steroids have been examined in the regions where absorption characteristic of the carbon–carbon double bond is known to occur. The presence of a double bond containing at least one directly linked hydrogen atom can usually be detected from measurements in the neighborhood of 3030 cm.$^{-1}$.

A comparative study of steroids containing ethylenic linkages at different positions has shown that the frequency of the maximum in the region of the C=C stretching vibration (1580–1680 cm.$^{-1}$) is specific for a given location of the bond in the steroid molecule. In conjugated dienes, α,β-unsaturated ketones and the estrogens these bands are intense. In steroids containing non-conjugated ethylenic double bonds the bands, although weak, can generally be observed.

Absorption associated with the carbon–hydrogen bending vibrations in the neighborhood of 800–970 cm.$^{-1}$ is variable in the steroids and so far no unequivocal correlations with structure have been established in this part of the spectrum.

These observations have proved of value in the elucidation of the structure of new steroids isolated from urine.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE JOHNS HOPKINS UNIVERSITY]

Reactions with Heavy Metals and their Bearing on Poisoning and Antidote Action[1]

BY JAMES L. A. WEBB,[2] IQBAL SINGH BHATIA, ALSOPH H. CORWIN* AND ALVIN G. SHARP[3]

The successful use of 2,3-dimercaptopropanol (BAL) as an antidote for poisoning by certain heavy metals climaxes years of investigation in numerous laboratories concerning the mechanism of poisoning by heavy metals. It has been shown that the specific action of the metal is to form derivatives similar to the mercaptides with critical sulfhydryl groups in such a manner as to remove the necessary sulfhydryls from the biochemical systems in which they are functioning. A brief review of the literature on this subject may be found in a publication by Peters, Stocken and Thompson.[4] Our interest in the field stems from investigations which have been under way for a number of years concerning the toxic action of mercurials and other divalent metal derivatives.

The present paper reports our preliminary observations on the chemistry of the displacement reactions which are of interest in connection with heavy metal poisoning. Data on the pharmacological findings will be published elsewhere.

General Principles.—It has been shown that sulfhydryl compounds are essential for the growth of many, and probably all, cells.[5] Recently a large group of enzymes has been shown to contain –SH groups essential for enzymatic activity. This activity is inhibited by mercury and arsenic compounds[6] and is restored by glutathione.[7] The poisoning thus results from metallic combination with essential sulfhydryl groups. *Detoxicant* action is a preliminary combination of a substance with the metallic poison in a compound so firm that the metal is not available for reaction with essential sulfhydryls. *Antidote* action is observed after combination has taken place with the essential sulfhydryls but when the affinity of the antidote for the metal is greater than that of the essential sulfhydryls and displacement takes place. This latter reaction can obviously be favored by the mass action effect of large amounts of antidote but will be most favorable if the affinity of the antidote for the metal is high. For this reason a search for sulfur compounds with high affinity for metals is in order. Peters[4] and his collaborators succeeded in this quest by the use of two sulfhydryl groups in the same compound. An alternative approach is to use a single sulfur atom with substituent groups chosen to give a great increase in chemical affinity for metal. This high chemical affinity may or may not be added to the chelation effect to secure the desired end. The general method of attack is outlined below.

The Poisoning Reaction.—In the equations given below, we have used mercury as the metal but it is our belief that such equations also apply to other heavy metals such as cadmium, lead, and even silver, with appropriate modifications.

Toxic mercurials may be divided into five types: (I) HgX_2, (II) $R'HgX$, (III) R'_2Hg, (IV) $R'HgSR''$, and (V) $(R'S)_2Hg$. It is to be expected from the literature that compounds of types I and II would react readily with sulfhydryl compounds. Poisoning by Type III compounds, if it were due to the mechanism suggested, would

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* Harvard University Ph.D. 1932.

