days, and its weight became constant after 48 days, thus showing that the substance which held water so tenaciously in Dextrins Nos. 2 to 4 had been removed by the treatment with ammonium sulfate.

The properties of the material thus obtained are included in Tables II and III, the digestion having been made with the same sample of saliva used with the other dextrins. That saliva preserved with toluene is stable for years was announced by the author at the Cleveland meeting of the American Chemical Society (1918), and independently soon thereafter by Myers and Scott.[1]

It will be noticed from Table III that the last traces of amylodextrin have been removed and that the ratio of the red color with iodine to the time required for digestion to the achromatic point, 18, is the same as that obtained for Dextrin No. 1, which this dextrin most closely resembles. But the red color and the time required for digestion are only 75% of the values given by Dextrin No. 1; that is to say, Dextrin No. 5 contained only 75% as much erythrodextrin as Dextrin No. 1. This loss of erythrodextrin must be attributed to a partial conversion to achro-odextrin during the heating with barium carbonate. The lessened content of erythrodextrin also accounts for the smaller ratio of red to yellow observed on adding the same proportion of iodine-water (Table III).

With this evidence of the individuality of erythrodextrin the author's efforts in this direction will be necessarily terminated, at least temporarily; but erythrodextrin nearly free from amylodextrin will continue in extensive use in this laboratory as an accurate and ready means of determining relative amylolytic activity.

CHICAGO, ILL.

[CONTRIBUTION FROM THE PHARMACOLOGY DEPARTMENT, UNIVERSITY OF MINNESOTA.]

MERCURY COMPOUNDS OF SOME PHENYL CARBINOLS.[2]

BY MERRILL C. HART AND ARTHUR D. HIRSCHFELDER.

Received October 21, 1920.

In spite of the large number of organic mercury compounds which have hitherto been prepared[3] we have been unable to find references to any compounds of mercury and arsenic with phenyl carbinols.

In view of the relatively low toxicity of phenyl carbinols, the presence of carbinol groups in many of the most active natural alkaloids and the interesting local anesthetic and anti-spasmodic properties possessed by

[1] Myers and Scott, THIS JOURNAL, 40, 1713 (1918).

[2] This work was done with the aid of funds granted by the United States Interdepartmental Social Hygiene Board, for the investigation of the antiseptic and chemotherapeutic action of phenolic alcohols and their derivatives upon the gonococcus and the spirochaete.

[3] F. C. Whitmore, *J. Ind. Eng. Chem.*, 11, 1083 (1919).

phenyl carbinols and their esters[1] it seemed to us that mercury compounds of this group might prove useful as antiseptics and perhaps might also possess valuable chemotherapeutic properties.

Since Hirschfelder, Lundholm, and Norrgard[2] found that out of a number of phenyl carbinols investigated, saligenin (*o*-oxybenzyl alcohol) possessed the lowest toxicity for the tissues and also the best action as a local anesthetic and since this substance is one of the salicyl group which are useful as sedatives, antipyretics and antiseptics, saligenin was selected as the starting point in our research.

The compounds of saligenin and of *p*-hydroxy-*m*-nitrophenyl carbinol and mercury which are reported below have been found to be efficient antiseptics, about as strong as mercuric chloride but much less irritant to the tissues, so that they are being used successfully in the treatment of gonorrheal urethritis. Their antiseptic and therapeutic properties will be reported elsewhere.

Using the same method that was used in the preparation of the mercury compounds of saligenin and *p*-hydroxy-*m*-nitrophenyl carbinol, we have attempted the preparation of mercury compounds of benzyl alcohol, phenylethyl alcohol,[3] cumin alcohol and nitrosaligenin ($(2)CH_2OH(4)\text{-}NO_2C_6H_3OH$), but found no evidence of combination.

Experimental Part.

