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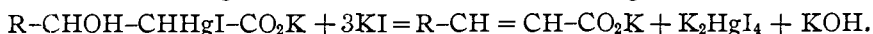
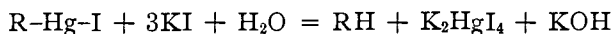
REACTION OF ALKALI HALIDES WITH MERCURY DERIVATIVES OF PHENOL.¹

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Mercury derivatives of phenol lose their mercury quantitatively when treated with a solution of potassium iodide. Ordinarily, an aromatic mercury compound does not react with iodides to give mercuric iodide. Under some conditions, one half of the mercury is removed as the iodide and the other half remains combined in a derivative of mercury diphenyl, $2R-Hg-I + 2KI = K_2HgI_4 + R_2Hg$. In a study of the mercury derivatives of *p*-bromo-dimethylaniline,² it was found that the reaction of potassium iodide with 5-bromo-2-dimethylamino-phenylmercuric acetate gave a considerable amount of *p*-bromo-dimethylaniline as well as the expected mercury diphenyl derivative. The formation of metallic mercury during the reaction made it appear that the alcohol or some other substance was acting as a reducing agent. However, this could not explain the formation of all of the bromo-dimethylaniline, since the amount of this substance produced was greater than the free mercury would require. A search through the literature revealed a number of cases in which mercury attached to carbon is replaced by hydrogen under the influence of iodide solutions. While this reaction is universal for Hg-N compounds, it is unusual for Hg-C compounds. Since there is undoubtedly some relation between the therapeutic value of mercury carbon compounds and the stability of the Hg-C linkage, it seemed desirable to study the conditions under which this linkage between mercury and carbon is broken by inorganic halides.

Biilmann found that mercury derivatives of malonic acid and of its esters³ when treated with potassium iodide solution yield mercuric iodide and one molecule of potassium hydroxide for every Hg-C linkage. With potassium iodide mercury is removed in a different way from the products of the action of mercuric salts upon various unsaturated acids.⁴ In this case the original unsaturated acid is recovered. The difference in the 2 reactions may be shown by the equations



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² THIS JOURNAL, 41, 1851 (1919).

³ Biilmann, *Ber.*, 35, 2581 (1902); 42, 1070 (1909).

⁴ Biilmann, *ibid.*, 35, 2571 (1902); 43, 568 (1910); also compare Manchot, *Ann.*, 420, 183 (1920).

In the second case the replacement of the mercury by hydrogen is accompanied by, or followed by, the loss of water. The mercury derivative of cyano-acetic acid¹ behaves in a manner similar to that of the mercury malonic derivatives. The mercury derivative of camphor² is said to be "decomposed" rapidly by an acetone solution of potassium iodide.

In the aromatic series a few cases of this replacement are recorded. Dimroth found that *p*-aminophenylmercuric acetate,³ when treated with potassium iodide gave a small amount of inorganic mercury. This may be due to the formation of mercuric iodide during the formation of the mercury diphenyl derivative, or during a splitting of the Hg-C linkage, accompanied by the formation of aniline and alkali. Pesci found that salts of *o*-(chloromercuri)benzoic acid⁴ when treated with sodium halides give sodium benzoate, mercuric halide, and sodium hydroxide.

2-5-Cresylmercuric acetate⁵ is said to be "decomposed" by potassium iodide. Brieger and Schulemann in their exhaustive study of the mercuriation of the various naphthalene intermediates⁶ of the coal tar dye industry found that the mercurated naphthols are very sensitive to alkali halides. In some cases they titrated the alkali formed and drew conclusions as to the completeness of the splitting of the Hg-C linkage. They found that potassium iodide gives a quantitative replacement, while the bromide and chloride give it to a decreasing extent. In other cases they did not determine the alkali formed, but studied the "loosening" effect of the halide by treating with sulfides. In many instances, the pure mercury compound gave no action with ammonium sulfide, but, when treated with potassium iodide and then with the sulfide, gave mercuric sulfide. The bromide and chloride of potassium had a similar but weaker effect. Brieger and Schulemann found that the mercurated naphthylamines were split much less readily than the corresponding naphthols.

In view of the many cases of this peculiar replacement of organic mercury, and the lack of details, it seemed desirable to study the reaction with some substances simpler than the complicated intermediates used by Brieger and Schulemann. The mercurated phenols⁷ prepared by Dimroth offered an ideal subject for the study.

Dimroth's method of treating a solution of phenol with mercuric acetate solution was discarded because of the large amount of dimercurated product formed. It was found that phenol, without a solvent, heated

¹ Petterson, *J. prakt. Chem.* [2] **86**, 458 (1912).

² Marsh and Fleming-Struthers, *J. Chem. Soc.*, **95**, 1777 (1909).

