

USE OF MERCURIC ACETATE IN ORGANIC PREPARATIONS—PART I

Mercury Compounds of Amides and Imides

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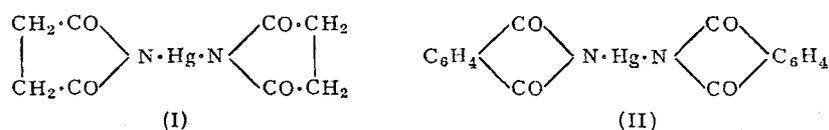
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FROM time immemorial, compounds of mercury have been valued as anti-septics, diuretics and antisyphilitics. Inorganic compounds are easily ionised and absorbed in the system and hence are toxic. Further, compounds like mercuric chloride are caustic due to their capacity to precipitate proteins. There has therefore been a persistent search for suitable organo-mercury compounds which do not give mercury easily in an ionised condition and are not toxic but possess the useful properties above mentioned. As a result, a large number of organo-mercury compounds have been made. According to Kolmer and Raiziss, these compounds can be divided into the following four groups: (1) Simple organic, (2) Pseudo complex organic, (3) Half complex organic and (4) Fully complex organic. (See *Pharmaco Therapeutics* by Cohen and Githens. D. Appleton & Co., Ltd., New York, 1928, p. 657.) The compounds belonging to class 1 (*e.g.*, mercury salicylate) ionise more or less completely in water and hence have strong bactericidal action but they are also toxic. Compounds coming under classes 2 and 3 (*e.g.*, mercury succinimide, flumerin, mercurio-chrome, etc.) ionise less readily or do not ionise at all and the presence of mercury can be detected only by means of ammonium sulphide. The minimum of toxic properties is found in these two groups and at the same time the antipathogenic action is fully available. In the last group of compounds (*e.g.*, metaphen), mercury is so firmly bound that it cannot be removed or split off even by boiling with water and ammonium sulphide. Hence they are very slow in their action.

The mercury compound of succinimide (I) which is said to have been employed with good results in cases of syphilis and pulmonary tuberculosis has been prepared till now by the action of mercuric oxide on succinimide in aqueous or alcoholic solution¹ or by the action of mercuric chloride on the potassium derivative of succinimide.¹ The same methods have been used for obtaining the mercury derivative of phthalimide¹ (II). It is now found that the preparations can be made far more conveniently by mixing an

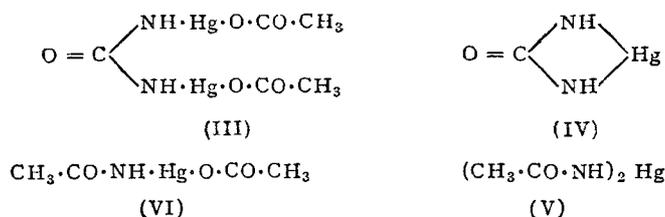
alcoholic solution of the respective imide with a similar solution of mercuric acetate. The reaction is quick and the yield and purity of the product very high. It has been observed that even with a large excess of mercuric acetate, the same di-imido mercuri compounds are produced and no other products are formed. Mercury phthalimide is more sparingly soluble in water than the succinimide compound and hence may be preferred where greater retention of mercury in the body and slower action are desired.



Liebig² (1853) noted the formation of a compound of urea with mercuric oxide having the formula $\text{CON}_2\text{H}_4, 2 \text{HgO}$. With mercuric nitrate and urea, he obtained a product of the composition $2 \text{CO} (\text{NH}_2)_2, \text{Hg} (\text{NO}_3)_2, 3 \text{HgO}$. Ruspaggiari³ (1897) reported the preparation of compounds containing the

divalent group $\text{CO} \begin{array}{l} \text{NH} \cdot \text{Hg}' \\ \text{NH} \cdot \text{Hg}' \end{array}$, and using mercuric acetate, he isolated a

