

obvious that the concentration of the permanganate is changed but very little. That acetates are not oxidized to oxalates in neutral solutions containing small concentrations of permanganate has been shown by the action of this reagent toward ethyl alcohol and acetaldehyde.⁵ In some unpublished experiments on propylene glycol this same fact has also been observed. The time employed for the experiments at 75° was approximated from that employed at 50° on the basis of the Ostwald rule in which we used a differential of 10°.

Summary

1. Potassium acetate may be oxidized to potassium oxalate with alkaline potassium permanganate under certain definite conditions.

2. The yield of oxalic acid is a function of the concentration of the reacting materials, the temperature and the duration of the experiment.

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ORGANIC MERCURY COMPOUNDS PREPARED FROM ORTHO- CHLOROMERCURI-PARA-NITROBENZOYL CHLORIDE¹

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Received March 1, 1922

Very few mercury derivatives of aromatic esters are known. These have been prepared by direct mercurization of the esters by mercuric acetate. Methyl benzoate gives mono- and dimercurated compounds, the structures of which have not been definitely established.³ *o*-Chloromercuribenzoic methyl ester has been obtained from methyl alcohol and sulfidomercuri-benzoyl chloride.⁴ The esters of *ortho*- and *para*-amino-benzoic acids and their mono- and di-alkyl derivatives give mono- and dimercurated compounds.⁵ Esters of salicylic acid react with mercuric acetate giving mono-mercurated compounds.⁶

Mercurated acid chlorides were unknown until recently, when *o*-chloromercuri-benzoyl chloride was prepared from thionyl chloride and the

¹ THIS JOURNAL, 41, 1273, 1390 (1919).

² Presented at the Rochester Meeting of the American Chemical Society, April 1921.

³ This work was done under a grant from the United States Interdepartmental Social Hygiene Board, Washington, D. C., Dr. Valeria H. Parker, Secretary. Some of the organic mercury compounds prepared will be tested for their pharmaceutical value by Dr. A. S. Loevenhart of the University of Wisconsin.

⁴ Schoeller and Schrauth, *Ber.*, 53, 636 (1920).

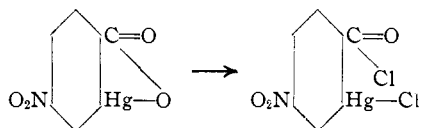
⁵ Sachs, *ibid.*, 53, 1741 (1920).

⁶ Schoeller and Hueter, *ibid.*, 47, 1930 (1914). Schoeller, Schrauth and Liese, *ibid.*, 52 1777 (1919). Ref. 3, p. 634.

⁶ Ref. 3, p. 639.

anhydride of *o*-hydroxymercuri-benzoic acid.⁴ Undoubtedly, it was thought that halides of phosphorus could not be used for making acid chlorides containing mercury, as it has long been known that these halides react with organomercury compounds with the elimination of the mercury.⁷ During the first part of the present work thionyl chloride was used, but it was soon found possible to use phosphorus pentachloride without removing the mercury from the molecule.

The present paper is a report of the preparation and properties of a number of esters and other derivatives of mercurated *p*-nitrobenzoic acid obtained from the corresponding mercurated acid chloride. When the mercuric salt of *p*-nitrobenzoic acid is heated to 200° it gives the inner anhydride of *o*-hydroxymercuri-*p*-nitro-benzoic acid.⁸ The anhydride suspended in chloroform reacts with phosphorus pentachloride to give the desired acid chloride.



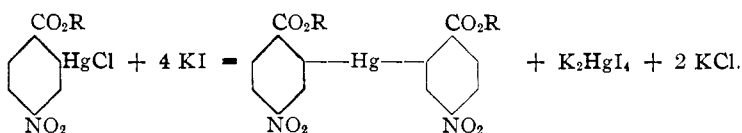
It was found difficult to obtain the acid chloride in a form pure enough for analysis. The derivatives were prepared directly from the crude product. The *n*-butyl, *n*-propyl, *isopropyl*, ethyl and methyl esters were made from the alcohols and the crude chloride. The melting points of these compounds increase regularly from the *n*-butyl ester to the methyl ester. The acid chloride was also treated with ethylene chlorohydrine, ethylene bromohydrine, and diethylamino-ethyl alcohol. Esters were formed in each case, but only the first of these has as yet been obtained in pure form. The chloride reacted normally with aniline giving an anilide.

The action of inorganic iodides on the mercurated esters was studied. The reaction consists in the change of the compounds of the type, RHgX , to those of the type, R_2Hg . The mercurated esters thus resemble the mercurated hydrocarbons, the mercurated dimethylanilines, and the acetylated mercury phenols, rather than the free mercury phenols from which the mercury is entirely removed by the action of inorganic halides.⁹ An equivalent amount of alkali is formed during this removal of mercury. In the case of the mercurated esters no alkali is formed. The reaction is as follows

⁷ Buckton, *Ann.*, **108**, 105 (1858). Cahours, *Ber.*, **6**, 568 (1875). Michaelis, *Ann.*, **293**, 196, 248, 303 (1896).

