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No. 195

MERCURY COMPOUNDS OF HYDROXYBENZALDEHYDES

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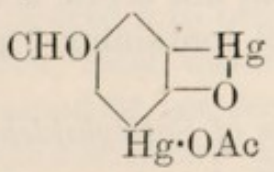
CXXVIII.—*Mercury Compounds of Hydroxybenzaldehydes.*

By Thomas Anderson Henry and Thomas Marvel Sharp.

When a solution of one of the three hydroxybenzaldehydes is boiled with mercuric acetate, mercury compounds are formed in which either one or two mercuric acetate residues, ·Hg·OAc, become attached to carbon atoms in the ring. The entry of these residues appears to be facilitated by the presence of the hydroxyl group, since benzaldehyde on similar treatment reduces the mercuric salt, the only crystalline substance so far isolated being mercurous acetate. Further, of the large number of organic compounds of mercury known none is derived from aromatic aldehydes except that recently prepared from vanillin by Paolini (*Gazzetta*, 1921, [ii], **51**, 188).

In the present paper, it is shown that with salicylaldehyde mercuric acetate residues are introduced at positions 3 and 5; with *p*-hydroxybenzaldehyde substitution presumably occurs at the same positions, but further action takes place between one of the ·Hg·OAc residues and the neighbouring hydroxyl group, with the loss of a molecule of acetic acid and the formation of the anhydrosubstance represented by formula I.

(I.)



This, on boiling with acetic acid, regenerates the normal 3 : 5-diacetoxydimercuri - 4 - hydroxybenzaldehyde. With *m* - hydroxy-

benzaldehyde, only one mercuric acetate residue is introduced, and its position has not yet been determined.

There is evidence also of the formation of a monomercurated derivative in the case of salicylaldehyde, but it has not so far been possible to obtain the substance in a pure state.

Mercury has been estimated in these compounds usually by destroying the organic matter with sulphuric acid and potassium permanganate and estimating the metal as sulphide, but in a few cases mercury, carbon, and hydrogen have been determined simultaneously by Abelmann's method (*Ber.*, 1914, **47**, 2935) and in others carbon has been estimated by Robinson's wet combustion method (T., 1916, **109**, 215).

Organic mercury compounds have acquired a new interest in recent years, owing to their increasing use in medicine, since they have the advantage over inorganic mercury compounds of not precipitating proteins, and of not being decomposed to any considerable extent by the metal of surgical instruments. Unfortunately, the utility of most of them is limited by their slight solubility in water, and this feature is shared by those now described. They yield sparingly soluble sodium salts, the bactericidal action of which is being examined by Major Brown, M.B., C.M., of the Wellcome Bureau of Scientific Research, who finds that *Bacillus typhosus* is killed in five minutes by solutions containing 0·034 and 0·002 per cent. of the ortho- and meta-compounds respectively, but only in twenty-five minutes by a solution containing 0·053 per cent. of the para-compound.

Experimental.

Preparation of the Mercury Compounds.—To one molecular proportion of the hydroxybenzaldehyde in a convenient quantity of 50 per cent. alcohol is added one or two molecular proportions of mercuric acetate dissolved in 50 per cent. alcohol containing 1 per cent. of acetic acid. This mixture is boiled under reflux until no more crystalline matter separates, when the flask is cooled and the mercury compound filtered off, washed with water, alcohol, and ether in succession, and dried. In the case of the meta-compound, no separation occurs until the reaction liquid has been concentrated. The compounds usually separate in a pure state, but they can be crystallised, if necessary, from hot acetic acid, or in the case of the meta-compound from alcohol containing 5 per cent. of acetic acid.

Derivatives of Salicylaldehyde.

3 : 5-*Diacetoxydimercurisalicylaldehyde.*—This substance, obtained as described, in a yield of 68·5 per cent. of the theoretical, forms a

colourless, crystalline powder consisting of minute, distorted cubes and melts at 133° (corr.) with decomposition. It is insoluble in most solvents, but dissolves in hot acetic acid and sparingly in acetal; with sulphuric acid it gives an orange coloration [Found : C = 20·01, 20·04; H = 1·92, 1·77; Hg = 62·6. $C_{11}H_{10}O_6Hg_2$ (639·2) requires C = 20·65; H = 1·56; Hg = 62·76 per cent.].