compound having the formula of di-acetoxymercuri urea (III). It has now been found that urea reacts readily with mercuric acetate in aqueous or alcoholic solutions to give rise to two different compounds depending on the proportion of mercuric acetate employed. Using one molecule of mercuric acetate for each molecule of urea, a colourless micro-crystalline compound melting above 340°C . and having a formula (IV) is obtained. Using two molecular proportions of mercuric acetate or excess, a second compound having the formula (III) as suggested by Ruspaggiari³ could be isolated. Both the compounds are similar in their solubilities and reactions towards alkali and ammonium sulphide and belong to the category of pseudo-complex organic compounds. But the formation of two different compounds is evident from the analytical results for mercury and nitrogen and from the relative yields of the compounds based upon the amount of urea used as starting material. The compound IV can be used with advantage in place of mercury succinimide as it has very similar properties, as the raw material, urea is very cheap and as the compound has a high mercury content.



In the formation of these compounds, urea obviously behaves like a diamide in which a hydrogen atom of each amide group is capable of being replaced by mercury. It is well known that acetamide reacts with mercuric oxide when heated at 180° C. to give rise to mercury acetamide⁴ (diacetamido mercury) (V). When mercuric acetate is used in the place of mercuric oxide in the above reaction and heated for 1 hour a very complex change takes place. The clear liquid mixture that is first produced rapidly evolved acetic acid and as a result of further decomposition globules of mercury began to collect and the whole mass solidified. From the product no pure compound could be isolated. For the preparation of mercury acetamide (V), the use of mercuric oxide is therefore the most convenient.

When two molecules of acetamide are allowed to react with one molecule of mercuric acetate in alcoholic solution, a colourless crystalline compound resembling mercury acetamide in most of its properties is obtained. But on detailed analysis, it is found to be different and to have the formula of acetoxymercuri acetamide (VI).

When larger quantities of mercuric acetate are employed, a colourless crystalline compound melting at 225° C. and containing 72.0 per cent. mercury and 3.9 per cent. nitrogen is formed. No definite composition could be given to this substance and it is still under investigation.

Experimental

In preparing solutions of mercuric acetate in water or in alcohol a few drops of acetic acid were always added in order to render them clear.

Mercury succinimide (I).—When to a clear solution of succinimide (2 g.) in alcohol (15 c.c.) was added a similar solution of mercuric acetate (3.3 g.) in alcohol (60 c.c.) a colourless crystalline solid separated immediately. It was filtered, washed with a little alcohol and air dried. The yield was 3 g. (nearly 75 per cent.). The substance appeared as rectangular rods under the microscope and melted at 262° C. with decomposition. It was readily soluble in cold water and the solution did not precipitate mercuric oxide on the addition of alkali. It however formed mercuric sulphide when treated with ammonium sulphide solution. (Found: Hg, 50.3; $C_3H_3O_4N_2Hg$ requires Hg, 50.5 per cent.)

In the above preparation, succinimide and mercuric acetate were used in the proportion 2 : 1. Using double the above quantity of mercuric acetate (1 : 1) did not produce any change in the yield or the nature of the product.

Mercury phthalimide (II).—When a clear solution of phthalimide (2 g.) in hot alcohol (25 c.c.) was added to a cold solution of mercuric acetate

(2.2 g.) in alcohol (40 c.c.), a colourless crystalline compound (needles) separated immediately on stirring. The precipitate was allowed to settle, filtered, washed with a little alcohol and dried in air. The yield was 3.2 g. (nearly quantitative). The substance did not melt below 300° C., was insoluble in cold water but dissolved to some extent in hot water. In other respects it resembled mercury succinimide closely. (Found: Hg, 39.8; $C_{16}H_8O_4N_2Hg$ requires Hg 40.6 per cent.) Using excess of mercuric acetate did not introduce any change.