[1] Studies on Heavy Metal Poisoning, paper I. A portion of this paper is from the doctoral dissertation of Iqbal Singh Bhatia, The Johns Hopkins University, 1949. Another portion of this paper was presented before the Div. of Med. Chem. of the Am. Chem. Soc. at the New York Meeting, Sept., 1947.

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[4] Peters, Stocken and Thompson, *Nature*, **156**, 616 (1945).

[5] Volonsky, *Compt. rend. Soc. Biol. Paris*, **109**, 528 (1932), *Compt. rend. Acad. Sci. Paris*, **197**, 712 (1933); *Ann. inst. Pasteur*, **52**, 76 (1934); see also Fildes and Richardson, *Brit. J. Exptl. Path.*, **18**, 292 (1937).

[6] Barron and Singer, *Science*, **97**, 356 (1943); *J. Biol. Chem.*, **157**, 221 (1945).

[7] Hellerman, Chinard and Dietz, *J. Biol. Chem.*, **147**, 443 (1943).

necessitate cleavage of a mercury to carbon bond, Equation 1

$$R'_2Hg + RSH \longrightarrow RSHgR' + R'H \qquad (1)$$

This seems drastic to proceed under physiological conditions. The known toxicity of these compounds makes the experiment a critical one. Either the reaction must proceed or the mechanism of poisoning must be abandoned or modified.

We have found that the reaction of cleavage of type III compounds does occur in the test tube at room temperature and at blood *p*H when dithizone, $C_6H_5N{=}NC(SH){=}NNHC_6H_5$,[8] is used as the sulfur containing molecule. We shall abbreviate this as (DzS)H. Because of the solubility relationships, the reaction is most easily demonstrated in non-aqueous media

$$(RC_6H_4)_2Hg + (DzS)H \longrightarrow RC_6H_5 + RC_6H_4Hg(SDz) \qquad (2)$$

$R = H$ or CH_3

In aqueous media, it is difficult to stop reactions with compounds of type I, II or III at the first stage of the reaction, or to isolate a free carboxylic acid such as that derived from compound IVa below. The presence of acid tends to carry the reaction on as in equation 4.

$$\underset{\text{(IIIa)}}{Hg(C_6H_4COOH)_2} + (DzS)H \longrightarrow \underset{\text{(IVa)}}{(DzS)HgC_6H_4COOH} + C_6H_5COOH \qquad (3)$$

$$2(DzS)HgC_6H_4COOH \longrightarrow (DzS)_2Hg + \underset{\text{(Va)}}{Hg(C_6H_4COOH)_2} \qquad (4)$$

That acid causes the cleavage of the second C–Hg bond is shown by the reaction of ethylmercuric dithizonate with hydrochloric acid

$$\underset{\text{(IVb)}}{2(DzS)HgC_2H_5} + H^+ + Cl^- \longrightarrow (DzS)_2Hg + C_2H_5HgCl + [C_2H_6] \qquad (5)$$

The mercuric bis-dithizonate was identified as such by comparison with a sample prepared by the reaction of two moles of dithizone with one mole of mercuric chloride

$$HgCl_2 + 2(DzS)H \longrightarrow (DzS)_2Hg + 2H^+ + 2Cl^- \qquad (6)$$

On reaction of equimolar quantities of dithizone and mercuric chloride, monodithizone mercuric chloride is formed

$$HgCl_2 + (DzS)H \longrightarrow (DzS)HgCl + H^+ + Cl^- \qquad (7)$$

Because of its decomposition when heated, mercuric bis-dithizonate is best identified by the absorption spectrum of a saturated solution. The same material is also readily prepared from the unbuffered reaction of two moles of dithizone with one mole of ethylmercuric chloride

$$C_2H_5HgCl + 2(DzS)H \longrightarrow (DzS)_2Hg + H^+ + Cl^- + [C_2H_6] \qquad (8)$$

In a bicarbonate buffer, this reaction stops at the first stage according to the equation

$$C_2H_5HgCl + (DzS)H + OH^- \longrightarrow (DzS)HgC_2H_5 + H_2O + Cl^- \qquad (9)$$

We conclude that the observed toxicity of the disubstituted mercurials is entirely consistent with the assumption that these substances may react with biological sulfhydryl groups under mild conditions.