Preparation of Saligenin.—Hutchinson's[4] method, modified slightly by Hurd was used for the preparation of saligenin. Salicyl amide was prepared from methyl salicylate by shaking the oil in a mechanical shaker with strong ammonia water for several hours. When the oil was all in solution it was evaporated on a steam-bath to a small volume. On cooling the salicyl amide crystallized out, and was filtered off, washed with water and dried.

Seventy-five g. of the salicyl amide was dissolved in 800 mils of water and 1000 mils of alcohol. To this solution, agitated in a mechanical stirrer, there was added gradually in the course of 2 hours 2700 g. of a 2.75% sodium amalgam[5] and 215 g. of glacial acetic acid. The dilute alcohol solution was separated from the mercury and after being neutralized with a slight excess of sodium hydrogen carbonate, evaporated under

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[1] D. I. Macht, *J. Pharmacol.*, 11, 263 (1918); A. D. Hirschfelder, A. Lundholm, and H. Norrgard, *Science*, N. S., 51, 21 (1920); *J. Pharmacol.*, 15, 263 (1920); D. I. Macht, *ibid.*, 11, 419 (1918).

[2] *Loc. cit.*

[3] The phenylethyl alcohol was kindly furnished by Dr. W. J. Hale of the Dow Chemical Company, Midland, Michigan, and the cumin alcohol by Dr. W. Schwartze and Dr. Max Phillips, of the Bureau of Chemistry, Department of Agriculture, Washington, D. C.

[4] A. Hutchinson, *Ber.*, 24, 173 (1891); Chas. D. Hurd, private communication.

[5] Prepared by Nef's method. J. U. Nef, *Ann. Chem.*, 280, 307 (1893).

reduced pressure to approximately half its volume. This was extracted 5 times with ether. The ether extract on evaporation yielded an oil that solidified on cooling. This was crystallized once from toluene and yielded 43 g. of a yellowish crystalline mass, 63% of the theoretical yield. This product required further purification before it could be used for the preparation of the mercury compound. A 4% aqueous solution of this was made, treated with animal charcoal and after being cooled in ice water, filtered. The filtrate was evaporated under reduced pressure to a small volume, extracted with ether, and the ether removed. The residue from the ether extract was crystallized once from toluene. This method gave a product that consisted of beautiful white, flaky crystals melting sharply at 86° and soluble in water to a clear colorless solution.

Preparation of the Mercury Compound of Saligenin.—Fifteen g. of saligenin was dissolved in 250 mils of 95% alcohol. To this was added a warm filtered solution of 80 g. (2 moles) of mercuric acetate in 150 mils of water to which 5 mils of acetic acid had been added to prevent hydrolysis of the mercuric acetate. This solution was heated on the reflux condenser for 30 minutes and allowed to stand overnight. Hard clumps of needle-like crystals radiating out from a common center had formed. These were filtered off, washed with a little water, alcohol, and ether, and dried. They weighed 67 g. The filtrate on being allowed to stand for several weeks separated 8 g. more of this compound. This reaction also occurred at ordinary temperature by merely mixing solutions of the 2 substances and allowing them to stand for several weeks.

Properties and Salts of the Mercury Compound of Saligenin.—This compound was very insoluble in water and in all the ordinary organic solvents. It dissolved in hot acetic acid with the separation of mercurous acetate on cooling. It was soluble in hot acetic anhydride and in the fixed alkalies. It was not soluble in ammonium hydroxide. In water suspension it was not acted upon by hydrogen sulfide. In alkaline solution it gave gradually with hydrogen sulfide in the course of several hours a precipitate of black mercuric sulfide.

It had no definite melting point. It began to turn brown at 160° and at 169° gas began to form. The material became porous and fluffy with no further change except a gradual darkening up to 250°.

The chloride of this compound is extremely insoluble, the bromide, and iodide less so. The sulfate is insoluble and the nitrate soluble.

The sodium salt of this compound was prepared by pouring gradually a concentrated solution of the mercury saligenin in 10% sodium hydroxide into 95% alcohol. A yellow granular solid separated which was filtered off, washed with alcohol and ether, and dried in a desiccator. This sodium salt when first made is extremely soluble in water giving clear, slightly yellow solution, but on exposure to the air it gradually takes up carbon dioxide and becomes more or less insoluble.

