The second question is: Does anesthetic ether ever contain benzene? We have examined four brands of anesthetic ether. In only one case was an absorption pattern obtained and this was much fainter than has been found with U.S.P. ether or C.P. anhydrous ether containing the impurity.

The latter part of Dr. de Laszlo's article does not deal with a question of fact but rather with the interpretation of ultraviolet absorption spectra. Since the validity of the experimental results contained in our paper has been disproved, a further discussion of interpretation does not seem profitable at this time. However, on the basis of the quantum theory, we find little reason for supposing any absorption or emission spectrum to be essentially continuous.

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[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORY OF HYNSON, WESTCOTT & DUNNING]

SALICYLSULFONPHTHALEIN AND ITS TETRABROMO AND MONOMERCURY DERIVATIVES

BY WILTON C. HARDEN

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Since the synthesis of the first sulfonphthaleins by Remsen and his students[1] many new members of this class of compounds have been described by Orndorff and his co-workers,[2] Clark and Lubs,[3] Cohen[4] and others.

The purpose of the present paper is to describe still another sulfonphthalein, namely, salicylsulfonphthalein. The only mention of this compound in the literature is contained in some German patents[5] describing certain dyestuffs prepared by the condensation of *o*-sulfobenzaldehyde with various phenols, cresols and substituted phenols and cresols. In this manner salicylic acid was condensed with *o*-sulfobenzaldehyde to give a red dye.

The author has prepared this compound by condensing salicylic acid with the anhydride of *o*-sulfobenzoic acid and found it to possess some interesting properties. Its tetrabromo and its monohydroxymercuri derivative have also been prepared and will be discussed.

Since nearly all of the sulfonphthaleins are useful indicators in the determination of hydrogen-ion concentration and since salicylsulfon-

[1] (a) Remsen, *Am. Chem. J.*, **6**, 180 (1884); (b) Remsen and Saunders, *ibid.*, **17**, 352 (1895); (c) Sohon, *ibid.*, **20**, 257 (1898).

[2] (a) Orndorff and Sherwood, THIS JOURNAL, **45**, 486 (1923); (b) Orndorff and Shapiro, *ibid.*, **46**, 2856 (1924); (c) Orndorff and Purdy, *ibid.*, **28**, 2212 (1926); and others.

[3] Clark and Lubs, *J. Wash. Acad. Sci.*, **5**, 609 (1915); **6**, 481 (1916); **6**, 483 (1916).

[4] (a) Cohen, *U. S. Public Health Reports*, **38**, 199 (1923); (b) **41**, 53, 3051 (1926).

[5] Friedländer, (**1908–1910**), vol. 9, p. 195; D. R. P. 189,938–198,909 and others.

phthalein contains in addition to the sulfonic acid group two carboxyl groups, it was thought that a study of its color changes in solutions of varying P_H would be of interest. For this purpose a 0.1% solution in 70% alcohol was used. Five-tenths of a cc. of this solution was added to 10 cc. of various buffer mixtures prepared according to Clark.[6] As would be expected the compound is an excellent indicator; it is yellow at all P_H's below 6.6 and shades through a brown to a bluish red at P_H 8.2. The fact that at P_H 7.0–7.2 the color is distinctly brown, while below this point it is yellow and on the alkaline side red, should make the indicator a useful one in those cases where an indicator which shows a marked color change at the neutral point is desired. The color change of the tetrabromo derivative, that is, tetrabromosalicylsulfonphthalein, was determined in a similar manner. This indicator was found to change from a yellow at P_H's lower than 3.2 through a brownish-purple to a clear purple at P_H 4.6. Color standards prepared using these indicators have shown no appreciable fading after several months' exposure to ordinary light. Since these compounds have at least a potential value as indicators, the author suggests that they be called, in accordance with the usual custom, Salicyl Red and Salicyl Purple in place of the longer salicylsulfonphthalein and tetrabromosalicylsulfonphthalein. No attempt has been made to determine the apparent dissociation constants or spectrophotometric data for these indicators.

The monohydroxymercuri derivative of the unhalogenated sulfonphthalein has also been prepared and the germicidal properties of the three compounds have been studied *in vitro*. The mercury derivative, as would be expected, is the only one to show any marked germicidal power.

Experimental Part

Preparation of Salicylsulfonphthalein (Salicyl Red).—The salicylic acid used was the ordinary U. S. P. variety. The anhydride of *o*-sulfobenzoic acid used was prepared by the method described by White and Acree.[7] Fifty g. of salicylic acid was intimately ground in a mortar with 24 g. of the anhydride. This amount of salicylic acid represents about a 50% excess. This mixture was transferred to an Erlenmeyer flask, 2 cc. of concd. sulfuric acid and 10 cc. of fuming stannic chloride added and the flask heated in an oil-bath for four hours at 120–130°. At this temperature the mixture slowly melts and begins to redden. At the end of four hours the temperature was raised slowly (1/2 hour) to 160–180°. At this temperature the melt becomes more intense in color and begins to harden. The temperature was kept at 170° for several hours longer and the semi-fused mass then poured into 4 liters of hot water. If the melt is allowed to cool it becomes caked and great difficulty is experienced in removing it from the flask. Sodium carbonate was then added until the solution was alkaline. Since the dye is a relatively strong acid, care must be taken in this operation to prevent the solution

[6] Clark, "The Determination of Hydrogen Ions," Williams and Wilkins Co., Baltimore, 1922, 2nd edition.