In neutral media, toxic activity of compounds of the type R'HgSR'' (IV), the mercaptides, should have been removed by the combination with sulfur. The fact that these compounds are observed to be toxic may be due to an exchange reaction in which the mercury attaches itself to critical enzymatic sulfhydryl groups according to equation 10

$$R'HgSR'' + RSH \rightleftharpoons R'HgSR + R''SH \qquad (10)$$

We have found that exchanges of the type of equation (10) can be demonstrated in the laboratory and that they proceed at room temperature and blood *p*H. Examples are the exchanges with ethylmercuric thiosalicylate and with *m*-tolylmercuric thioglycolate. Only the former was stopped at the first stage of reaction

$$C_2H_5HgSC_6H_4COO^- + (DzS)H \rightleftharpoons (DzS)HgC_2H_5 + HSC_6H_4COO^- \qquad (11)$$

The new reactions formulated above clarify the toxic action of complex mercurials in a manner consistent with the assumption that toxic activity is due to combination with critical enzymatic sulfhydryl groups.

The Antidote Reaction.—Reactions (10) and (11) above may be used as the prototype of poisoning reactions if the compound RSH or dithizone is taken as the analog of an enzymatic sulfhydryl group, or they may be used as the prototype for an antidote reaction, if the original sulfur mercury compounds are thought of as the poisoned enzymatic system and the RSH or dithizone as the antidote. The reagents and products in equations (10) and (11) are identical in type. In a homogeneous system lacking unusual structural features, the reaction should tend to go in the direction which will create the stronger Hg–S bond. As a working hypothesis, we may assume that the reaction between a sulfur-containing compound and a mercurial is a polar reaction and that the sulfur atom is the electron-donating reagent and the mercurial the electron-attracting reagent.[9] According to this hypothesis, dithizone should form stable bonds to metals, as is observed in the laboratory, because of the numerous resonating forms which can contribute to its ability to donate electrons.

In our work with mercurial dithizonates, especially mercuric bis-dithizonate (Va), a curious reversible reaction with light has been observed.

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[8] For a discussion of the structure of dithizone, see Corwin and Jackson, THIS JOURNAL, 71, 3698 (1949).

[9] See Corwin and Naylor, THIS JOURNAL, 69, 1004 (1947).

When a dilute solution of (Va) in benzene is irradiated, the color changes from orange-yellow to blue.[10] In the dark the reaction is reversed. This experiment may be repeated as many times as desired. We are seeking an explanation of this photochemical reaction. It is obviously of importance in connection with the colorimetric use of dithizone derivatives in analytical chemistry.[11]

One of us (A. G. S.) wishes to acknowledge a grant from the Rockefeller Foundation which financed the early part of this research.

Experimental

Dithizone.—The dithizone for the following experiments was purchased from the Eastman Kodak Company and purified by the method of the AOAC.[12]

Preliminary Tests on Mercurials.—Isotonic sodium chloride was acidified to *p*H 2 with hydrochloric acid. Mercurials were added to concentrations of $^1/_{50,000}$ to $^1/_{100,000}$, depending upon their solubility. They were treated with a chloroform solution of dithizone in test-tubes with shaking. A change to an orange color indicated a positive reaction. The reactions were positive and rapid on the following mercurials: inorganic salts of mercury, phenyl or ethyl mercuric chloride (or acetate or nitrate), diphenyl mercury, merthiolate, mercurophen, metaphen. Mercuric sulfide and metallic mercury required heating to give a positive test.