Mercury carbamide (IV).—To a cold solution of urea (1 g.) in water (10 c.c.) a solution of mercuric acetate (6 g.) in water (40 c.c.) was added. (In preparing the clear solution of mercuric acetate, the minimum of acetic acid should be used as otherwise the yield of the product would be considerably diminished.) There was immediate precipitation of a colourless crystalline solid and the reaction was complete in a few minutes. The solid was filtered, washed with a little water and dried in air. The yield was 3.2 g. and the substance appeared as small crystalline plates under the microscope. On heating it turned yellow at 230° C. and decomposed at 340°–345° C. It was sparingly soluble in cold water but dissolved appreciably in boiling water. (Found: Hg, 76.8; C, 4.9; N, 11.0; $C_2H_2ON_2Hg$ requires Hg, 77.6; C, 4.6; N, 10.8 per cent.) The compound was not decomposed by alkalis but ammonium sulphide precipitated mercuric sulphide. It was readily decomposed by acids including acetic acid and hence the need for avoiding excess of this during the course of preparation.

The above reaction could be carried out in methyl alcoholic solution also, though a large volume of alcohol had to be employed owing to the comparatively lower solubility of mercuric acetate in this solvent. The yield was however better (3.8 g.).

Di-acetoxymercuri carbamide (III).—A cold solution of urea (1 g.) in water about (10 c.c.) was added to a clear aqueous solution of mercuric acetate (15 g.) in water (80 c.c.). On stirring a colourless crystalline solid rapidly separated. It was allowed to settle, filtered, washed with water and dried in air. The yield of the dry substance was 6 g. It appeared as rectangular plates and prisms under the microscope and on heating decomposed at about 270° C. It was sparingly soluble in water and alcohol in the cold and dissolved to some extent in hot water. In this and most other respects it resembled mercury carbamide. (Found: Hg, 70.2; N, 5.2; $C_5H_8O_3N_2Hg_2$ requires Hg, 69.4; N, 4.9 per cent.) Using a large excess of mercuric acetate (30 g.) did not produce any change in the yield or the composition of the product.

Acetoxymercuri acetamide (VI).—When a clear solution of acetamide (1 g.) in alcohol (about 10 c.c.) was added to a similar solution of mercuric acetate (3.5 g.) in alcohol (60 c.c.) a colourless crystalline solid began to separate gradually on stirring. After leaving overnight, the precipitate was filtered, washed and air-dried. The yield was 1.2 g. The substance appeared as long narrow rectangular plates under the microscope and melted at 195° with decomposition. It could be easily recrystallised from alcohol and was readily soluble in water. In its properties it behaved like pseudo-complex organic compounds. (Found: Hg, 63.1; N, 4.8; $C_4H_7O_3NHg$ requires Hg, 63.1; N, 4.4 per cent.)

In the above experiment two molecular proportions of acetamide were employed for one of mercuric acetate. When it was repeated using 7 g. of mercuric acetate (1 : 1) dissolved in alcohol (about 120 c.c.) and the precipitate was collected just as before, it looked pure and crystalline (rectangular prisms) and the yield was found to be almost double. It resembled the above acetoxymercuri acetamide very closely in its properties but it melted with decomposition at 225° C. and was found to have a different composition. (Found: Hg, 72.0; N, 3.9 per cent.)

Summary

Mercury compounds of succinimide and pthalimide have been obtained easily and in a pure condition by treating the respective imides with mercuric acetate in alcoholic solution. Carbamide (urea) forms two compounds when it reacts with mercuric acetate in different proportions: (1) Mercury carbamide and (2) Di-acetoxymercuri carbamide. The preparation of mercury acetamide is best effected only through the use of mercuric oxide. When mercuric acetate in alcoholic solution is employed, acetoxymercuri acetamide is formed.

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| 2. Liebig | .. <i>Ibid.</i> , 1853, 85, 289. |
| 3. Ruspaggiari | .. <i>Gaz.</i> , 1897, 27, I, 1; 1897, 27, I, 12. |
| 4. Schöller and
Schrauth | <i>Ber.</i> , 42, 784. |