of phenol and 4-methyl-benzophenone chloride on the steam-bath. It is a wine-red amorphous powder, soluble in most organic solvents except carbon tetrachloride and petroleum ether. It can be precipitated from its alkaline solutions by either carbon dioxide or acetic acid. It could not be crystallized.

Summary.

The results of this work show that the condensation of 4-methyl-benzophenone chloride with phenol is analogous to that between benzophenone chloride and phenol, and indicate that the corresponding carbinol exists in 2 tautomeric forms.

The author wishes to express his indebtedness to Professor M. Gomberg, under whose guidance this work was pursued.

ANN ARBOR, MICH.

[CONTRIBUTION FROM THE HYGIENIC LABORATORY, U. S. PUBLIC HEALTH SERVICE, AND THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO.][1]

PHENYLACETIC-PARA-ARSONIC ACID.

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While arsphenamine[2] and neo-arsphenamine[3] have been found to be probably the best arsenical preparations for the treatment of disease involving infections by the spirochetes, and have been proved a great boon to mankind, they are nevertheless without question dangerous drugs, demanding extraordinary care in manufacture and skill in administration. That there is ample room for improvement is universally recognized. While engaged in investigation of arsenicals for the Hygienic Laboratory of the U. S. Public Health Service, we have started work on the study of preparation of other arsenicals which might lead to an equally efficient and less dangerous drug than the preparations now used.

As a first series in this direction it is the intention to use the carboxyl group of phenyl-acetic acid as the salt-forming group instead of the phenol group of arsphenamine in order to avoid the sensitiveness of the aromatic nucleus[4] to oxidation which makes the arsphenamine so liable to decomposition. Whether the availability of the arsenic in the body will thereby be also reduced in such a way as to make the derivatives of no therapeutic value, the event must tell.

[1] This work was carried out by Mr. Robertson, chemist in the employ of the U. S. Public Health Service, under the direction of Mr. Stieglitz in his capacity of Expert Advisor to the Hygienic Laboratory of the U. S. P. H. S. and is published with the consent of the Surgeon-General. The work was done at the University of Chicago.

[2] The official American name for the drug introduced as "salvarsan;" or known scientifically as the hydrochloride of 3,3′-diamino-4,4′-dihydroxy-1,1′-arsenobenzene.

[3] The American name for the drug introduced as "neo-salvarsan" and known as sodium 3,3′-diamino-4,4′-dihydroxy-1,1′-arsenobenzene methanal-sulphoxylate.

[4] As distinguished from the arsenic atoms.

The preparation of phenyl-acetic-*p*-arsonic acid, $HOOC.CH_2.C_6H_4.AsO_3H_2$, is a first step in this direction and will be described in this preliminary report.

Experimental Part.

p-Nitrobenzyl Cyanide.—Benzyl cyanide was nitrated by the method of Pschorr, Wolfes and Buckow.[1] It was found that an ordinary nitrating mixture (400 cc. of conc. nitric acid, 300 cc. of conc. sulfuric acid to 125 g. benzyl cyanide) gave as good a yield as the more expensive fuming nitric acid. The crude mixture of *o*-, *p*- and *m*-nitrophenyl-acetonitrile is pressed, and then recrystallized once from 95% alcohol and twice from 80% alcohol. The third recrystallization gave a distinct improvement in purity with only a 3 to 4% loss in the mother-liquor.

p-Nitrophenyl-acetic Acid.—The hydrolysis of *p*-nitrobenzyl cyanide by conc. hydrochloric acid in sealed tubes, described by Gabriel,[2] is inconvenient with large quantities. Instead, 100 g. of the nitrile is hydrolyzed by being heated under a reflux condenser for an hour in 900 cc. of sulfuric acid (70% by weight). Yield, after one recrystallization from hot water, 91%. M. p., 151° to 152°, as in the literature.

p-Aminophenyl-acetic Acid.—The method of reduction developed by Jacobs and Heidelberger[3] was modified as follows.