Reaction of Dithizone with Compounds of Type HgX_2 (I) and R'HgX (II).—Dithizone reacts rapidly with mercuric chloride under widely different conditions of *p*H and solvent. When a benzene solution of dithizone is shaken with a neutral aqueous solution of mercuric chloride, the benzene solution changes from green to orange immediately. The water solution becomes acid due to the liberation of hydrochloric acid. Dithizone and mercuric chloride also react rapidly in non-aqueous solvents.

(a) **Mono-dithizone Mercuric Chloride.**—A solution of 0.543 g. (0.002 mole) of mercuric chloride in 50 cc. of C. P. ether was mixed with stirring with a saturated solution of dithizone in C. P. ether, that is, 0.513 g. (0.002 mole) of dithizone in approximately 400 cc. of ether, cooled in ice and filtered. The filtered reaction material was extracted four hours with 130 cc. of C. P. benzene which was then evaporated to approximately 80 cc. and allowed to cool. The orange material thus deposited gave a strong halogen test. The crystals had a characteristic appearance of five-leafed rosettes made from twisted ribbons and with a fine four-pointed rosette superimposed on the end of each leaf.

Anal. Calcd. for $C_{13}H_{11}N_4ClSHg$: Hg, 40.8. Found: Hg, 39.8. The analytical discrepancy is ascribed to the fact that the material is difficult to purify and tends to decompose to give mercuric bis-dithizonate (see below). Absorption maximum in benzene, 485 mμ.

The benzene solution of this compound is sensitive to sunlight or to intense artificial light. The orange solution changes to a deep clear blue. The reaction is reversible when the solution is removed from the light; the orange color is restored. The rate at which the color change takes place is dependent upon the concentration of the substance and the intensity of the illumination. In very dilute solution the change is rapid and takes place within a few seconds.

(b) **Mercuric bis-Dithizonate.**[13]—Five and forty-two hundredths grams of mercuric chloride (0.02 mole) was dissolved in 40 cc. of ethanol and 10.24 g. (0.04 mole) of dithizone suspended in 700 cc. of benzene was added to the alcoholic solution. The color changed from green to orange instantaneously. The reaction mixture was refluxed on a steam-bath for one hour under an atmosphere of nitrogen. The hot solution was concentrated under vacuum to 150 cc. Sufficient ethanol was added to cause incipient precipitation. On cooling, red crystals were obtained; m. p. 225–226° (dec.).

Anal. Calcd. for $C_{26}H_{22}N_8S_2Hg$: Hg, 28.2. Found: Hg, 28.0.

This substance is reversibly light sensitive, similar to mono-dithizone mercuric chloride; absorption maximum in 95% ethanol, 490 mμ.

(c) ***p*-Chloromercuric Benzoic Acid and Dithizone.**—Three and fifty-six hundredths grams (0.01 mole) of *p*-chloromercuric benzoic acid was suspended in 10 cc. of benzene in a round bottom flask and 2.54 g. (0.01 mole) of dithizone, suspended in 100 cc. of benzene, was added. The mixture was refluxed seventeen hours on a steam-bath. After removing the solid white material (unchanged starting material), the filtrate was washed several times with water and 0.1 *N* sodium bicarbonate alternately and finally with two 50-cc. portions of water. The benzene layer was then dried over calcium chloride, filtered, concentrated to 30 cc. under water-pump vacuum on a steam-bath. Ten cubic centimeters of cold ethanol was added to precipitate the product. Approximately 2.1 g. of mercuric bis-dithizonate was obtained.

The white material obtained by filtration of the original reaction mixture was dissolved in sodium hydroxide and reprecipitated. It was then identified as starting acid.

(d) **Ethylmercuric Dithizonate.**—Six hundred milligrams (0.00236 mole) of dithizone was suspended in 30 cc. of benzene and to this 15 cc. of water and 0.591 g. of sodium bicarbonate was added; 0.624 g. (0.00236 mole) of ethylmercuric chloride was added, the flask was fitted with a standard taper stopcock which was opened slightly and carbon dioxide was passed through. The flask was placed on a shaker and the color changed to red in approximately four minutes. Shaking was continued for four hours to make sure that the benzene layer was homogeneous and that the reaction was complete.