[7] White and Acree, THIS JOURNAL, 41, 1190 (1919).

from frothing over. The purple alkaline solution was next heated to boiling and filtered while hot. It was then transferred to a large evaporating dish, strongly acidified with hydrochloric acid and concentrated on the water-bath. Some of the dye separates out at this stage as a green tar and should be removed, redissolved in sodium carbonate and reprecipitated. After several such treatments the dye is obtained in a pure form as a red, amorphous powder. The main body of the solution was evaporated to about one-third of its original volume and allowed to cool. The dye separates from this solution contaminated with large amounts of salicylic acid. This was removed by repeated extractions with ether, in which the dye is insoluble. The dye was then further purified by repeated solution in sodium carbonate and reprecipitation with hydrochloric acid.

Anal. Calcd. for $C_{21}H_{14}O_9S$: S, 7.24. Found: 7.38.

Preparation of Tetrabromosalicylsulfonphthalein (Salicyl Purple).—4.5 g. of Salicyl Red prepared as described above was suspended in 100 cc. of glacial acetic acid and a solution of 7.0 g. of bromine in glacial acetic acid added. The solution was warmed on the steam-bath for several hours and allowed to stand overnight. The next day it was again warmed on the steam-bath and aspirated while warm to remove hydrobromic acid and some of the acetic acid. This is essentially the method described by Cohen[4a] for the preparation of tetrabromo-*m*-cresolsulfonphthalein. When the solution had been evaporated to about one-half its original volume, it was cooled in the ice-box for several hours, when a small crop of crystals separated. These were filtered off and the filtrate poured into dilute hydrochloric acid. The dye separated as an amorphous, yellow powder which was dissolved in sodium carbonate, reprecipitated, dried and analyzed.

Anal. Calcd. for $C_{21}H_{10}O_9Br_4S$: Br, 42.18; S, 4.20. Found: Br, 42.20; S, 4.52.

Preparation of Monohydroxymercuri-salicylsulfonphthalein.—4.4 g. of Salicyl Red was dissolved in sufficient normal sodium hydroxide to form the disodium salt. To this solution was added a solution of 3.18 g. of mercury acetate to which had been added several drops of acetic acid. There was no apparent action in the cold and no precipitation of the mercury salt of the dye. If such a salt is formed in this case, it is probably soluble. The solution was boiled for several hours when it lost its red color and became quite brown. The boiling was continued until a small test-tube portion showed no free mercury when tested with ammonium sulfide. It was then filtered and poured into dilute hydrochloric acid. The mercurated material came down at once as a brown powder which was filtered by suction and washed repeatedly with warm water.

Anal. Calcd. for $C_{21}H_{14}O_{10}SHg$: Hg, 30.4. Found: Hg, 29.84.

Bacteriological and Pharmacological Part

The method used for testing the germicidal properties of these compounds was a modification of the Hygienic Laboratory method for determining phenol coefficients. The procedures used are, briefly, as follows: 0.1 cc. of a twenty-four hour broth culture of the test organism is added to 5 cc. of the diluted sample at 37°. Body temperature is used because of the possible application of these materials for combating infections within the human body. At the end of one, five and fifteen minutes, subculture was made into 10 cc. of sterile broth and this incubated at 37° for forty-eight hours, at which time they were observed for growth. It was found that a 1% solution of the mercurated salicylsulfonphthalein kills *B. Typhosus* and *Staph. Aureus* within one minute. It also kills

B. Typhosus in 1–1000 dilution within five minutes and in 1–2000 dilution within fifteen minutes. *Staph. Aureus* is killed by a 1–500 dilution within five minutes but is not killed by 1–1000 dilution in fifteen minutes. One per cent. solutions of Salicyl Red and Salicyl Purple do not kill either *B. Typhosus* or *Staph. Aureus* in fifteen minutes under the same conditions.

A preliminary pharmacological investigation shows that the mercurated derivative apparently is eliminated from the body through the digestive system, while the other two compounds, like most sulfonphthaleins, are eliminated through the urinary tract.

The author wishes to express his thanks to Drs. G. F. Reddish and David I. Macht for the bacteriological and pharmacological investigation of these compounds.

Summary

1. Salicylsulfonphthalein (Salicyl Red) has been prepared and its indicator properties have been studied.

2. Tetrabromosalicylsulfonphthalein (Salicyl Purple) has been prepared and its indicator properties have been studied.

3. The monohydroxymercuri derivative of salicylsulfonphthalein has been prepared.

4. A preliminary bacteriological and pharmacological study of these compounds has been made.

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[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF JOHNS HOPKINS UNIVERSITY]

THE ALKYLATION OF BENZENE, TOLUENE AND NAPHTHALENE

BY T. M. BERRY[1] AND E. EMMET REID

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It was shown by Balsohn[2] that ethylene may be substituted for ethyl chloride in the Friedel and Crafts synthesis. Milligan and Reid[3] found that the reaction is facilitated by high-speed stirring to such an extent that this becomes a convenient method for the ethylation of benzene.

The present investigation has to do with a further study of the reaction and with its extension to propylene and cyclohexene.

The ethylene (or propylene) is passed into the benzene at such a rate that only an occasional bubble escapes. If an excess of gas passes through, hydrogen chloride is carried away and the reaction slows down. It is

[1] From the Ph.D. dissertation of T. M. Berry, June, 1923.

[2] Balsohn, *Bull. soc. chim.*, [2], **31**, 539 (1879).

[3] (a) Milligan and Reid, THIS JOURNAL, **44**, 206 (1922); (b) *Ind. Eng. Chem.*, **15**, 1048 (1923).