The acetate of the mercury saligenin had in general the same solubilities as its parent substance. It was slowly soluble in sodium hydroxide solutions.

The most interesting fact about this compound is the very great affinity of the saligenin molecule for the mercuric ion. After 15 g. of saligenin had been refluxed with 80 g. of the mercuric acetate for 2 hours and allowed to stand for several hours the mercuric ion was removed quantitatively from solution. No precipitate could be obtained with hydrogen sulfide, showing the practically complete removal of the mercuric ion from solution.

Purification and Analysis of the Mercury Compound of Saligenin.—The crystals of this compound as originally obtained were slightly contaminated with very faint traces of mercurous acetate. This was removed by cooking the finely powdered material with large quantities of water and then drying with alcohol and ether. By this method the material was obtained free from mercurous acetate and completely soluble in 10% alkali solutions. Material for check analyses was also prepared by dissolving the mercury saligenin in 10% sodium hydroxide solution, filtering and reprecipitating by just making the solution acid with acetic acid. The precipitate was filtered off, washed with water, alcohol and ether, and then dried.

The mercury in these compounds was determined by the method of Jamieson[1] by precipitating it as the double thiocyanate with zinc. A 0.2500 g. sample was dissolved in 3 mils of nitric acid to which 2 mils of hydrochloric acid were added. This was heated on the steam-bath until all the chlorine had been boiled off. The residue was then diluted to 50 mils and nearly neutralized with sodium hydrogen carbonate. The mercury was then precipitated by adding 25 mils of a solution containing 39 g. of ammonium thiocyanate and 29 g. of zinc sulfate to the liter. The solution was stirred vigorously for about 10 minutes and then allowed to stand for one hour. The precipitate of the mercury double salt was then filtered off in a weighed Gooch crucible, washed and dried to constant weight at 105°.

This method of analysis was checked by the method used by Whitmore[2] for the analysis of the organic mercury compounds derived from *p*-bromodimethyl aniline. By this method the mercury compound was decomposed by heating with fuming nitric acid in a sealed tube for 36 hours at a temperature of 200°. The mercury was then precipitated as the sulfide using freshly prepared ammonium sulfide. The precipitate was

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[1] G. S. Jamieson, *J. Ind. Eng. Chem.*, **11**, 4, 206 (1919).

[2] F. C. Whitmore, THIS JOURNAL, **41**, 1848 (1919).

filtered off on a weighed Gooch crucible, washed with water and carbon disulfide, dried, and weighed in the usual manner.

Analysis and Probable Formula of the Mercury Compound of Saligenin.—The mercury compound, purified by digesting with large quantities of hot water, alcohol, and ether was used for analysis. The material was completely soluble in sodium hydroxide solution. It was air dried to constant weight and analyzed.

Subs., 0.2500: $HgZn(SCN)_4$, 0.4138.

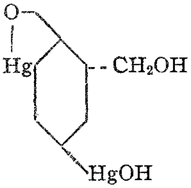
Calc. for $C_7H_6O_3Hg_2 \cdot 3.5H_2O$: Hg, 66.62. Found: Hg, 66.63.

The material was then dried to constant weight at 100° and analyzed.

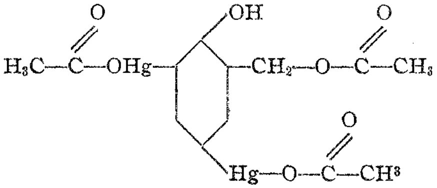
Subs., 0.2227: $HgZn(SCN)_4$, 0.4127.

Calc. for $C_7H_6O_3Hg_2$: Hg, 74.41. Found: Hg, 74.60.

These figures agree very closely with those for a compound of mercury with saligenin (Formula I) containing 3.5 molecules of water at ordinary temperature. The mercury in this condition being weakly basic the acetate radicals having been hydrolyzed off during the process of purification and the basic mercury reacting to form an inner anhydride with phenolic hydroxyl *ortho* to it.