The benzene layer was separated and washed five times with water, using a total of 200 cc. Next it was washed twice with 2 *N* ammonia then again with water. It was dried over calcium chloride. The benzene layer was then filtered and the calcium chloride washed with 10 cc. of benzene. The total filtrate was transferred to a 100 cc. round-bottom flask. The solution was concentrated under water-pump vacuum at 60° until a thick, oily layer was deposited in the inside of the flask. Approximately 10–15 cc. of ethanol was added and the material crystallized; m. p. 158–158.5°, absorption maximum in 95% ethanol 480 mμ.

Anal. Calcd. for $C_{15}H_{16}N_4SHg$: N, 11.5. Found: N, 11.65.

(e) **Ethylmercuric Dithizonate and Acid.**—One gram of ethylmercuric dithizonate was dissolved in 50 cc. of ethanol in a round-bottom flask and three drops of concentrated hydrochloric acid were added. The color changed from orange to green immediately. This indicated the formation of dithizone. The mixture was refluxed for fifteen minutes on a steam-bath. During this period a garlic-like odor was given off. About 20 cc. of cold benzene was added and by using vacuum and water-bath, the volume of the solution was reduced to 30 cc. After cooling, red crystals melting at 212° were obtained. These were recrystallized from benzene and ethanol; m. p. 224–225° (dec.). This material was further identified as mercuric bis-dithizonate spectrophotometrically by the method described below.

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[10] Compare Sandell, "Colorimetric Determination of Traces of Metals," Interscience Publishers, Inc., New York, N. Y., 1944, p. 93.

[11] Compare Lewis, Magel and Lipkin, THIS JOURNAL, **64**, 1779 (1942). The phenomenon which we have observed differs from that described by these investigators in that the presence of a rigid solvent is not necessary and phosphorescence is not observed.

[12] Assn. Official Agricult. Chem., Official and Tentative Methods of Analysis, p. 369 (1940).

[13] After this paper was prepared for publication, Irving, Andrew and Risdon, *J. Chem. Soc.*, 541 (1949), described the preparation of this compound by a slightly different method.

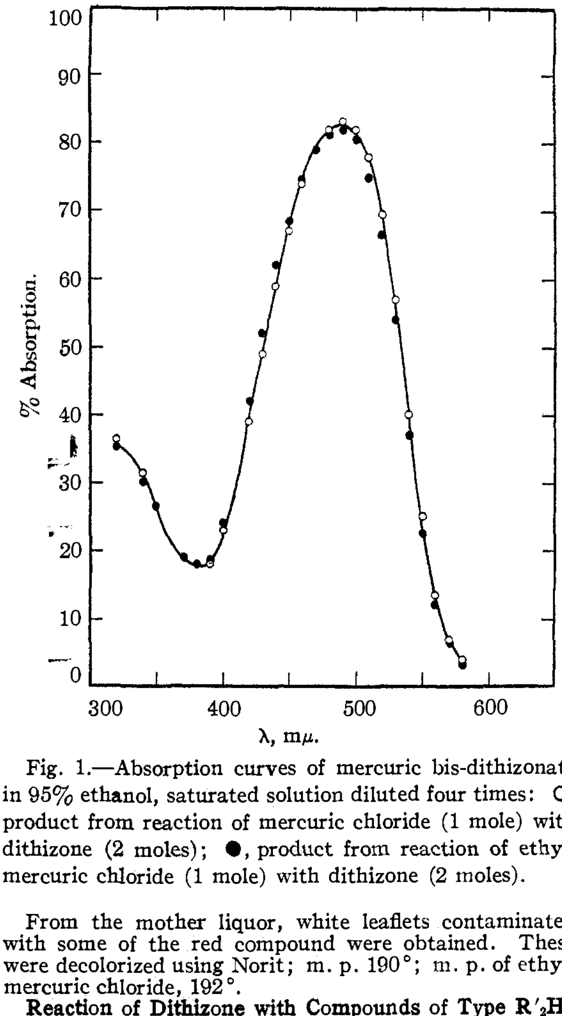

Fig. 1.—Absorption curves of mercuric bis-dithizonate in 95% ethanol, saturated solution diluted four times: O, product from reaction of mercuric chloride (1 mole) with dithizone (2 moles); ●, product from reaction of ethylmercuric chloride (1 mole) with dithizone (2 moles).

