonephthalein.

8. *Pure* tetrabromo-phenolsulfonephthalein has been found to be *colorless*. It has been shown to have the lactoid and not the carbinol sulfonic acid structure. Like phenolsulfonephthalein it is a tautomeric substance and gives rise to both colored quinoid and colorless lactoid derivatives. Its hydrate, its salts and its monomethyl ether are colored and have the quinoid structure. The hydrate when dried in a vacuum over sulfuric acid gives the *colored*, quinoid modification of tetrabromo-phenolsulfonephthalein, which is converted into the colorless, lactoid form on heating. The diacetate and dibenzoate of tetrabromo-phenolsulfonephthalein are colorless and are derivatives of the lactoid modification.

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