3. The acyl group does not enter in either the 9 or 10 position.

4. Whereas it has been impossible to nitrate retene itself, these acyl derivatives nitrate easily.

5. By reduction of acetylretene semicarbazone, ethylretene has been secured.

6. The work has considerable significance for the chemistry of the terpenes and resins.

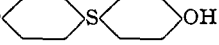
NEW YORK, N. Y.

[CONTRIBUTION FROM THE CHEMICAL AND BACTERIOLOGICAL RESEARCH LABORATORIES OF HYNSON, WESTCOTT & DUNNING, INC.]

PREPARATION AND BACTERIOLOGICAL STUDY OF SOME SYMMETRICAL ORGANIC SULFIDES[1]

BY FITZGERALD DUNNING, BROWN DUNNING, JR., AND W. ERIC DRAKE

RECEIVED JUNE 18, 1931 PUBLISHED SEPTEMBER 5, 1931

In the course of a study of the influence of the structure of compounds containing two hydroxyphenyl groups upon the bacteriological properties, we have prepared some derivatives and analogs of 4,4′-dihydroxydiphenylsulfide, HO  OH, where the phenol residue may be substituted by CH_3, OH, Cl, Br, etc. Johnson and his co-workers have published[2] results dealing with the preparation and study of the bactericidal properties of a number of unsymmetrical organic sulfides. Due to differences in methods of testing, comparisons with values found by these investigators are not in order.

According to Tassinari[3] symmetrical organic sulfides are formed when a cold carbon disulfide solution of a phenol is treated with sulfur dichloride.

Table I lists the sulfides which have been prepared by a modification of this method, the details of which appear below.

TABLE I

DATA ON SULFIDES

Phenol used	Empirical formula of sulfide	Sulfur, % Calcd.	Sulfur, % Found	Melting point, °C.	Solubility: NaOH	Solubility: Alcohol	Solubility: Benzene
Phenol	$C_{12}H_{10}O_2S$	14.68	14.73	151	Soluble	Soluble	Soluble hot
Resorcin	$C_{12}H_{10}O_4S$	12.80	13.00	165–167	Soluble	Soluble	Soluble hot
m-Cresol	$C_{14}H_{14}O_2S$	13.07	12.98	142.5	Soluble	Soluble	Soluble hot
p-Chlorophenol	$C_{12}H_8O_2Cl_2S$	11.15	10.95	173	Soluble	Soluble	Soluble hot
p-Bromophenol	$C_{12}H_8O_2Br_2S$	8.51	8.66	180	Soluble	Soluble	Soluble hot
Thymol	$C_{20}H_{26}O_2S$	9.70	9.80	152.5–153.5	Soluble hot	Soluble hot	Slightly hot

[1] Paper read before the Section on Medicinal Chemistry, at the Indianapolis Meeting of the American Chemical Society, April, 1931.

[2] Hilbert and Johnson, THIS JOURNAL, **51**, 1526 (1929); Bass and Johnson, *ibid.*, **52**, 1146 (1930).

[3] Tassinari, *Gazz. chim. ital.*, **17**, 83 (1887); **19**, 343 (1889); **20**, 362 (1890).

It was found, limited of course by the conditions of our experiments, that no ortho-substituted phenols would react with sulfur dichloride to give a sulfide, regardless of the nature of the substituent group present in the phenol. No meta- or para-substituted phenols, furthermore, would react when the substituent group was a so-called meta-orienting group. Tassinari[3] reports similar findings with nitrophenols, but has made a compound from *o*-cresol.

Indefinite results were obtained when *p*-cresol, hydroquinone, *m*-chlorophenol and *m*-bromophenol were used. Difficulty in repeating the experiments made with these phenols led us to decide against including these compounds in this study.

No attempts have been made to explain the behavior of these reactions from a theoretical point of view.

Experimental

The general method adopted for the preparation of the compounds in this report is: two moles (or a proportionate amount) of the desired phenol is dissolved in two liters of carbon tetrachloride or anhydrous ether (particularly for resorcinol). The reaction is carried out in a three-necked, round-bottomed flask fitted with a mechanical stirrer, thermometer, dropping funnel and a reflux condenser. The condenser is connected to an absorption tower as hydrochloric acid is copiously evolved. A cold solution ($-10°$) of one mole of sulfur dichloride in carbon disulfide is added gradually by means of the dropping funnel. The reaction proceeds vigorously at room temperature with little attendant rise in temperature of the reaction mixture. The total time for addition is generally about one hour. Hydrochloric acid is evolved and a white or yellow precipitate separates. This precipitate is filtered off, and may be recrystallized from benzene. White crystals of the desired sulfide are thereby obtained.

Sulfur dichloride may be prepared by passing chlorine into sulfur monochloride at $-15°$ until the calculated amount of chlorine has been taken up.[4] The compounds were analyzed for sulfur by the usual Parr bomb oxidation method.