³ *Z. anorg. Chem.*, **33**, 314 (1903).

⁴ Pesci, *Gazz. chim. ital.*, **32**, II, 277 (1902); *Centralbl.*, **1902**, II, 1454.

⁵ Dimroth, *Ber.*, **35**, 2853 (1902). Compare Brieger and Schulemann, *J. prakt. Chem.*, [2] **89**, 104 (1914).

⁶ *Ibid.*, 97 ff.

⁷ *Habilitationschr.*, Tubingen, **1900**; *Centralbl.*, **1901**, I, 452; *Ber.*, **35**, 2855 (1902).

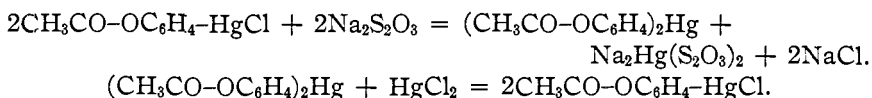
with mercuric acetate on the steam-bath gives a mixture of the *ortho* and *para* compounds free from the disubstituted product. These were separated by Dimroth's method of forming the chlorides; the *p*-hydroxyphenylmercuric chloride is insoluble in hot water, while the *ortho* compound is soluble. At temperatures above that of the steam-bath, the total yield was decreased somewhat, but the amount of *ortho* compound increased slightly.

The 3 mercurated phenols were boiled with aqueous potassium iodide. In each case the solid soon dissolved and the solution became alkaline. After boiling for 30 minutes the alkali was titrated with standard acid and phenolphthalein. The *ortho* and *para* compounds gave almost one molecule of alkali while the *di*- compound gave almost 2.

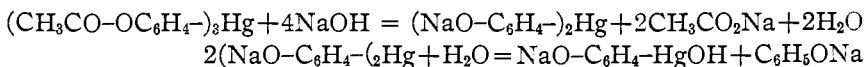
$\text{HO-C}_6\text{H}_4\text{-HgCl} + \text{KI} + \text{H}_2\text{O} = \text{HO-C}_6\text{H}_5 + \text{K}_2\text{HgI}_4 + \text{KOH} + \text{KCl}$.
The dimercuric chloride compound would give 2 molecules of potassium hydroxide. When potassium bromide was used in place of the iodide, only a small amount of alkali was formed. Potassium chloride gave no alkali even on prolonged boiling.

It seemed desirable to find out whether this unusual removal of mercury from the aromatic nucleus depended on the presence of the phenolic hydroxyl. To answer this question the acetyl derivatives of the *o*- and *p*-hydroxyphenylmercuric chlorides were prepared and treated with potassium iodide. There was no splitting of the Hg-C linkage in these cases. The solutions remained neutral. If splitting had occurred the alkali formed would probably have saponified the phenyl acetate to form sodium acetate and free phenol. No phenol was obtained as was shown by distillation of the neutral mixture with steam and a test of the distillate with ferric chloride. The acetylated *o*-hydroxyphenylmercuric chloride reacted with aqueous potassium iodide to form the organomercuric iodide. The hot mother liquor from this iodide gave a small amount of the corresponding mercury diphenyl derivative, *o,o'*-mercuri-bis(phenyl acetate). The same reaction, carried out in alcohol solution, gave only the iodide. The acetylated *p*-hydroxyphenylmercuric chloride gave only the corresponding iodide.

As the yield of the substituted mercury diphenyl is often larger with sodium thiosulfate than with potassium iodide, the former reaction was tried with the acetylated mercury phenols. In each case, a fair yield of the mercury diphenyl derivative was obtained. The proof of the structure of these compounds lies in the fact that they react quantitatively with mercuric chloride to give the original acetylated hydroxyphenylmercuric chlorides.



Dimroth was able to change the *o*-hydroxyphenylmercuric chloride to the corresponding mercury diphenyl derivative but did not carry out the reaction with the *para* compound. Dimroth's work was repeated and confirmed. It seemed possible that the missing *para* mercury diphenyl derivative might be made by saponifying the corresponding acetylated substance. When this was tried the product was found to be a monophenylmercuric derivative. In other words, one of the phenyl groups had been removed from the mercury by the action of hot sodium hydroxide. Apparently this is a new method of splitting a Hg-C linkage. It is another example of the "loosening" effect of hydroxyl or, in this case of the ONa group, on a mercury atom attached to the same nucleus. The reactions involved may be written thus:



Neutralization with dil. acetic acid precipitated $(\text{HO}-\text{C}_6\text{H}_4-\text{Hg})_2\text{O}$ instead of the corresponding hydroxide.¹ An analogous reaction occurs and a similar product is obtained with the acetylated *ortho* diphenyl derivative. Both the complex organomercuric oxides were converted to the original chlorides by treatment with acetic acid and sodium chloride. The same conversion was brought about by treatment with ethyl acetate and then with sodium chloride solution.² All the organic mercury compounds studied reacted with ammonium sulfide only on standing. They reacted slowly with cold conc. hydrochloric acid, but rapidly with the hot acid to give inorganic mercury salts which formed an immediate precipitate with hydrogen sulfide.

