[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Pyridine Mercurials

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The preparation and properties of di-3-pyridylmercury, bis-(3-pyridylmercuri)-ammonium chloride, 6-chloro-3-pyridylmercuric chloride and 2-pyridylmercuric chloride are described.

Mercuration of pyridine was first studied by Sachs and Eberhartinger[1] in 1923, and subsequently by McCleland and Wilson[2] and by Swaney, Skeeters and Shreve.[3] The last investigators developed optimal conditions for obtaining a monomercurated product. They recommended heating a mixture of pyridine, mercuric acetate and water in a sealed glass vessel at 155° for about 2.5 hours. The yield of 3-pyridylmercuric acetate was about 50%. Isomers were not found, but no rigorous search was made for traces. The acetate is soluble in water, and treatment of such a solution with sodium chloride causes precipitation of the very insoluble 3-pyridylmercuric chloride.

3-Pyridylmercuric chloride has been prepared[4] also from the double salt of 3-pyridinediazonium chloride and mercuric chloride by treating it with copper powder in cold acetone; but similar treatment of 6-chloro-3-pyridinediazonium chloride led to the production of no mercurial.

Technical pyridylmercuric acetate was made available through the courtesy of Mallinckrodt Chemical Works, hence we became interested in investigating some of its properties and in studying other pyridine mercurials. Pyridylmercuric salts have been produced commercially for use as fungicides and for prevention of mildew.

New evidence was obtained regarding the structure of the starting mercurial. Since cleavage of carbon-to-mercury bonds by halogen is a general reaction, it seemed safe to assume that any 2- or 4-pyridylmercuric chloride would be cleaved by bromine to form 2- or 4-bromopyridine just as the 3-isomer is cleaved to yield[2] 3-bromopyridine. Fractional distillation of the mixed bromopyridines would remove most of the 3-isomer in a lower boiling fraction. If any 2- or 4-isomers were present in the residue they should react with hot aniline to form 2- or 4-anilinopyridine, but no solid derivative was obtained at this point when the test was performed. Hence, no evidence was obtained for any 2- or 4-isomers in the original mercurial.

Information supplied by Mallinckrodt stated that 3-pyridylmercuric chloride was virtually insoluble in water (0.2 and 2 g. per liter, respectively, at 25°, 100°) or alcohol (0.8 g. per liter of warm 70% ethanol), and was insoluble also in solutions of sodium bicarbonate, sodium carbonate, but soluble in 1% solution of sodium hydroxide. In contrast, the compound was stated to be insoluble in ammonium hydroxide, but soluble in this medium if certain ammonium salts such as ammonium acetate or ammonium carbonate were present.

The solubility of pyridylmercuric chloride in sodium hydroxide is in noteworthy contrast to phenylmercuric chloride which is insoluble in alkali solutions. This demonstrates the solubility of 3-pyridylmercuric hydroxide. Sodium chloride, added to such a solution, causes no precipitation, but ammonium chloride does cause precipitation. This is reasonable since ammonium chloride reacts with sodium hydroxide to yield ammonium hydroxide which is incapable of holding pyridylmercuric chloride in solution.

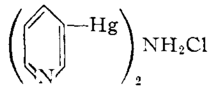
In studying the behavior of pyridylmercuric chloride and ammonium hydroxide we found that part of it did dissolve, but that the quantity taken into solution was unrelated to the quantity of ammonia used. Thus 10 ml. of ammonium hydroxide dissolved about half of a 1-g. sample and also about half of a 0.5-g. sample. Even as little as 0.1 g. of pyridylmercuric chloride failed to dissolve completely in 10 ml. of ammonium hydroxide although five times this amount dissolved when 1 g. was taken initially.

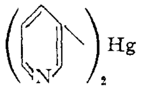
That portion of 3-pyridylmercuric chloride which was solubilized by ammonium hydroxide must have been converted into 3-pyridylmercuric hydroxide, following the equation (Py = pyridyl)

$$\text{PyHCl} + \text{NH}_4\text{OH} \rightleftharpoons \text{PyHgOH} + \text{NH}_4\text{Cl}$$

The equilibrium shown explains the behavior of the solution on evaporation. Ammonia was evolved and the white solid residue consisted of pyridylmercuric chloride (insoluble) and ammonium chloride. Ammonium chloride persisted in the residue since it was a product not only of this equation but also of the one given below.