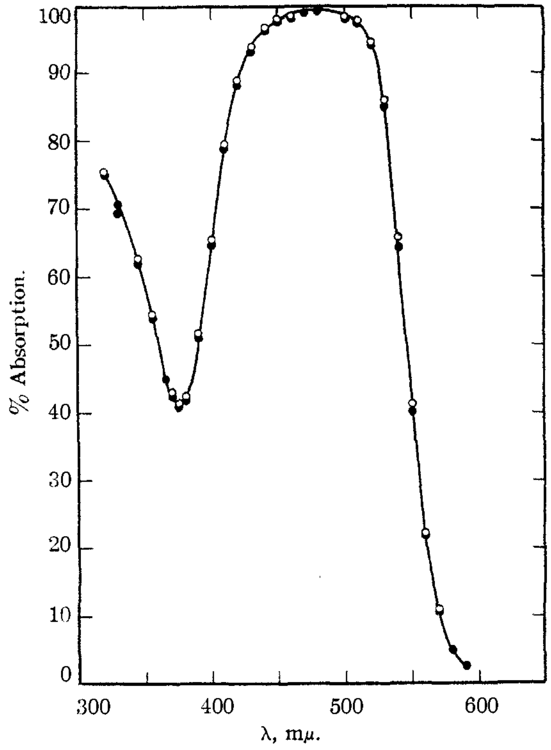

Fig. 2.—Absorption curves of ethylmercuric dithizonate in 95% ethanol; saturated solution diluted four times: O, product from reaction of ethylmercuric chloride (1 mole) with dithizone (1 mole); ●, product from reaction of merthiolate (1 mole) with dithizone (1 mole).

From the mother liquor, white leaflets contaminated with some of the red compound were obtained. These were decolorized using Norit; m. p. 190°; m. p. of ethylmercuric chloride, 192°.

Reaction of Dithizone with Compounds of Type R'_2Hg (III). (a) **Phenylmercuric Dithizonate.**—One and one-half grams (0.006 mole) of dithizone was dissolved in 200 cc. of benzene and 2.1 g. (0.006 mole) of diphenylmercury was added. The benzene solution gradually changed from green to reddish orange, showing that the reaction proceeds at room temperature. For preparative purposes, however, it is best to hasten the reaction by heating. Under these conditions it must be protected from air.

The reaction mixture was heated on a steam-bath while a slow stream of nitrogen was swept through it. After eight hours, the reaction was stopped. The material obtained by evaporating the benzene to dryness was extracted with ether in a Soxhlet extractor. Evaporation of the ether gave a crystalline product, m. p. 162–163°. After two recrystallizations from ethanol, beautiful, long, needle-shaped crystals were obtained which looked like long wires under the microscope; m. p. 174–175° (dec.); absorption maxima in 95% ethanol, 266 mμ and 475 mμ.

Anal. Calcd. for $C_{19}H_{16}N_4SHg$: Hg, 37.6. Found: Hg, 37.3.

This substance can be prepared more rapidly from phenylmercuric nitrate: 6.78 g. (0.02 mole) of phenylmercuric nitrate was weighed into a round-bottom flask and 5.12 g. (0.02 mole) of dithizone and 300 cc. of benzene were added. The color became red at once. A small amount of dithizone was added (0.1 g.) to make sure that there was no unreacted phenylmercuric nitrate. The color became green, showing the excess of dithizone. This was removed with 5 *N* ammonia. The benzene layer was filtered off. The residue was less than 0.5 g. The filtrate was concentrated after drying over calcium chloride. Addition of ethanol gave a compound which was shown by its melting point to be identical with phenylmercuric dithizonate prepared from diphenylmercury. The benzene insoluble residue was mercury bis-dithizonate.

