

chloride. The precipitate of the sodium salt was twice recrystallized from hot water. The yield of pure product was 44 g. or 66% of the theoretical. The analytical data and yields of the four sulfonates are included in Table I.

The sulfur analyses were made by the Parr bomb method. The solubility determinations consisted of weighing the residues obtained by evaporation of the water from 25-cc. portions of saturated solutions of the various salts.

Summary

Four new *p*-alkylphenol-*o*-sulfonic acids have been made and the solubilities of their sodium salts in water determined. Of the compounds studied only the *n*-propyl- and *n*-butylphenolsulfonates have a measurable antiseptic action:

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[CONTRIBUTION FROM THE MCCARTHY NEUROLOGICAL FOUNDATION AND THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY, MEDICAL SCHOOL, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, AND THE LABORATORY OF BIOLOGICAL CHEMISTRY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS]

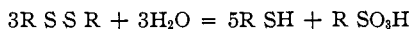
THE MECHANISM OF THE PRODUCTION OF THIOL ACIDS (R SH) AND SULFONIC ACIDS (R SO₃H) FROM DITHIO ACIDS (R S S R). III. THE ACTION OF COPPER SALTS^{1,2}

BY PAUL W. PREISLER AND DORIS B. PREISLER

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Dithio acids (R S S R) have been shown to be simultaneously converted into thiol acids (R SH) and sulfonic acids (R SO₃H) by the action of Ag⁺,^{3,4} BrHg⁺,⁵ and Hg⁺⁺,^{6,7} the final result may be expressed by the equation



in which the formation of R SH and R SO₃H appears to be accelerated by reactants which remove the R SH by precipitation (Ag⁺, Hg⁺⁺) or by formation of un-ionized complexes (BrHg⁺).

The reaction between cupric salts and dithio acids has been studied by a quantitative method in which the corresponding sulfonic acid barium salt and the di-cuprous derivative of the thiol acid were isolated and identified. Of several possible reactions, the most probable is expressed by the equation

¹ Presented at the Meeting of the American Chemical Society in Buffalo, N. Y., September, 1931.

² The authors are indebted to the Smith, Kline and French Co., of Philadelphia, and to the Science Research Fund of Washington University, who have shared the expenses of this investigation with the respective institutions.

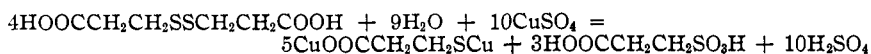
³ Vickery and Leavenworth, *J. Biol. Chem.*, **86**, 129 (1930).

⁴ Preisler and Preisler, *ibid.*, **89**, 631 (1930).

⁵ Preisler and Preisler, *ibid.*, **95**, 181 (1932).

⁶ Andrews and Wyman, *ibid.*, **87**, 427 (1930).

⁷ Simonsen, *ibid.*, **94**, 323 (1931).



This presents an interesting example of oxidation and reduction in which two substances in higher states of oxidation are both reduced at the expense of a further oxidation of part of one of the reactants. Reactions of this kind may be the cause of lower yields when copper salts are used in the isolation of R SH and R S S R compounds.

Experimental

Because of the ease of the isolation of the products, dithiodihydracrylic acid was selected for study of the reaction of dithio acids with copper sulfate and copper perchlorate. The quantity of di-cuprous compound that was isolated depended upon the acidity, the temperature, the concentrations and the presence of oxygen. Conditions were adjusted so as to obtain a high yield of products, since complete reaction apparently did not take place within reasonable time under the conditions studied. The maximum yield obtained was approximately 57% of the original dithio acid as a di-cuprous derivative.

Isolation of the Di-cuprous Thiol Derivative.—(CuSO_4 reaction): 100 cc. of 0.2 *M* CuSO_4 , 0.0025 *N* in H_2SO_4 , and 325 cc. of water were placed in a flask fitted with a reflux condenser and heated in a boiling water-bath. Nitrogen, purified by passing over hot copper, was continuously passed through the solution to remove oxygen.