⁸ Blumenthal, *Biochem. Z.*, **32**, 60 (1911).

⁹ Whitmore, *THIS JOURNAL*, **41**, 1841 (1919). Whitmore and Middleton, *ibid.*, **43**, 622 (1921).

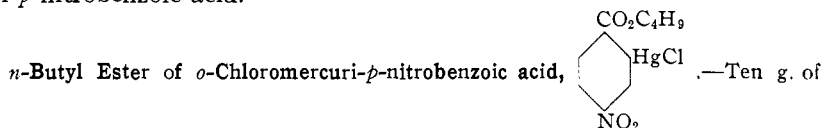


These derivatives of mercury diphenyl are less soluble than the corresponding chlorides and their melting points are higher. They react in the usual way with mercuric chloride forming the compounds of the type, RHgCl . They can be saponified without breaking the C-Hg linkage. The acid obtained by this process is *o*-mercuri-*bis*(*p*-nitrobenzoic acid), which has been prepared by a regulated alkaline reduction of *o*-hydroxymercuri-*p*-nitrobenzoic acid.⁸

The acid chloride prepared by Sachs was also prepared by means of phosphorus pentachloride. The *n*-butyl ester prepared from it was identical with that prepared from a sample of the acid chloride made with thionyl chloride.

Experimental

The mercuric salt of *p*-nitrobenzoic acid was prepared from the sodium salt by precipitation with a nearly neutral solution of the calculated amount of mercuric nitrate. The precipitate was washed thoroughly and dried. Fifty g. of the mercuric salt was heated for 3 hours at 200–220° in a small flask immersed in an oil-bath. When samples of more than 100 g. were heated, explosions sometimes occurred. After heating the mixture, it was cooled and the *p*-nitrobenzoic acid which formed was removed by repeated extractions with small amounts of ether. The residue insoluble in ether consisted of the nearly pure anhydride of *o*-hydroxymercuri-*p*-nitrobenzoic acid.



the anhydride was suspended in 100 cc. of chloroform and treated in the cold with 7 g. of phosphorus pentachloride. Vigorous action ensued. The mixture was then heated under a reflux condenser about 30 minutes. The solution was then cooled and filtered. The precipitate was washed with chloroform to remove phosphorus oxychloride and allowed to dry. The dry acid chloride was then treated with 10 cc. of *n*-butyl alcohol and heated until it completely dissolved. As this product cooled, white crystals of the *n*-butyl ester separated. These are fairly soluble in ethyl alcohol, benzene, chloroform, acetone, ether, and carbon tetrachloride. The product was recrystallized from hot ethyl alcohol until it showed a constant melting point of 125–126° (uncorr.). Nine g. of the ester was obtained from 10 g. of the crude anhydride; yield, 70%. Most of the loss occurs in the conversion of the acid to the acid chloride which is never complete.

Analyses. Subs., 0.1754: Hg, 0.0770. Subs., 0.1991, 0.2033: CO₂, 0.2071, 0.2146. Calc. for C₁₁H₁₂O₄NCIHg: C, 28.8; Hg, 43.8. Found: C, 28.4, 28.8; Hg, 43.9.¹⁰

¹⁰ The analyses for mercury were carried out by the "gold crucible method" de-

***n*-Propyl Ester.**—The procedure given above was employed, except that 10 cc. of *n*-propyl alcohol was used instead of butyl alcohol. The product, after repeated crystallizations from ethyl alcohol, melted at 145–150°. No sharper melting point could be obtained. The ester is moderately soluble in ethyl alcohol, chloroform, ether, carbon tetrachloride, acetone and benzene.

Analyses. Subs., 0.1943, 0.1911: Hg, 0.0887, 0.0871. Calc. for C₁₀H₁₀O₄NClHg: Hg, 45.2. Found: 45.6, 45.6.

Isopropyl Ester.—The same procedure was used as with the other esters. The purified product melted at 179–180°.

Analyses. Subs., 0.1981, 0.2089: Hg, 0.0897, 0.0943. Calc. for C₁₀H₁₀O₄NClHg: Hg, 45.2. Found: 45.3, 45.1.

Ethyl Ester.—The purified product melted at 220–222°. Its properties and solubilities are similar to those of the other esters.

Analyses. Subs., 0.1945, 0.1800: Hg, 0.0899, 0.0842. Calc. for C₉H₈O₄NClHg: Hg, 43.6. Found: 46.2, 46.8.