(b) **p-Tolylmercuric Dithizonate.**—The reaction was performed similarly to that described for the phenyl compound above: 6 g. of di-p-tolylmercury and 4 g. of dithizone reacted in 450 cc. of benzene for twenty hours on a steam-bath. After isolation and purification the m. p. was 200–201° (dec.); yield 9.5 g.

Anal. Calcd. for $C_{20}H_{18}N_4SHg$: Hg, 36.6. Found: Hg, 36.4.

(c) **p,p'-Dicarboxydiphenylmercury and Dithizone.**—Four hundred forty-three milligrams (0.001 mole) of p,p'-dicarboxydiphenylmercury was suspended in 30 cc. of dilute sodium bicarbonate solution and at intervals portions of a benzene solution of 0.256 g. (0.001 mole) of dithizone were added, shaken, and allowed to stand until the benzene layer became orange. This procedure was repeated until all of the dithizone had been added. The benzene solution was separated and allowed to evaporate very slowly in the dark. Deep orange needles formed which were washed with ether and benzene. A benzene solution of this material was reversibly light sensitive.

Anal. Calcd. for $C_{26}H_{22}N_8S_2Hg$: Hg, 28.2. Found: Hg, 27.8, 27.6.

The material is identified as mercury bis-dithizonate.

Reaction of Dithizone with Compounds of Type $R'HgSR''$ (IV). (a) **Sodium Ethylmercuric Thiosalicylate and Dithizone.**—Three and seven hundredths grams (0.0076 mole) of sodium ethylmercuric thiosalicylate[14] was dissolved in 50 cc. of water in a 250-cc. round-bottom

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[14] "Merthiolate" obtained through the courtesy of the Eli Lilly Co., whom the authors wish to thank for their coöperation.

flask; 0.5 g. of sodium bicarbonate and 100 cc. of benzene were added and then 1.93 g. (0.0076 mole) of dithizone was added in small amounts with continuous rotation of the flask. At each addition the color became red. The flask was shaken mechanically for fourteen hours. The color remained red.

The aqueous layer was separated and acidified with acetic acid after the benzene soluble material had been removed by washing with benzene. A very light, pinkish compound was obtained from the water; m. p. 288–289°. This was identified as the disulfide of thiosalicylic acid.

The benzene layer was washed twice with 25 cc. of water and then with 15-cc. portions of 5 *N* ammonia until the aqueous layer became almost colorless. This insured the complete removal of dithizone. After a final washing with water the benzene solution was dried with calcium chloride and the product was isolated as described above except that the temperature was kept below 50°; m. p. 158–158.5°. This material was identified further spectrophotometrically as ethylmercuric dithizonate.

(b) ***m*-Tolylmercuric Thioglycolate.**—*m*-Tolylmercuric thioglycolic acid was prepared by the reaction of equimolar quantities of *m*-tolylmercuric chloride and the sodium salt of thioglycolic acid in aqueous bicarbonate solution. Upon acidification of the reaction mixture, *m*-tolylmercuric thioglycolic acid precipitated. This material was reprecipitated three times from bicarbonate solution with hydrochloric acid solution and then recrystallized several times from ethanol. White needles were obtained, m. p. 190–193° (dec.), when placed in a bath preheated to 185°.[15]

A benzene solution of dithizone was shaken with a water solution of the sodium salt of *m*-tolylmercuric thioglycolic acid. The benzene layer changed color immediately from green to orange. After separation, the water layer has a strong sulfhydryl test with nitroprusside. The nitroprusside test had been negative for the aqueous solution of the sodium salt of the mercurial before reaction with dithizone. The odor of thioglycolic acid in the water layer was unmistakable. Upon evaporation of the benzene solution, an orange solid was obtained and identified as mercury bis-dithizonate.