The substance dissolves in sodium hydroxide solution, forming a neutral yellow liquid from which carbon dioxide causes the separation of a yellow precipitate of 3 : 5-*dihydroxydimercurisalicylaldehyde*, which darkens on heating, but does not melt up to 300° [Found : Hg = 72·66. $C_7H_6O_4Hg_2$ (555·2) requires Hg = 72·24 per cent.].

Dilute hydrochloric acid added to a solution of the sodium salt causes precipitation of 3 : 5-*dichlorodimercurisalicylaldehyde*, which darkens at 260°, sinters at 270°, but does not melt up to 310° [Found : Hg = 67·75 per cent. $C_7H_4O_2Cl_2Hg_2$ (592·1) requires Hg = 67·74 per cent.].

On shaking the finely powdered diacetoxy-derivative with excess of a 10 per cent. solution of iodine in potassium iodide, it is almost immediately replaced by a yellow precipitate, which on recrystallisation from methyl alcohol melts at 107·5° (corr.) [Found : C = 22·69; H = 1·17; I = 67·79. $C_7H_4O_2I_2$ (373·8) requires C = 22·48; H = 1·07; I = 67·90 per cent.].

This di-iodo-compound is identical with 3 : 5-di-iodosalicylaldehyde prepared by Seidel (*J. pr. Chem.*, 1899, [ii], **59**, 114) by the action of iodine on salicylaldehyde in presence of mercuric oxide. A specimen thus prepared melted at 107·5° and showed no depression of melting point on admixture with the di-iodo-derivative prepared from diacetoxydimercurisalicylaldehyde. The phenylhydrazone crystallises in yellow needles and melts at 172·5—173·5° (corr.). On oxidation with permanganate in acetone, the di-iodosalicylaldehyde is converted into 3 : 5-di-iodosalicylic acid, m. p. 225° (decomp.; corr.) [Found : I = 65·73. $C_7H_4O_3I_2$ (389·8) requires I = 65·1 per cent.].

The mercury compound formed from salicylaldehyde must therefore be 3 : 5-diacetoxydimercuri-2-hydroxybenzaldehyde.

The mother-liquor, which contains no free mercuric acetate, since it gave no precipitate with solution of sodium hydroxide or ammonium sulphide, was then poured into brine, when a voluminous, white precipitate formed, which, after washing with water, alcohol, and ether, and drying, contained 64 per cent. of mercury, and appeared to be a mixture of chloromercuri- and dichlorodimercuri-salicylaldehydes : it was insoluble in the usual solvents, but on extraction with hot acetal there remained undissolved a pale pink, amorphous

powder, which proved to be 3 : 5-dichlorodimercurisalicylaldehyde (see above) [Found : Hg = 67·47. $C_7H_4O_2Cl_2Hg_2$ (592·1) requires Hg = 67·74 per cent.]. The acetal solution on cooling deposited a pink solid which contained 58 per cent. of mercury instead of 53·4 required for a monochloromercuri-compound, and so far the latter has not been obtained in a pure state. Reduction of the amount of mercuric acetate used in the initial reaction to one molecular proportion merely reduced the ratio of pure diacetoxy-compound to mixed chloro-compounds formed from 8 to 1 to 0·8 to 1.

p-*Hydroxybenzaldehyde.*

The *p*-hydroxybenzaldehyde used was prepared by the method described in British Patent 161679, depending on the condensation of phenol with formaldehyde; a yield of 42·6 per cent. of the theoretical was obtained.

4 : 5-*Anhydro*-3-*acetoxymercuri*-5-*hydroxymercuri*-4-*hydroxybenzaldehyde* (Formula I).—This substance results as already stated (p. 1055) from the application of the general method to *p*-hydroxybenzaldehyde.

It occurs as a colourless, crystalline powder, which under the microscope is seen to be composed of masses of minute cubes, is insoluble in water and most organic solvents, and has no definite melting point [Found : C = 18·79, 18·31; H = 1·44, 1·47; Hg = 69·15. $C_9H_6O_4Hg_2$ (579·2) requires C = 18·64; H = 1·03; Hg = 69·24 per cent.].