Fifty cc. of 0.1000 *N* di-sodium dithiodihydracrylate was added and the mixture heated for five hours. The light yellow precipitate was filtered off on a sintered glass crucible, washed with water containing a little sulfuric acid and then with acetone; amount of precipitate isolated (average of six experiments), 0.661 g., representing 57% of the original dithiodihydracrylic acid.

Analysis of the Di-cuprous Derivative.—Thiol determination: 0.30 to 0.45 g. of the precipitate was dissolved in excess potassium iodide and hydrochloric acid and titrated² with 0.1000 *N* potassium iodate: found, SH (average of six experiments), 14.26%; theoretical, 14.30%.

Copper determination: A 0.15 to 0.20 g. sample was dissolved in bromine water. After the removal of the excess of bromine by evaporation on the steam-bath, 3 g. of potassium iodide was added and the solution titrated with 0.1000 *N* sodium thiosulfate; found, Cu (average of six experiments), 54.3%; theoretical, 55.0%.

Isolation of the Di-cuprous Thiol Derivative.—($\text{Cu}(\text{ClO}_4)_2$ reaction): Sulfonic acid could not be isolated successfully from the sulfate solutions so similar experiments were carried out with perchlorate solutions: 150 cc. of 0.1 *M* copper perchlorate, 0.01 *N* in perchloric acid and 300 cc. of water were heated in a boiling water-bath, nitrogen was passed through, and 40.00 cc. of 0.1000 *N* di-sodium dithiodihydracrylate was added. The mixture was allowed to react for eight hours, after which the precipitate was filtered off. Amount of precipitate obtained (average of six experiments), 0.439 g., representing 47% of the original dithiodihydracrylic acid. To establish the identity of the compound, analyses for copper content, using 0.17 to 0.23 g. samples, were made: found (average of six experiments), 54.9%; theoretical, 55.0%.

Isolation of the Barium Salt of the Sulfonic Acid.—To the filtrate from the di-cuprous thiol compound was added 15 cc. of *N* barium perchlorate and then the mixture was saturated with hydrogen sulfide. After warming to coagulate, the copper sulfide (and a little barium sulfate) was filtered off and the filtrate was evaporated to about 10 cc. on the steam-bath. The solution was neutralized with *N* sodium hydroxide and one drop excess *N* perchloric acid was added; the white or gray precipitate which

formed was removed by centrifugalization. This precipitate is, perhaps, due to a decomposition of the dithiodihydracrylic acid present, since this gives a similar precipitate and a small amount of sulfonic acid when treated in a like manner. The solution and washings were evaporated to 50 cc., 150 cc. of 95% ethyl alcohol was added and the mixture warmed, whereupon precipitation of the barium sulfonate took place. This concentration of alcohol prevents the precipitation of the barium salt of the dithio acid. The mixture was cooled to about 7° and the crystalline precipitate filtered off on a sintered glass crucible. Isolated (average of five experiments) 0.284 g. of anhydrous Ba(OOCCH₂CH₂SO₃), representing approximately 24.5% of the original dithio acid.

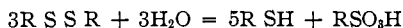
Analysis of the Barium Sulfonate.—A 0.1 to 0.18 g. sample of the precipitate was placed in a platinum dish and dried at 180° to obtain the anhydrous salt and then quickly weighed. The material was ignited in a muffle, treated with a few drops of sulfuric acid and again ignited. Found, Ba (average of five experiments), 46.8%. Theoretical, 47.5%.