Methyl Ester.—The product, purified by crystallization from methyl alcohol, melted at 240–245°.

Analyses. Subs., 0.2206, 0.2008: Hg, 0.1077, 0.0976. Calc. for C₈H₆O₄NClHg: Hg, 48.2. Found: 48.9, 48.6.

Chloro-ethyl Ester.—This ester was prepared from the crude acid chloride and ethylene chlorohydrine in the usual way. Its solubilities and properties resembled those of the other esters. Crystallization from ethyl alcohol gave a product melting at 163–164°.

Analyses. Subs., 0.2010, 0.2023, 0.2323: Hg, 0.0865, 0.0879, 0.1000. Calc. for C₇H₆O₃NCl₂Hg: Hg, 43.2. Found: 43.0, 43.4, 43.1.

Attempts at Preparation of the Bromo-ethyl and Alkamine Esters

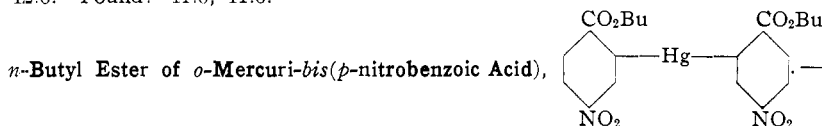
The acid chloride was found to react readily with ethylene bromohydrine and with diethylamino-ethyl alcohol, but no homogeneous product was obtained from either reaction. Further attempts are being made to prepare these esters in a state of purity.

Determination of the Position of the Mercury in the Esters

When the mercurated esters reacted in the cold with bromine water, they gave products which, after saponification and acidification, were converted into *o*-bromo-*p*-nitrobenzoic acid: this was identified by its melting point (163°) and by analyses for bromine.

Anilide of *o*-Chloromercuri-*p*-nitrobenzoic Acid.—Ten g. of the crude acid chloride was heated with 6 cc. of aniline until solution took place. The anilide separated as the mixture cooled. It was washed free from aniline with benzene and recrystallized from ethyl alcohol. The product was soluble in hot ethyl alcohol, slightly soluble in ether and insoluble in most other organic solvents.

Analyses. Subs., 0.2112, 0.2001: Hg, 0.0878, 0.0832. Calc. for C₁₃H₉O₃N₂-ClHg: Hg, 42.0. Found: 41.6, 41.6.



scribed on p. 365 of "Organic Compounds of Mercury" (Chemical Catalog Co., N. Y. C. 1921) by one of us (W.). In the analysis of organic mercury compounds containing nitro groups the heating must be carried out very cautiously to avoid slight explosions which are likely to blow foreign material against the amalgam.

Eight g. of the *n*-butyl ester of *o*-chloromercuri-*p*-nitro-benzoic acid in 100 cc. of ethyl alcohol was refluxed with 5 g. of potassium iodide for 1 hour. As the reaction mixture cooled, the mercuri-*bis* compound separated in colorless crystals. The mother liquor contained large amounts of inorganic mercury. The product was recrystallized from ethyl alcohol; m. p., 158°; yield, 5 g. or 95%. Its solubilities resembled those of the corresponding chloromercuri compound but were slightly less.

Analyses. Subs., 0.2521, 0.1461: Hg, 0.0791, 0.0459. Subs., 0.1781, 0.2214: CO₂, 0.2585, 0.3240. Calc. for C₂₂H₂₄O₃N₂Hg: C, 40.9; Hg, 31.1. Found: C, 39.6, 39.9; Hg, 31.4, 31.4.

One g. of this compound was heated with 0.43 g. of mercuric chloride (one mol) in 50 cc. of ethyl alcohol for 30 minutes. The corresponding chloromercuri compound, 1.2 g. separated as the product cooled; m. p., 125°. The chloride was analyzed.

Analysis. Subs., 0.1923: Hg, 0.0839. Calc. for C₁₁H₁₂O₄NCIHg: Hg, 43.8. Found: 43.7.

Five g. of the ester of the mercuri-*bis* compound suspended in 100 cc. of ethyl alcohol was heated with 5 g. of sodium hydroxide. When all of the solid had dissolved, the solution was cooled. The sodium salt which separated was collected, dissolved in water, and the solution acidified. The amorphous precipitate was *o*-mercuri-*bis*(*p*-nitrobenzoic acid),³ as was shown by analyses for mercury.

n-Propyl Ester.—Seven g. of the corresponding chloromercuri ester was heated under a reflux condenser with 5 g. of potassium iodide in 100 cc. of alcohol for 1 hour. Colorless crystals of the mercuri-*bis* compound separated as the solution cooled. After recrystallization from ethyl alcohol, it melted at 189°; yield 4.6 g., or 92%.