(I).



(II).

The Acetate of the Mercury Compound of Saligenin.—Assuming that the Formula I for the mercury compound of saligenin is correct it should form an acetate with 3 acetyl radicals going into the molecule, 2 on the mercury groups and one on the alcohol group. To test this out the acetate was prepared by dissolving the mercury saligenin in hot acetic anhydride and then filtering very rapidly. On continued heating an insoluble amorphous compound is formed probably due to the combination of 2 or more molecules from the dehydrating effect of the acetic anhydride. The acetate is best prepared using small quantities of the materials. On cooling, the acetic anhydride deposits beautiful rod-shaped, flat-sided crystals of the acetate. These were filtered off and washed with a little ether and dried in a vacuum desiccator. From 60 g. of the mercury saligenin, 19 g. of the crystalline acetate was obtained. These crystals were dried to constant weight at 100° and analyzed.

Subs., 0.2500: $HgZn(SCN)_4$, 0.3556.

Calc. for $C_{13}H_{14}O_7Hg_2.H_2O$: Hg, 57.21. Found: Hg, 57.26.

These figures agree very closely with those for a triacetate of the mercury compound, the probable formula of which corresponds to Formula II. This acetate contains one molecule of water of crystallization which it loses on being heated to 110°.

The Mono Mercury Compound of Saligenin.—We attempted to isolate a monomercury compound of saligenin. Equimolecular quantities of the saligenin and of the mercuric acetate were allowed to react at ordinary temperature. The mercury compound of saligenin containing 2 atoms of mercury was formed, and no evidence of a more soluble, monomercury compound of saligenin was discovered in the filtrate.

The Mercury Compound of *p*-Hydroxy-*m*-Nitrophenyl Carbinol.

Preparation of *p*-Hydroxy-*m*-Nitrophenyl Carbinol.[1]—This compound was prepared by the action of bromomethyl alcohol on *o*-nitrophenol.

The bromomethyl alcohol was prepared by the method of L. Henry.[2] 125 mils of 40% formaldehyde was treated in the cold with approximately 270 g. of dry hydrogen bromide in the course of 7 hours. After some time a heavy, dark red liquid separated out which consisted essentially of bromomethyl alcohol. This was then quickly separated from the supernatant aqueous hydrobromic acid by means of a separatory funnel. The bromomethyl alcohol was kept in a tightly stoppered bottle in the cold, as it decomposes at a temperature of 20° or more.

o-Nitrophenol was allowed to stand for several days with a slight excess of bromomethyl alcohol in the presence of a small amount of fused zinc chloride. The *o*-nitrophenol dissolved in the bromomethyl alcohol at first and then gradually the mixture solidified. The solid was then suspended in water and distilled with steam to remove any unchanged *o*-nitrophenol. The water solution remaining in the distilling flask was then filtered and allowed to crystallize. Beautiful long, yellow needles were obtained which after another crystallization from water melted sharply at 97°. The yields by this method were very good.

Preparation of the Mercury Compound of *p*-Hydroxy-*m*-Nitrophenyl Carbinol.—25 g. of the *p*-hydroxy-*m*-nitrophenyl carbinol was dissolved in 500 mils of 95% alcohol. To this was added a warm filtered solution of 94 g. (2 moles) of mercuric acetate in 200 mils of water containing 15 mils of glacial acetic acid. This mixture was refluxed for 6 hours and then allowed to stand at ordinary temperature for some time. Gradually a fine, light, yellow needle-like, crystalline compound separated. This was filtered off at the end of 7 days, and was found to weigh 29 g. Further small crops were obtained by concentrating the filtrate.

Properties and Salts of the Mercury Compound of *p*-Hydroxy-*m*-Nitrophenyl Carbinol.—This substance was contaminated by a slight

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[1] We have also prepared a carbinol, nitrosaligenin ((2) $CH_2OH(4)NO_2C_6H_3OH$) by the action of bromomethyl alcohol on *p*-nitrophenol. This method will probably be found useful for the synthesis of other phenyl carbinols.