The insoluble residue, following treatment of pyridylmercuric chloride with ammonia, was not the original pyridylmercuric chloride but was bis-(3-pyridylmercuri)-ammonium chloride (I). Its melting point (170°) clearly differentiates it from the original pyridylmercuric chloride (265° dec.), but compound I differs also in evolving ammonia when boiled with alkali. Its formation is explained by an extension of the previous equation


I


II

$$2\text{PyHgOH} + 2\text{NH}_4\text{Cl} \rightleftharpoons 2\text{PyHgCl} + 2\text{NH}_4\text{OH} \rightleftharpoons (\text{PyHg})_2\text{NH}_2\text{Cl} + \text{NH}_4\text{Cl} + 2\text{H}_2\text{O}$$

The reversibility of these equations in the presence of ammonia is witnessed experimentally by the fact that ammonium chloride and ammonia cause

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[1] G. Sachs and R. Eberhartinger, *Ber.*, **56**, 2223 (1923).

[2] N. McCleland and R. Wilson, *J. Chem. Soc.*, 1263 (1932).

[3] M. W. Swaney, M. J. Skeeters and R. N. Shreve, *Ind. Eng. Chem.*, **32**, 360 (1940); Shreve and Skeeters, U. S. Patent 2,206,309, July 2, 1940.

[4] A. N. Nesmeyanov and I. F. Lutsenko, *J. Gen. Chem. U. S. S. R.*, **11**, 382 (1941).

pyridylmercuric chloride to dissolve in water, presumably as pyridylmercuric hydroxide.

Compound I is similar to bis-(phenylmercuri)-ammonium chloride, $(C_6H_5Hg)_2NH_2Cl$, which was prepared by Pesci[5] on passing ammonia into a suspension of phenylmercuric chloride in boiling water.

Di-3-pyridylmercury (II) was synthesized in good yield from both I and 3-pyridylmercuric acetate by reaction with sodium thiosulfate

$$2PyHgOAc + 2Na_2S_2O_3 \longrightarrow Py_2Hg + Na_2Hg(S_2O_3)_2 + 2AcONa$$

The compound also was obtained, although in poor yields, by treating the double salt of 3-pyridinediazonium chloride and mercuric chloride with copper powder. No dipyridylmercury resulted on treatment of 3-pyridylmercuric chloride with sodium iodide[6] (in water or alcohol). There was some conversion, however, to a very insoluble yellow solid which was believed to be simply pyridylmercuric iodide. On treatment of the latter with sodium stannite solution, there was blackening because of liberation of mercury, which is typical of compounds of the structure RHgX but not of the structure R_2Hg.

It is interesting to note that strong acids give rise to salts of II and do not cleave the C–Hg bond under ordinary conditions. Thus, treatment with alcoholic solutions of hydrogen chloride or picric acid yield the dihydrochloride or dipicrate, respectively; but fusion of the dihydrochloride (222°) does yield pyridine and mercuric chloride

$$Hg(C_5H_5NCl)_2 \longrightarrow 2C_5H_5N + HgCl_2$$

New syntheses of pyridine mercurials were developed also by way of the sulfinic acids.[7] This

$$RSO_2H + HgCl_2 \longrightarrow RHgCl + SO_2 + HCl$$

method was used in the preparation of 6-chloro-3-pyridylmercuric chloride and 2-pyridylmercuric chloride, although in poor yields. The first of these compounds is the one which could not be made by the diazo method.[4] The second compound is of interest in that mercury is attached to carbon at position 2. Since completion of this study, Gilman and co-workers[8] have reported the synthesis of di-2-pyridylmercury in low yield by reaction of 2-pyridyllithium and mercuric chloride at −20°. In view of the fact that di-3-pyridylmercury yields 3-pyridylmercuric chloride on reaction with mercuric chloride it is of interest to note that 2-pyridylmercuric chloride was not mentioned as a product.

Experimental

Analysis for mercury was performed by the "gold crucible method."