Analyses. Subs., 0.1638, 0.1705: Hg, 0.0538, 0.0549. Calc. for C₂₀H₂₀O₃N₂Hg: Hg, 32.5. Found: 32.8, 32.2.

Treatment of this compound with mercuric chloride in alcohol gave the *n*-propyl ester of *o*-chloromercuri-*p*-nitrobenzoic acid melting at 145–150°.

Ethyl Ester.—This ester was prepared in the same way as were the *n*-butyl and *n*-propyl esters and resembled them in properties; m. p., 227–232°.

Analyses. Subs., 0.1909, 0.1877: Hg, 0.0650, 0.0644. Calc. for C₁₃H₁₆O₃N₂Hg: Hg, 34.1. Found: 34.1, 34.3.

***n*-Butyl Ester of *o*-Chloromercuri-benzoic Acid.**—Seven g. of the anhydride of *o*-hydroxymmercuri-benzoic acid was treated with 5 g. of phosphorus pentachloride in 50 cc. of chloroform. Vigorous action took place. As soon as this had ceased, the mixture was cooled and the acid chloride was collected on a filter. It was washed with chloroform and allowed to dry. The product was heated with 10 g. of *n*-butyl alcohol until all of it dissolved. After several recrystallizations from alcohol it melted at 115°.

Two g. of the *o*-chloromercuri-benzoyl chloride prepared by the thionyl chloride method⁴ was treated with *n*-butyl alcohol in the same way. The purified product melted at 116°. The melting point of the mixture of the two products was not lower.

Analysis. Subs., 0.1668: Hg, 0.0813. Calc. for C₁₇H₁₈O₂ClHg: Hg, 48.4. Found: 48.7.

Summary

1. Phosphorus pentachloride can be used as well as thionyl chloride for making acid chlorides of mercurated aromatic acids.
2. The acid chloride of *o*-chloromercuri-*p*-nitrobenzoic acid was used to prepare the following esters of the acid: methyl, ethyl, *n*-propyl, *iso*-propyl and *n*-butyl.

3. These compounds react with inorganic iodides to form the corresponding compounds of the type, R_2Hg .

4. These compounds can be saponified without breaking the C-Hg linkage.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF TUFTS COLLEGE]

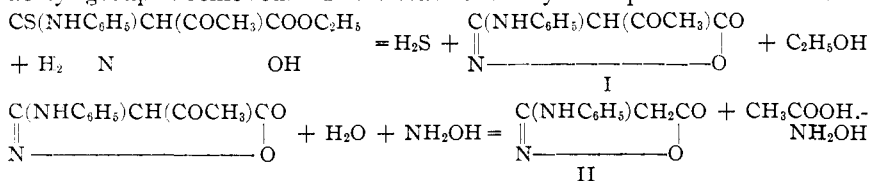
THE ACTION OF HYDROXYLAMINE AND OF HYDRAZINE ON THE ARYL MONOTHIO-AMIDES OF ETHYL ACETYLMALONATE

BY DAVID E. WORRALL

Received March 10, 1922

Sodium aceto-acetic ester reacts easily and smoothly with phenyl- and *para*-substituted phenyl mustard oils to form substituted mono-thio-amides of the general formula, $CH_3COCH(CSNHR)COOC_2H_5$. These thio-amides¹ undergo acid hydrolysis when dissolved in aqueous alkali, so that the acetyl as well as the ethoxy groups are removed. Since the resulting acids, $CH_2(CSNHR)COOH$, lose carbon dioxide when heated, a new and interesting method is offered for the preparation of thio-acetanilide and related compounds. The *ortho*- and *meta*-substituted mustard oils form addition products that are hydrolyzed to ketones in the presence of alkali but as the latter readily undergo further hydrolysis, ultimately the derivatives of thio-acetanilide are formed. Consequently, the various aromatic mustard oils can be used for the preparation of thio-acetanilides. It will be shown in this paper that the mustard oils are also useful for the preparation of certain heterocyclic compounds of the isoxazole and hydrazole series, all of which are new.

A well-known reaction of aceto-acetic ester is the condensation with hydroxylamine to form an isoxazolone. Ethyl acetylmalonate mono-thio-anilide, $CH_3COCH(CSNHC_6H_5)COOC_2H_5$, contains the same grouping and in addition the thio-anilide radical which also is known to react as in thio-acetanilide, with hydroxylamine. Consequently, a reaction would be expected between the mustard oil addition product of aceto-acetic ester and substances such as hydroxylamine. It was found that they react very readily indeed, and that it is sulfur and not oxygen which is attacked by hydroxylamine or hydrazine. The ring is closed by the subsequent elimination of the elements of ethyl alcohol; also, through hydrolysis, the acetyl group is removed. These reactions may be expressed as follows.



¹ Worrall, THIS JOURNAL, 40, 415 (1918).