The *p*-nitrophenyl-acetic acid (20 g.) is dissolved in a small amount of warm dil. ammonia, and the solution stirred into a boiling solution of about 8 mols, or 250 g. of ferrous sulfate (commercial crystals) in 300 cc. of water. Conc. commercial ammonia is added cautiously until the solution reacts alkaline; then the mixture is boiled actively for 10 minutes. The liquid is now filtered into 30 cc. of glacial acetic acid and allowed to cool; a mass of glistening, mother-of-pearl scales of the amino-acid separates out. Yield, 75 to 77%. The use of 2 mols excess of ferrous sulfate instead of one (*loc. cit.*) seems to improve the yield slightly.

Phenyl-acetic-p-arsonic Acid ($HOOC.CH_2.C_6H_4.AsO_3H_2$).—The preparation just described was converted into the corresponding acid by the Bart[4] reaction. With the aid of gentle heat, a quantity of *p*-aminophenyl-acetic acid (12.25 g.) is dissolved in 90 cc. of 4-*N* hydrochloric acid. This solution is cooled and diazotized with 5.75 g. of sodium nitrite. A red color appears intermittently after the diazo reaction is well started, and its permanent disappearance marks the end of the reaction.

Arsenious oxide (8.25 g.) and anhydrous sodium carbonate (58 g.) are dissolved in 400 cc. of hot water. Without filtration, the mixture is placed

[1] Pschorr, Wolfes and Buckow, *Ber.*, **33**, 170 (1900).

[2] Gabriel, *ibid.*, **15**, 834 (1882).

[3] THIS JOURNAL, **39**, 1437 (1917).

[4] *J. Soc. Chem. Ind.*, **30**, 1087 (Patent, 1911), and *Zentr.*, **1912**, II, 882 (D. R. P. 250264).

in a liter flask provided with a mechanical stirrer, and heated to 50° by a water-bath.

The catalyst for the reaction is prepared as follows. About 15 g. of common salt is mixed with 50 g. of ice, and a little water added to keep the excess of ice immersed. The whole is placed in a tall beaker containing 2 copper strips, and a current of 2 to 4 amperes is passed through the mixture until the heat of the electrolysis has melted the ice. A quantity of finely divided, colloidal cuprous hydroxide is thus produced in a form favorable for catalysis.

Without any attempt to separate or even coagulate the cuprous hydroxide, the whole electrolyte is poured into the sodium arsenite solution prepared above, and the stirrer set in rapid motion. When the temperature of the contents reaches 50°, the diazo-solution is introduced in a fine stream from a small wash-bottle kept cool with ice.

The resulting brown mixture is poured into a decided excess of conc. hydrochloric acid. (The reverse operation gives much trouble with foaming.) Most of the tar is now easily skimmed off. Washed animal-charcoal is added, the solution filtered into a liter beaker and evaporated to small volume. A second filtration will now remove traces of tar still persisting. The filtrate is now taken to dryness in the liter beaker over the steam-bath. The solid residue is coarsely powdered and extracted twice with absolute alcohol. When the alcoholic filtrate is evaporated, the crude arsonic acid remains as a brown syrup, which will crystallize on the addition of water. Yield, only 20%. The product is recrystallized from hot water with the aid of more charcoal, and, on repeated treatment, is obtainable as white, glistening leaflets, often crystallizing in clumps. It is slightly soluble in cold water, very soluble in hot water and in alcohol. If suddenly placed in a melting-point bath previously heated to about 195°, it melts quietly; but if heated with the bath from room temperature, it undergoes some invisible decomposition, or dehydration, and then does not melt below 270°. At very high temperatures it melts with discoloration and evolution of gas.

Subs., 0.2182: CO_2, 0.2961; H_2O, 0.0701.
Calc. for $C_8H_9O_5As$: C, 36.91; H, 3.49. Found: C, 37.01; H, 3.60.
Subs., 0.1253, 0.049: *N* iodine, 19.27 cc.
Calc.: As, 28.83. Found: 28.58.

Phenyl-acetic-*p*-arsonic acid, when neutralized with alkali and heated with sodium hydrosulfite, gives a light yellow precipitate of an arseno-derivative, soluble in sodium carbonate. A further investigation of this compound, as well as the arseno-derivatives of substituted phenyl-acetic acids is planned.

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