Experimental.

Preparation of the *o*- and *p*-Hydroxyphenylmercuric Chlorides.—Twelve g. of phenol (about 1.5 molecules) was heated on the steam-bath and 25 g. of mercuric acetate was added gradually while the mixture was stirred constantly. When all the acetate had dissolved, boiling water was added and the mixture was boiled for a few minutes. Then a hot solution of 5 g. of sodium chloride was added. The *p*-hydroxyphenylmercuric chloride precipitated at once. The mixture was filtered while hot. The solution, on standing, deposited crystals of the *ortho* compound. The properties of these substances agreed with those recorded by Dimroth. When the preparation was carried out as described, no dimercury compound was formed. This was proved by the complete solubility of the mixture in boiling water. The amounts of *ortho* and *para* compounds formed varied only slightly with the temperature of reaction. With 25-g. portions of mercuric acetate (about 85% pure), the following amounts of *para* and *ortho* compounds were obtained, at 100°, 18 g. of *para* and 7 g. of *ortho*; at 125°, 16 g. of *para* and 8 g. of *ortho*; at 150°, 14 g. of *para* and 8 g. of *ortho*.

Preparation and Properties of the Acetyl Derivatives of the Hydroxyphenylmercuric Chlorides.—Fourteen g. of the *o*-hydroxyphenylmercuric chloride was treated with a slight excess of acetyl chloride (3 cc.) and warmed gently. After the evolution

¹ Compare Dimroth, *Ber.*, 35, 2854 (1902).

² Compare THIS JOURNAL, 41, 1854, Summary, 3 (1921).

of hydrochloric acid had ceased, the substance was pressed on a porous plate and then washed many times with water. Twelve g. of the acetyl derivative was obtained (about an 80% yield). The *para* compound was prepared in a similar way. Melting points (uncorr.): *ortho*, 170–1°; *para*, 235°.

Analyses.—Calc. for C_8H_7OClHg : Hg, 54.05. Found: *ortho*, 54.1, 54.0, 54.0; *para*, 53.8, 53.5.

Reaction of Potassium Iodide with the Mercurated Phenols.—When the *o*-hydroxyphenyl mercuric chloride, the corresponding *para* compound, and the *o,p*-diacetymercuriphenol were boiled with excess of potassium iodide solution they dissolved, the solutions became alkaline, and phenol and inorganic mercury compounds were formed. The alkali was titrated with standard acid. The procedure was as follows. 1 g. of the mercury compound was boiled for half an hour with 50 cc. of water and 2 g. of potassium iodide. Water was added to replace that lost by evaporation. The base was then titrated with 0.1 *N* sulfuric acid. One g. of the *o*-hydroxyphenylmercuric chloride gave 30.12 cc. of 0.1 *N* potassium hydroxide, while that calculated was 31.90. One g. of the *para* compound gave 29.12 cc. of 0.1 *N* potassium hydroxide, as compared with calculated 31.90 cc. One g. of the dimercury acetate compound gave 32.50 cc. of 0.1 *N* hydroxide, compared with 32.6 cc. calculated for 2 molecules.

An experiment was tried with the *ortho* compound in which potassium bromide or chloride was used instead of the iodide. The compound boiled with the chloride gave no alkali. Long boiling of it with the bromide gave only a slight alkalinity. Similar results were obtained with the *para* and with the di-compounds.

Reaction of Potassium Iodide with the Acetylated Compounds.—When the acetyl derivative of the *o*- or *p*-hydroxyphenylmercuric chlorides was boiled with potassium iodide solution, no alkali or phenol was formed. Thus, 1.5 g. of the *ortho* acetylated compound was boiled for one hour with 50 cc. of water and 2 g. of potassium iodide. The solution was still neutral. The solution was distilled with steam and the distillate was tested with ferric chloride. No color resulted. When the aqueous filtrate from the organomercuric iodide was cooled, it yielded 0.2 g. of white needle shaped crystals melting at 125°. This substance was proved to be the mercury diphenyl derivative, mercury di-(*o* hydroxyphenyl acetate), $(CH_3CO-OC_6H_4)_2Hg$. The yield was only about 20%. The *para*-acetylated compound is changed to the organomercuric iodide only after long boiling with potassium iodide.