The technical pyridylmercuric acetate which was supplied by Mallinckrodt Chemical Works was of 83% purity (*Anal.:* Hg, 49.7, 49.4; calcd., 59.4). In a typical conversion of it to pyridylmercuric chloride, 75 g. of the acetate was dissolved in 3 liters of water at 80° and a solution of 13 g. of sodium chloride in 50 ml. of water was added dropwise, yielding 53 g. of white precipitate and another 2.5 g. of needle-shaped crystals on cooling the filtrate; yield 81%, showing a nearly complete conversion. The 3-pyridylmercuric chloride melted at about 245° when heated rapidly on a preheated melting point block. A solution of it in concentrated sodium hydroxide was colorless, indicating absence of free mercuric salts. Recrystallization of 2 g. of it from one liter of water gave needles of m.p. 265–268° dec. Both this and the unrecrystallized material analyzed 63.4–63.7% Hg (calcd. 63.8).

When aqueous sodium bromide and sodium iodide solutions were added dropwise to comparable hot solutions of the acetate precipitates were formed also, presumably of pyridylmercuric bromide (m.p. 275° dec.) and iodide (m.p. 280° dec.), respectively. The chloride and bromide were both white solids whereas the iodide was yellow. The iodide was considerably less soluble in hot water than the chloride.

Reaction with Bromine.—Ten grams of bromine was added during 3.5 hours to a stirred suspension of 20 g. of pyridylmercuric chloride and 6.6 g. of sodium bromide in water at 50–60°. After 15 hours at 20°, 5.7 g. of hydrochloric acid was added and the solution was filtered from 16.4 g. of residue. After making the filtrate alkaline it was ether extracted thereby removing 3 ml. of liquid, b.p. 120–169°. On redistillation of the latter, 1.6 g. (16% yield) of liquid boiled at 168–171.5°. To the residue was added 1.5 g. of aniline and this mixture was refluxed for 30 hours. On fractionation, all the aniline came over at 180–182°, leaving no solid residue and showing no replacement of halogen by aniline.

When pyridylmercuric chloride was treated with a solution of bromine in ethanol or in carbon disulfide the yield of liquid bromopyridine was negligible.

Reaction with Iodine.—Refluxing 0.2-g. samples of pyridylmercuric chloride for 30 minutes with 25 ml. of 0.1 *N* iodine solution containing 1 g. of potassium iodide and 3 ml. of chloroform, then titrating with 0.1 *N* sodium thiosulfate, proved to be a quantitative operation, giving mol. wt. values of 324 and 333, compared to the theoretical value of 314.

Reaction with Ammonia.—A mixture of 10 g. of 3-pyridylmercuric chloride (m.p. 245°) and 100 g. of ammonium hydroxide was stirred occasionally for 30 minutes, then filtered. The solid (A) weighed 5.1 g. (m.p. 168–180°), and from the filtrate, on evaporation, was obtained 4.8 g. of solid (B), m.p. 204–214°.

Part, but not all, of solid B dissolved when it was mixed with 100 g. of ammonium hydroxide. Solid B contained ammonium chloride which was extracted by water leaving a residue of pyridylmercuric chloride, m.p. 240°. *Anal.:* Hg, 63.80, 63.91; calcd., 63.85.

Solid A contained no ammonium chloride and liberated no ammonia when cold alkali was added, but fumes of ammonia were liberated when it was boiled with dilute alkali. Solid A was rinsed with ammonium hydroxide, dried and analyzed. It melted at 170°. Amide nitrogen was obtained by collecting the ammonia liberated on boiling A with alkali in a 4% boric acid solution and titrating the latter with standard acid until the brom cresol purple indicator changed to yellow.

Anal. Calcd. for $C_{10}H_{10}ClHg_2N_3$: Hg, 65.9; Cl, 5.83; amide N, 2.30. Found: Hg, 66.0; Cl, 5.28; amide N, 2.22.

Di-3-pyridylmercury.—To a solution of 50 g. of sodium thiosulfate in 50 ml. of water was added 10 g. of 3-pyridylmercuric acetate. The solid dissolved, but the solution became cloudy in 3 minutes, and after 30 minutes 4.5 g. of white solid separated, m.p. 225–226°. This is an 85% yield of di-3-pyridylmercury.