[2] L. Henry, *Bull. acad. roy. med. belg.*, [3] **26**, 615; *Ber. Gesellsch.*, **27**, 336 (1894).

amount of mercurous acetate, otherwise it was completely soluble to a deep reddish-yellow solution in alkaline solutions. It was slightly soluble in water and insoluble in all of the ordinary organic solvents. It was soluble in hot acetic acid and hot acetic anhydride and could be crystallized from these solvents. In aqueous suspension it did not give a precipitate of mercuric sulfide with hydrogen sulfide. In alkaline solution it gave gradually in the course of several hours on treatment with hydrogen sulfide, a black precipitate of mercuric sulfide. It did not melt when heated to 240°.

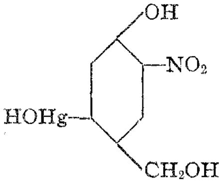
The chloride of this compound is very insoluble, the bromide, and the iodide less so. The sulfate is insoluble and the nitrate soluble. The acetate of this compound has in general the same solubilities as its parent substance. It was slowly soluble in solutions of alkali, giving a deep reddish colored solution.

Analysis and Probable Formula of the Mercury Compound of *p*-Hydroxy-*m*-Nitrophenyl Carbinol.—The crude compound was purified for analysis by crystallizing it 3 times from 20% acetic acid. Beautiful long light yellow needle like crystals were obtained. These were completely free from the presence of mercurous acetate as was shown by their complete solubility in dilute sodium hydroxide solution. These were washed with alcohol and ether, dried to constant weight at 100° and analyzed for mercury. The sample in this case was dissolved by heating on the steam-bath for one hour with 3 mils of fuming nitric acid. The solution of the mercury compound was then diluted to 50 mils, nearly neutralized with sodium hydrogen carbonate and the mercury precipitated and weighed in the same manner given above for the analysis of the mercury saligenin.

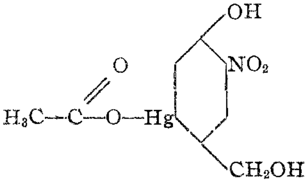
Subs., 0.2500: $HgZn(SCN)_4$, 0.3250.

Calc. for $C_7H_7O_5NHg$: Hg, 52.02. Found: Hg, 52.33.

These figures correspond very closely to a compound of mercury with *p*-hydroxy-*m*-nitrophenyl carbinol (Formula III). As in the case of the compound of mercury with saligenin, the acetate is hydrolyzed from the mercury, due to the weak basicity of the mercury in this position. The mercury in this compound evidently was not *ortho* to the phenolic hydroxyl because there was no evidence of losing water to form an inner anhydride similar to the mercury compound of saligenin, when this compound was heated to 110° for some time.



(III).



(IV).

The Acetate of the Mercury Compound of *p*-Hydroxy-*m*-Nitrophenyl Carbinol.—If the mercury compound of *p*-hydroxy-*m*-nitrophenyl carbinol has the structure corresponding to Formula III it should form an acetate with one or two radicals of the acetic acid going into the molecule depending on whether the alcohol group was acetylated or not. This compound was prepared by dissolving the mercury compound in hot acetic anhydride and then filtering very rapidly. It was necessary to filter very rapidly in this case, as in the preparation of the acetate of the mercury saligenin, to prevent the formation of an insoluble amorphous compound probably due to the combination of 2 or more molecules from the dehydrating effect of the acetic anhydride. On cooling, beautiful needles, of a little lighter yellow than the parent substance, separated. These were filtered off, washed with a little alcohol and ether, and dried to constant weight at 100°. They were analyzed for mercury, using the same method used for the analysis of the mercury compound of *p*-hydroxy-*m*-nitrophenyl carbinol.

Subs., 0.2500: $HgZn(SCN)_4$, 0.2916.
Calc. for $C_9H_9O_6NHg$: Hg, 46.91. Found: Hg, 46.95.