Reaction of Sodium Thiosulfate with the Acetylated Compounds.—Seven g. of the *ortho* acetyl derivative was dissolved in a thiosulfate solution containing 15 g. of the crystalline salt in 100 cc. of water. The mercury compound dissolved fairly readily to give a clear solution. As this solution stood, crystals of the mercury diphenyl compound separated. After 3 days, 3.6 g. of the *o, o'*-mercuribisphenol diacetate had separated as white needles, m. p. 125°. Yield, about 80%. They are slightly soluble, on heating, in alcohol, in benzene, and in chloroform; very slightly soluble in ether.

Analyses.—Calc. for $C_{16}H_{14}O_4Hg$: Hg, 42.62. Found: 42.7, 42.0.

Similarly, the *para* acetylated compound was treated with thiosulfate. The *para* diphenyl derivative separated from the thiosulfate solution as white crystals, m. p. 172–3°, much more slowly than did the *ortho* compound. The yield was poorer; 10 g. of the chloride gave only 3 g. of the diphenyl compound, about a 50% yield.

Analyses.—Calc. for $C_{16}H_{14}O_4Hg$: Hg, 42.62. Found: 42.4, 42.3.

Reaction of Mercuric Chloride with the Acetylated Diphenyl Derivatives.—The structure of the diphenyl derivatives was proved by splitting them with mercuric chloride to form the original chlorides. One g. of the *ortho* diphenyl derivative was boiled with 50 cc. of water containing 0.5 g. of mercuric chloride and yielded 1.4 g. of the *ortho* $CH_3CO-OC_6H_4-HgCl$, m. p. 170°. Similarly, the *para* diphenyl compound, gave the original chloride (m. p. 235°), quantitatively.

Reaction of the Acetylated Mercury Compounds with Sodium Hydroxide.—Three g. of [the *ortho* acetylated mercury diphenyl compound was boiled for 20 minutes with 50 cc. of 5% sodium hydroxide. The solution was cooled and made exactly neutral with dil. acetic acid. One and seven-tenths g. of a white amorphous substance separated. It did not melt, but darkened at a high temperature. Analyses indicated that it was the oxide obtained by Dimroth, di(hydroxyphenylmercuric) oxide.

Analyses.—Calc. for $C_{12}H_{10}O_3Hg_2$: Hg, 66.5. Found: Hg, 67.0, 66.7, 66.2.

When treated with dil. acetic acid and sodium chloride it gave the original chloride, hydroxyphenylmercuric chloride. When the oxide was boiled with ethyl acetate it dissolved readily. When this solution was boiled with sodium chloride solution the original chloride was formed.

The acetylated *para* mercury diphenyl compound was split in the same way by boiling with dilute sodium hydroxide. A similar complex oxide was formed. Like its isomer it was amorphous and did not melt.

Analyses.—Calc. for $C_{12}H_{10}O_3Hg_2$: Hg, 66.5. Found: Hg, 66.8, 67.0.

This complex oxide was changed to the *p*-hydroxyphenylmercuric chloride by treatment with dilute acetic acid and sodium chloride, and, also, by treatment with ethyl acetate and sodium chloride.

Reaction of the Acetylated Compounds with Sulfides and with Acids.—The *ortho* and *para* acetylated hydroxyphenylmercuric chlorides suspended in water and treated with hydrogen sulfide for 15 minutes gave no mercuric sulfide. After contact with ammonium sulfide for about half an hour, they commenced to blacken. The free mercury phenols acted a little more rapidly. The acetylated mercury diphenyl compounds gave no action with ammonium sulfide in less than 3 days; then a red precipitate began to form.

The acetylated hydroxyphenylmercuric chlorides treated with conc. hydrochloric acid and hydrogen sulfide showed no reaction. After standing for half an hour, or if they were heated, mercuric sulfide was formed. The acetylated mercury diphenyl compounds treated with conc. hydrochloric acid and hydrogen sulfide gave no mercuric sulfide, until the mixture had stood for about an hour or had been heated.

Summary.

1. Mercuric acetate reacts with an excess of phenol in the absence of a solvent to form only the *ortho* and *para* mercurated phenols. This differs from the action in water which gives a large amount of the di-product even in the presence of a large excess of phenol.

2. The hydroxyphenylmercuric chlorides and the corresponding dimercury acetate are split by iodides; mercuric iodide, phenol, and a base are formed. Bromides cause a partial splitting, chlorides none at all.

3. The acetylated compounds are not split by potassium iodide in the way that the phenols are. They give the organomercuric iodides and, in the case of the *ortho* compound, a small amount of the corresponding mercury diphenyl derivative.

4. Both of the acetylated chlorides react with conc. sodium thiosulfate solution to give the corresponding acetylated mercury diphenols.

5. The acetylated mercury diphenols, when treated with dil. sodium hydroxide, not only lose the acetyl groups but suffer a splitting of the Hg-C linkage which leaves a monophenylmercuric derivative. This, apparently, is a new method of breaking an Hg-C bond.