On steam distillation, after decomposition by phosphoric acid, it yields 9·61 per cent. of acetic acid ($C_9H_6O_4Hg_2$ requires acetic acid = 10·36 per cent.). Hot acetic acid dissolves this anhydro-substance, converting it into 3 : 5-*diacetoxydimercuri*-4-*hydroxybenzaldehyde*, which separates as the solution cools in minute, colourless, glistening plates. This, like the anhydro-compound, darkens on heating but has no melting point up to 300° [Found : C = 20·74; Hg = 63·02. $C_{11}H_{10}O_6Hg_2$ (639·2) requires C = 20·65; Hg = 62·76 per cent.].

The diacetoxy-compound dissolves with difficulty in sodium hydroxide solution, yielding a slightly turbid solution, which could not be filtered clear. It is decomposed by carbon dioxide, yielding a dull grey precipitate of 3 : 5-*dihydroxydimercuri*-4-*hydroxybenzaldehyde* [Found : Hg = 73·07. $C_7H_6O_4Hg_2$ (555·2) requires Hg = 72·24 per cent.], and by hydrochloric acid, giving the corresponding *dichlorodimercuri*-compound [Found : Hg = 67·07. $C_7H_4O_2Cl_2Hg_2$ (592·1) requires Hg = 67·74 per cent.].

On shaking the finely-ground anhydro-compound with excess of iodine dissolved in potassium iodide solution, a pale yellow substance

is obtained, which after crystallisation from alcohol forms colourless needles melting at 206·5° (decomp.; corr.). More of this substance can be isolated by removing the excess of iodine from the mother-liquor and acidifying with hydrochloric acid (Found: C = 22·41; H = 1·91; I = 67·75. Calc. for $C_7H_4O_2I_2$; C = 22·48; H = 1·07; I = 67·90 per cent.).

This di-iodo-compound is identical with the 3 : 5-di-iodo-4-hydroxybenzaldehyde prepared by Paal (*Ber.*, 1895, **28**, 2412) and shows no depression of melting point on admixture with a specimen made by Paal's method, although this author gives a lower melting point, 198—199°, than that now found. On oxidation with permanganate in alkaline solution the di-iodo-compound, prepared by either method, is converted into 3 : 5-di-iodo-4-hydroxybenzoic acid, which, however, melts at 261° (decomp.; corr.) instead of at 237° as recorded by Paal (*loc. cit.*). The authors find that by varying the rate of heating the melting point can be varied from 248° to 261°.

The mercury compound first formed from *p*-hydroxybenzaldehyde must therefore have the two mercury residues in positions 3 and 5, and since it yields only 1 molecule of acetic acid on distillation with phosphoric acid it must be 4 : 5-anhydro-3-acetoxymercuri-5-hydroxymercuri-4-hydroxybenzaldehyde (formula I).

m-*Hydroxybenzaldehyde.*

Acetoxymercuri-m-*hydroxybenzaldehyde*, $CH_3{\cdot}CO{\cdot}O{\cdot}Hg{\cdot}C_6H_3(OH){\cdot}CHO$. —This substance, obtained in almost quantitative yield by the general method (p. 1056), is much more soluble than the mercury derivatives already described and can be obtained only by concentrating the reaction liquid. It crystallises from acetic acid in colourless needles, m. p. 185—186° (corr.; decomp.), dissolves in solution of sodium hydroxide, forming a yellow liquid, and is coloured yellow by sulphuric acid [Found: C = 27·70, 27·78; H = 2·47, 2·55; Hg = 52·89. $C_9H_8O_4Hg$ (380·6) requires C = 28·38; H = 2·1; Hg = 52·70 per cent.].

It is decomposed by iodine in potassium iodide solution, yielding an *iodo*-m-*hydroxybenzaldehyde* [Found: I = 51·77. Calc. for $C_7H_5O_2I$ (247·9) I = 51·19 per cent.], which crystallises in yellow needles from dilute alcohol (15 per cent.), melts at 159—160°, and has powerful sternutatory properties.

On oxidation with permanganate in acetone it yields an *iodo*-m-*hydroxybenzoic acid*, melting above 233° to a cloudy liquid; this is not identical with 6-iodo-3-hydroxybenzoic acid (Limpricht, *Annalen*, 1891, **263**, 234), the only mono-iodo-derivative of

m-hydroxybenzoic acid so far known, and its constitution is being investigated.

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