Much the same observations were noticed when 1 g. of bis-(3-pyridylmercuri)-ammonium chloride (I) was mixed with 10 ml. of a saturated solution of sodium thiosulfate. At first compound I dissolved, then precipitation started increasing with time. The first crystallizations of the crude precipitate from alcohol gave di-3-pyridylmercury of m.p. 225° identical to that obtained above.

The dipyridylmercury was recrystallized from alcohol giving crystals of m.p. 239°. It is quite soluble in hot, but insoluble in cold alcohol. It is somewhat soluble in hot xylene and may be crystallized from it as platelets if a Soxhlet apparatus is used. Analysis was low for mercury, but it was noticed that traces of the sample sublimed undecomposed to the surface of the gold crucible, thus interfering with the method.

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(5) L. Pesci, *Gazz. chim. ital.*, **39**, I, 147 (1909).

(6) F. C. Whitmore and R. J. Sobatzki, THIS JOURNAL, **55**, 1128 (1933).

(7) W. Peters, *Ber.*, **38**, 2567 (1905); also, "Organic Syntheses," Coll. Vol. I, 1932, p. 505.

(8) H. Gilman, W. Gregory and S. Spatz, *J. Org. Chem.*, **16**, 1788 (1951).

Anal. Calcd. for $C_{10}H_8HgN_2$: Hg, 56.2; N, 7.85. Found: Hg, 55.2, 54.5; N (Dumas method by V. Hobbs), 7.31.

Pyridylmercuric chloride gives a positive reaction with sodium stannite. This is general for compounds of the structure RHgCl. In contrast, dipyridylmercury does not react with sodium stannite. Dipyridylmercury changed readily into pyridylmercuric chloride, m.p. 240–245°, when it was mixed in alcohol solution with alcoholic mercuric chloride.

Dipyridylmercury was converted into its salts, the dihydrochloride and the dipicrate, by mixing it in alcoholic solution with alcoholic solutions of the acids. The white dihydrochloride melted at 222° dec. and the yellow dipicrate melted at 255° dec.

Anal. of dihydrochloride. Calcd. for $C_{10}H_{10}Cl_2HgN_2$: Hg, 46.7. Found: Hg, 46.2, 46.7.

Anal. of dipicrate. Calcd. for $C_{22}H_{14}HgN_8O_{14}$: Hg, 24.6. Found: Hg, 24.3, 24.2.

Heating of a sample of the dihydrochloride to 200° (oil-bath) in a test-tube caused evolution of pyridine as judged by odor and the alkaline reaction of the vapor to litmus. Heating a sample of the dipicrate with alcoholic potassium hydroxide solution yielded a red solution from which white crystals of dipyridylmercury, m.p. 237–238°, separated on cooling.

Di-3-pyridylmercury from 3-Aminopyridine.—The method described in reference 9 for the synthesis of pentadecylamine[9] (*via* the urethan) was followed in the synthesis of 3-aminopyridine from nicotinamide. The urethan was not separated as such but, being water soluble, was dissolved in water after removal of the methanol and hydrolyzed directly by acidifying (HCl) and heating at 100° till effervescence ceased. After evaporation of the water the amine was taken up in hot benzene and precipitated with 2 volumes of ligroin; yield 40%, m.p. 62°.

Diazotization of 1.88 g. of this amine in 6 ml. of cold concd. hydrochloric acid with a solution of 1.4 g. of sodium nitrite in 6 ml. of water was followed by addition of 5.4 g. of mercuric chloride in 6 ml. of hydrochloric acid. The double salt[4] ($NC_5H_4N_2Cl{\cdot}HgCl_2$) separated. It was collected, washed and dried; yield 6.2 g.

Five grams of this salt was decomposed by mixing with 5 g. of copper bronze in 30 ml. of acetone with cooling in an ice-bath. Then 30 ml. of ammonium hydroxide was added. Most of the copper remained shiny. After 30 minutes the liquid had turned green, and after 15 hours it was diluted with an equal volume of water and filtered. The residue was transferred to a Soxhlet extraction cup and extracted with acetone for one hour. After evaporation of the acetone the 0.8 g. of residue was crystallized from a little alcohol. The crystals obtained melted at 232° and a mixture m.p. determination with authentic di-3-pyridylmercury of m.p. 239° showed no depression.