ANALYTICAL DATA AND PRODUCTS OF THE REACTION BETWEEN DITHIODIHYDRACRYLIC ACID AND CUPRIC SALTS

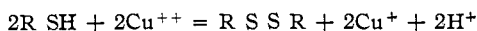
Reaction with CuSO ₄ CuOOCCH ₂ CH ₂ SCu			Reaction with CuOOCCH ₂ CH ₂ SCu		Cu(ClO ₄) ₂ Ba(OOCCH ₂ CH ₂ SO ₃)	
Isolated, g.	Cu, %	—SH, %	Isolated, g.	Cu, %	Isolated, g.	Ba, %
0.6679	54.6	14.18	0.4495	55.3	0.2820	47.2
.6598	54.3	14.30	.4338	54.7	.2706	46.7
.6574	54.4	14.35	.4363	54.9	.2888	46.7
.6566	54.2	14.26	.4371	54.5	.2959	46.7
.6559	54.1	14.16	.4408	55.0	.2849	46.5
.6678	54.3	14.33	.4374	54.8		
Av. 0.661	54.3	14.26	0.439	54.9	0.284	46.8
Calcd.	55.0	14.30		55.0		47.5

Discussion

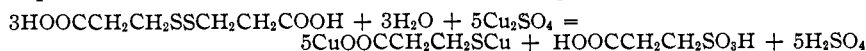
The action of copper salts in causing the formation of sulfonic acids and thiol acids from dithio acids is probably due to reduction of the Cu⁺⁺ to Cu⁺ with subsequent precipitation of the di-cuprous derivative. The reduction of Cu⁺⁺ may result from the reaction with the R SH formed when water reacts with the dithio acid according to



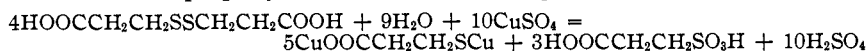
Cupric ion is then reduced as follows



Cuprous ion then reacts with the R SH present forming the insoluble di-cuprous derivative similar to the reaction with Ag⁺,⁴



The sum of the properly substituted equations gives



This series of reactions would require the conversion of 37.5% of the original dithio acid into sulfonic acid or a sulfonic acid—thiol derivative ratio of 0.60. The ratio calculated from the best experimental values is

0.52 and indicates that some Cu^{++} reduction is perhaps caused by material other than the —SH of the R SH.

The possibility of the occurrence of this series of reactions or any of its steps must be considered when isolating (as from biological material) R SH compounds (in the presence of oxidizing agents) or R S S R by means of cupric or cuprous salts, since sulfonic acids may result which cannot be easily reconverted into the original acids. Such reactions may also take part in the oxidation of R SH and R S S R when copper salts are used as catalysts.

The reaction is of chemical interest as an example of the interaction of two substances in higher states of oxidation to produce more reactive reducing substances and some of a more fully oxidized, unreactive product. The mechanism will be more fully discussed in a subsequent publication on the production of $\text{R SO}_3\text{H}$ from R S S R by oxidizing agents.

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[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE OF INDUSTRIAL RESEARCH]

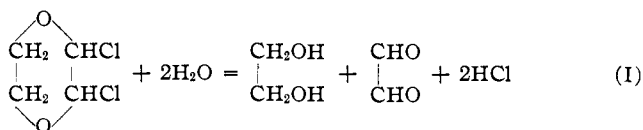
THE PREPARATION OF DI- AND ISOMERIC TETRACHLORODIOXANES

BY C. L. BUTLER AND LEONARD H. CRETCHER

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Dichlorodioxane was recently prepared by Böeseken, Tellegen and Henriques¹ for use as an intermediate in the preparation of stereoisomeric 1,4,5,8-naphthodioxanes. A convenient means of determining the structure of the dichloro derivative was found in the easy hydrolysis of the substance in boiling water. As the aqueous solution of the hydrolysis product yielded quantitatively one molecular equivalent of glyoxal-*p*-nitrophenylosazone on treatment with *p*-nitrophenylhydrazine, it was concluded that the chlorine atoms were in vicinal positions. The hydrolysis apparently proceeded according to equation I. In the present paper, this work was confirmed and the evidence in support of equation I



was completed by the identification of glycol, as dibenzoate, among the hydrolysis products. As far as the present authors are aware, no other experiments on the chlorination of dioxane have been made. Van Alphen²

¹ Böeseken, Tellegen and Henriques, *Proc. Roy. Soc. Amsterdam*, **34**, 631 (1931); *Rec. trav. chim.*, **50**, 909 (1931).

² Van Alphen, *ibid.*, **49**, 1040 (1930).