These figures correspond very closely to those for a mono-acetate of the mercury compound of *p*-hydroxy-*m*-nitrophenyl carbinol, the probable formula of which is shown in Formula IV.

Summary.

1. Saligenin heated on the steam-bath with 2 moles of mercuric acetate reacts with the formation of a dimercury compound of saligenin. The mercury is present as the free base in non-ionic form and probably attached to the ring *ortho* to the phenolic hydroxyl, with which it readily forms an inner anhydride, and *meta* to the alcohol group.

2. Saligenin has a remarkable affinity for the mercuric ion, 15 g. of which on being refluxed for 2 hours with 80 g. of mercuric acetate and allowed to stand for 2 hours removes the mercuric ion so completely from solution that the mixture gives no precipitate of mercuric sulfide with hydrogen sulfide.

3. The mercury compound of saligenin forms salts with the mineral acids. The chloride, sulfate, bromide and iodide are insoluble. The nitrate is soluble. It also forms a soluble sodium and potassium salt. It forms an acetate when crystallized from acetic anhydride, containing 3 acetyl groups, 2 on the mercury group and one on the alcohol group.

4. The aromatic alcohols which did not contain a phenolic hydroxyl group such as benzyl alcohol, phenylethyl alcohol, and cumin alcohol, as well as nitro-saligenin ($(2)CH_2OH(4)NO_2C_6H_3OH$) did not react with mercuric acetate to yield organic mercury compounds.

5. A new method has been developed for synthesizing *p*-hydroxy-*m*-nitrophenyl carbinol and nitro-saligenin by the action of bromomethyl

alcohol on *o*- and *p*-nitrophenol, respectively. This synthesis may prove useful for other carbinols.

6. The zinc thiocyanate method of Jamieson has been found satisfactory for determining the mercury in these aromatic mercury compounds.

7. *p*-Hydroxy-*m*-nitrophenyl carbinol heated on the steam-bath with mercuric acetate reacts with the formation of a monomercury compound. The mercury is present as the free base in non-ionic form and probably attached to the ring *para* to the nitro group.

8. The mercury compound of *p*-hydroxy-*m*-nitrophenyl carbinol forms salts with the mineral acids. The chloride, sulfate, bromide and the iodide were insoluble. The nitrate is soluble. It also forms soluble sodium, potassium and ammonium salts. It forms a mono-acetate when crystallized from acetic anhydride.

9. These organic mercury compounds have been found to be useful antiseptics.

MINNEAPOLIS, MINN.

NEW BOOKS.

Die Leichtflüchtigen Bestandteile im Magma. By PAUL NIGGLI. B. G. Teubner, Leipzig, 1920. viii + 272 pp., 20 x 28 cm., 132 figs. Price, M. 22.

The greater part of the experimental work hitherto carried out on silicate melts has been concerned almost entirely with mixtures of the involatile oxides which go to make up the rocks as they now exist. For this the main reason is that one must first investigate thoroughly the simpler systems before proceeding to the more complex, particularly as the difficulty of carrying out the experiments and of interpreting the results is enormously enhanced when one of the components is volatile within the temperature range in question. A subsidiary reason is that until recently it was not well recognized that the presence of a volatile component in a cooling melt could cause such marked differences as it does in fact; petrologists had, it is true, attributed certain things which they could not explain on the basis of the older chemistry to what they termed "mineralizers,"—somewhat mysterious, presumably volatile substances which had disappeared from the system after doing their work. But with careful investigation of such heterogeneous equilibria, from the theoretical perhaps more than from the experimental standpoint, it became apparent that the presence of a volatile component is competent to account for many phenomena, and that progress along many lines of petrological and volcanological research will be greatly accelerated by extension of accurate knowledge of the sequence of events to be expected when a silicate melt containing a component such as water, cools rapidly or slowly, in a confined space or otherwise.

In this monograph, which was awarded the prize offered by the Fürst-