Di-3-pyridylmercury from Pyridylmercuric Hydroxide and Copper.—Ten grams of 3-pyridylmercuric chloride was added to 50 ml. of cold ammonium hydroxide. After 30 minutes the solution was filtered and to the filtrate was added 10 g. of copper powder. Mercury plated out slowly on the copper, the mixture was left several days before filtering and evaporating the filtrate to dryness. The residue left on evaporation was recrystallized from alcohol, giving a small quantity of crystals, m.p. 227–234°, which did not depress the m.p. of authentic di-3-pyridylmercury.

2-Pyridylmercuric Chloride.—2-Pyridinethiol was prepared from 2-bromopyridine and thiourea,[10] after which it was chlorinated in acid solution adapting the method used by Caldwell[11] in the conversion of 5-acetamido-2-pyridinethiol into 5-acetamido-2-pyridinesulfonyl chloride. Thus, an excess of chlorine was passed at 0–5° into a solution of 22 g. of the thiol, 300 ml. of hydrochloric acid and 70 ml. of ice-water. The mixture was poured into 800 ml. of ice-water. A crystalline solid gradually separated at 0°. Part of this solid was dissolved in ethylene chloride at 40° and crystallized therefrom by cooling to −5°; m.p. 210° (solid A). The rest of the solid was suspended in 200 ml. of cold water, mixed with 40 g. of zinc dust, heated to boiling for 20 minutes, then made alkaline (Na_2CO_3) and filtered. The filtrate was neutralized and heated at the boiling point with 25 g. of mercuric chloride. A precipitate appeared in 15 minutes. This solid was collected after 2 hours, and mixed with dilute alkali, whereupon a black precipitate formed. This was filtered off and the filtrate neutralized with hydrochloric acid. The 2-pyridylmercuric chloride which precipitated was a white solid melting at 270°. Recrystallization from methanol brought the m.p. to 275°.

Anal. Calcd. for C_5H_4ClHgN: Hg, 63.8. Found: Hg, 63.5.

Solid A was not identified definitely, but it certainly was not the sulfonyl chloride. *Anal.* Found: C, 53.7; H, 3.37; N, 12.0, 11.7, 11.7. Recrystallization from acetone gave white needles still melting at 210° and with essentially the same analysis.

6-Chloro-3-pyridylmercuric Chloride.—A 25-g. portion of 2-chloro-5-pyridinesulfonyl chloride,[12] m.p. 51°, was suspended in vigorously stirred water and 23 g. of zinc dust was added gradually. The waxy globules of zinc-coated sulfonyl chloride soon disappeared and the liquid took on a green color after 30 minutes of boiling. The mixture was then made alkaline with sodium carbonate and filtered, washing the cake of zinc with hot sodium carbonate solution. The filtrate of the sulfinic salt then was neutralized and 32 g. of mercuric chloride was added. On heating to 100° a clear solution was obtained; after ten minutes, however, a white solid separated from the boiling solution, and this yield increased during the two hours of boiling. The collected solid was washed with water and dried (4.5 g.).

Recrystallization of the crude product, m.p. 130°, from alcohol did not free the solid of mercurous chloride. The crude product then was heated with hot 10% sodium hydroxide solution (80°) and filtered. The residue still contained undissolved organic material and was heated again with hot sodium hydroxide solution, filtering while hot. When the combined alkaline filtrates were neutralized with hydrochloric acid, a white solid separated. The cold suspension was filtered and the solid washed with water. The yield was 1.5 g. The solid was free from inorganic material, gave a positive test for RHgCl compound with sodium stannite, and melted sharply at 263°.

Anal. Calcd. for $C_5H_3Cl_2HgN$: Hg, 57.54. Found: Hg, 57.47.

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[9] "Organic Reactions," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 283.

[10] M. A. Phillips and H. Shapiro, *J. Chem. Soc.*, 584 (1942).

[11] W. T. Caldwell, *et al.*, THIS JOURNAL, **64**, 1695 (1942).

[12] A. Binz and C. Räth, *Ann.*, **487**, 116 (1931).