Bacteriological

These compounds have been tested for their bactericidal properties using the method developed by Reddish.[5] This method is one of those employed by the United States Food and Drug Administration in governmental regulatory work. Due to the insolubility of some of these compounds in water, 30% ethyl alcohol was used as a solvent.

Table II lists the bactericidal properties of the sulfides and also of the

[4] Abegg, Auerbach, Koppel, "Handbuch der anorganischen Chemie," **1927**, Vol. IV, p. 300.

[5] Reddish, *Am. J. Public Health*, **1927**, 320.

phenols from which they were prepared. The dilution recorded represents an average of ten or more tests on each compound, the greatest killing dilution being determined in each case by a series of tests.

TABLE II

GREATEST KILLING DILUTION

Solvent, 30% alcohol; test organism, *Staphylococcus aureus*

Compound	5 min.	10 min.	15 min.
Phenol	1–120	1–240	1–300
Resorcin	1–100	1–200	1–200
m-Cresol	1–250	1–600	1–750
p-Chlorophenol	1–750	1–2500	1–5000
p-Bromophenol	1–500	1–1375	1–2500
Thymol	1–1000	1–2000	1–3500
Sulfide from:			
Phenol	1–1500	1–2500	1–3500
Resorcin	1–350	1–525	1–800
m-Cresol	1–2000	1–3500	1–4500
p-Chlorophenol	1–7500	1–15,000	1–25,000
p-Bromophenol	1–5000	1–7500	1–15,000
Thymol	1–10,000	1–12,000	1–22,000

30% alcohol alone has no bactericidal effect on the strain of *Staphylococcus aureus* used in these tests.

It can be seen from the table that there is a relatively constant factor in the relationship of the killing power of these sulfides when compared to the phenols from which they are derived. For example, phenol under the conditions of the test kills in a dilution of 1–120 in five minutes, whereas 4,4′-dihydroxydiphenyl sulfide (made from phenol) kills in a dilution of 1–1500 in five minutes. Similar comparisons show that the sulfides exhibit a killing power approximately ten times as great as that of the analogous phenol (except in the case of resorcin). Regardless of the effect of substituent groups present in the phenol molecules, the linking of two phenol molecules by means of a sulfur atom results in a relatively constant enhancement of the bactericidal properties.

Some very interesting observations were made during this study regarding the effect of non-germicidal dilutions of alcohol on the killing powers of the germicides tested. It was found that, although both 20% alcohol and 30% alcohol have no germicidal properties when tested by the technique described, a much greater dilution of any given germicide will kill bacteria when 30% alcohol is used as a solvent than will kill when 20% alcohol is the solvent. A full report dealing with our investigation of this phenomenon will be published elsewhere.

Summary

1. Some symmetrical organic sulfides have been prepared by treating phenols with sulfur dichloride.

2. A study of the reaction between isomeric phenols and sulfur dichloride has been made.

3. It has been found that linking two phenol molecules by means of a sulfur atom results in a relatively constant factorial enhancement of their respective bactericidal properties.

4. Studies similar to this are now in progress and other series will be reported on later.

BALTIMORE, MARYLAND

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

THE STRUCTURE OF ENOL-ACETATES AND THE CORRESPONDING VINYLAMINES[1,2]

BY L. J. ROLL AND ROGER ADAMS

RECEIVED JUNE 19, 1931 PUBLISHED SEPTEMBER 5, 1931

At present there has been only one method devised for the determination of the structure of enols where two or more structures are possible. This is the ozonization method of Scheiber,[3] which consists merely in ozonizing any particular enol or equilibrium mixture of a keto and enol, and, after decomposing in the usual way, determining the structure of the products. There are in many instances, difficulties in the application of this method since it is frequently necessary to isolate and prove the constitution of secondary degradation products even if it is assumed that ozone during the course of the reaction does not cause any change in the equilibrium of the original mixture.

It has been the purpose of this investigation to determine the structure of some stable enol derivatives. This, of course, might be done merely by ozonization and isolation of the products, but many of the same difficulties would occur as in the ozonization of the enols themselves. Enol-acetates were selected for study. Although two possible enol-acetates of each 1,3-dicarbonyl compound may exist, in each instance studied, only a single compound was isolated. On the assumption that 1,3-dicarbonyl compounds in solution exist as equilibrium mixtures of the two enol and

[1] This communication was in completed manuscript form when a paper by Michael and Ross, THIS JOURNAL, **53**, 2394 (1931), appeared. During the course of this investigation the authors used a similar procedure to the one described in the Michael and Ross article for determining the structure of an enol ester. The compounds used in this research are different from those studied by Michael and Ross.

[2] This contribution is an abstract of a portion of a thesis submitted by L. J. Roll in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[3] (a) Scheiber and Herold, *Ber.*, **46**, 1105 (1913); *Ann.*, **405**, 295 (1914); (b) Lublin, *Chem.-Ztg.*, **39**, 433 (1915); (c) Scheiber and Hopfer, *Ber.*, **47**, 2704 (1914); *ibid.*, **53**, 697 (1920); (d) Weygand and Baumgärtel, *ibid.*, **62**, 574 (1929).