Spectrophotometric Identification of Dithizone Derivatives.—The method used is that of indirect solubility determination by the determination of the absorption spectrum of a saturated solution of the compound in question.[8] Comparative curves on two samples of mercuric bis-dithizonate and two of ethylmercuric dithizonate are given in Figs. 1 and 2. The method is reasonably rapid and very satisfactory for use on compounds which decompose on heating.

Summary

1. Dithizone will react with the mercury in mercurials of the types HgX_2, $R'HgX$, R'_2Hg, $R'HgSR''$, and $(R'S)_2Hg$.

2. Dithizone will cleave C–Hg bonds to form S–Hg bonds.

3. Alkyl and aryl mercuric dithizonates tested could be cleaved further to yield mercuric bis-dithizonate.

4. Mercury can exchange between different sulfur compounds.

5. Mercuric bis-dithizonate and certain other mercurial dithizonates are reversibly sensitive to light.

BALTIMORE 18, MARYLAND RECEIVED JUNE 21, 1949

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(15) See Kharasch, U. S. Patent 1,589,599 (June 22, 1926); Re 16,921, April 3, 1928; 1,672,615 (June 5, 1928).

[CONTRIBUTION NO. 68 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TENNESSEE]

The Rates of Ethanolysis of the Mono- and Dichloropropenes

BY HILTON A. SMITH* AND W. HOLMES KING

Introduction

Several studies of the rates of ethanolysis of chloropropenes have been published. The rates of reaction of allyl chloride and certain substituted allyl chlorides with sodium ethylate in absolute alcohol at 35 and 50° have been reported.[1] Andrews and Kepner[2] determined the rates of ethanolysis and hydrolysis of certain allyl chloride derivatives in 50% aqueous ethanol at 25°. Hatch and Alexander[3] report similar studies.

The purpose of the present work was to study the rates of ethanolysis of all of the dichloropropenes in absolute ethanol over the temperature range 25–65°, in order to compare their relative reactivities. Similar data on the monochloropropenes were also obtained.

Experimental

Dichloropropenes.—The preparation and properties of the dichloropropenes will be reported in connection with a study of their electric moments.[4] The same materials were used for rate studies.

Monochloropropenes.—The preparation and properties of the *trans*-1-chloropropene-1 (37° isomer) will also be given.[4] The *cis*-isomer was purified by refractionation of the cut distilling around 31°, obtained in the separation of the two isomers.[4] Both fractionations were carried out in an eight-foot Vigreux column.

2-Chloropropene-1 was purified by fractionation through the Vigreux column of foreshot materials obtained from the preparation of the 1-chloropropenes.[5]

Eastman Kodak Co. best grade allyl chloride was dried over anhydrous potassium carbonate, and purified by fractionation through the Vigreux column. The physical properties of the monochloropropenes are given in Table I.

TABLE I

PHYSICAL PROPERTIES OF THE MONOCHLOROPROPENES

Isomer	$n^{20}\text{D}$	Distillation temperature °C.	Distillation temperature Mm.
Allyl chloride	1.4142	44.2	737
trans-1-Chloropropene-1	1.4060	37.0	738
cis-1-Chloropropene-1	1.4060	30.8	738
2-Chloropropene-1		22.6–23.0	739

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* Harvard University Ph.D. 1934.

(1) Tamele, Ott, Marple and Hearne, *Ind. Eng. Chem.*, **33**, 115 (1941).

(2) Andrews and Kepner, THIS JOURNAL, **70**, 3456 (1948).

(3) Hatch and Alexander, *ibid.*, **71**, 1037 (1949).

(4) King and Smith, work to be published.

(5) These foreshot materials were donated by the Columbia Organic Chemicals Company, Inc., of Columbia, South Carolina. The authors are indebted to this Company for them.