by means of a mixed melting-point determination with its phenylhydrazone (m. p. 118°) and that of an authentic specimen of ethyl pyruvate.

Of the basic product twelve g. distilled at 114–116° (22 mm.) and was shown (see below) to be ethyl-β-piperidinopropionate; yield, 75% of the theoretical; d_{20}, 0.927.

Anal. Calcd. for $C_{10}H_{19}O_2N$: C, 64.85; H, 10.35. Found: C, 64.6; H, 10.0.

The methiodide melted at 100–102°. A mixed melting-point determination with the methiodide prepared from a known sample of the piperidino ester, whose preparation is described below, served to identify the compound.

The residue from the distillation proved to be diethyl-α,α'-dipiperidino-adipate. Four g. of this compound was isolated. After four recrystallizations from ether and one from petroleum ether the compound melted sharply at 94° (von Braun and Münch give 99° as the melting point).

Anal. Calcd. for $C_{20}H_{36}O_4N_2$: C, 65.2; H, 9.8. Found: C, 65.3; H, 9.8.

Ethyl-β-piperidinopropionate.—Seventeen g. of piperidine dissolved in 50 g. of dry benzene was refluxed with 6 g. of ethyl-β-chloropropionate. The product distilled at 113–116° (22 mm.). The methiodide melted at 100–102°.

Summary

Meso-diethyl-α,α'-dibromo-adipate is cleaved by piperidine to give a 75% yield of ethyl-β-piperidinopropionate.

Di-*n*-propylamine gives ethyl-β-di-*n*-propylaminopropionate in a yield of 85%.

The identity of ethyl-β-piperidinopropionate and of ethyl-β-di-*n*-propylaminopropionate has been established by mixed melting-point determinations of the methiodides with authentic specimens.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE COLLEGE OF LIBERAL ARTS, NORTHWESTERN UNIVERSITY]

THE REPLACEMENT OF CARBOXYL BY MERCURY IN CERTAIN 3-SUBSTITUTED PHTHALIC ACIDS. PRELIMINARY PAPER

BY FRANK C. WHITMORE AND PAUL J. CULHANE

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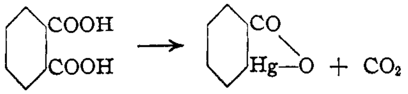
It has long been known that the treatment of phthalic acid with mercuric acetate gives an *o*-mercurated benzoic acid.[1] The present study was



undertaken to determine the mechanism of the mercuration and to find the effect of substituents on the reaction.

The first step in the reaction is the formation of an insoluble mercuric salt, as is the case in the mercuration of benzoic acid. The mercuric phthalate may then lose carbon dioxide with the replacement of the carboxyl by mercury. Another alternative is that the mercuric salt under

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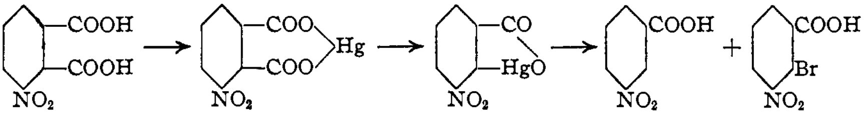
[1] Pesci, *Atti accad. Lincei*, [5] **10**, 1, 362 (1901).

the influence of heat may mercurate the benzene ring ortho to one of the carboxyls as happens in the mercuration of benzoic acid. The product would be a 3-mercurated phthalic acid which, on losing carbon dioxide, would give the observed product, *o*-mercurated benzoic acid. Working with phthalic acid it is impossible to distinguish between these mechanisms. Consequently, 3-substituted phthalic acids were studied. The mercuration of 3-nitrophthalic acid gave a nearly quantitative yield of a mercury compound which reacted with hydrochloric acid to give *m*-nitrobenzoic acid and with bromine to give 2-bromo-3-nitrobenzoic acid. This proves the reaction to be actually a replacement of carboxyl by mercury. In this case the replacement was limited to the 2-carboxyl. If mercuration had preceded the loss of carbon dioxide, the products would have been either *m*-nitrobenzoic acid and 2-bromo-5-nitrobenzoic acid or *o*-nitrobenzoic acid and 2-nitro-5-bromobenzoic acid. The actual course of the reactions was as follows.



Similar results were obtained with 3-bromophthalic acid and 3-chlorophthalic acid. In each case mercury compounds were obtained which gave 3-halogen benzoic acids on treatment with hydrochloric acid. 3-Iodophthalic acid reacted with mercuric acetate to give mercuric iodide and a complex organic mercury compound from which no substituted benzoic acid was obtained.

Experimental Part

Reaction of Sodium 3-Nitrophthalate with Mercuric Acetate.—A warm filtered solution of 211 g. of 3-nitrophthalic acid in 800 cc. of water and 80 g. of sodium hydroxide was mixed in a 3-liter long-necked flask with a hot solution of 350 g. of mercuric acetate in 700 cc. of water and 50 cc. of glacial acetic acid. The flask was provided with a reflux condenser and placed in an oil-bath which was gradually heated to 170°. Evolution of carbon dioxide commenced when this temperature was reached. After heating for seventy hours at 170°, no more carbon dioxide was evolved and a small test sample of the mixture was completely soluble in sodium hydroxide solution. The solid product was washed with water and with alcohol and dried to constant weight at 110°; yield of anhydro-2-hydroxymercuri-3-nitrobenzoic acid, 330 g. or 90%.

Anal. Subs., 0.1987, 0.2010: Hg, 0.1071, 0.1118. Calcd. for $C_7H_3O_4NHg$: Hg, 54.9. Found: 53.9, 55.6.

The analysis was made by the gold crucible method.[2] As is often the case with nitro compounds considerable difficulty was experienced because of the somewhat explosive decomposition of the mercury compounds.

Action of the Mercury Compound with Hydrochloric Acid.—A suspension of 36.6 g. of the mercury compound from 3-nitrophthalic acid, 100 cc. of concd. hydrochloric

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[2] Whitmore, "Organic Compounds of Mercury," Chemical Catalog Co., New York, 1921, p. 365.

acid and 50 cc. of water was heated under reflux for twenty minutes. Complete solution resulted. The crystals obtained by cooling the mixture were crystallized three times from hot water; m. p. 141–143°. Addition of a known sample of *m*-nitrobenzoic acid did not lower the melting point.

Action of Fuming Nitric Acid.—Anhydro-2-hydroxymercuri-3-nitrobenzoic acid dissolved completely in a large excess of hot fuming nitric acid. The mercury was not removed from organic combination even after refluxing for five hours. Dilution of the mixture precipitated unchanged material. The filtrate gave no test for inorganic mercury either with sodium hydroxide or hydrogen sulfide.

Action of Halogens on Anhydro-2-hydroxymercuri-3-nitrobenzoic Acid.—A solution of bromine in carbon tetrachloride was without action on the anhydro compound. On being stirred with an aqueous solution of potassium bromide and bromine, reaction took place, as evidenced by the disappearance of color. Since the reaction was slow, the following procedure was adopted. The anhydro compound (3.7 g.) was heated under reflux with 10 cc. of 2 molar potassium perbromide solution. This represented a 100% excess of bromine. The powdered mercury compound went into solution within two minutes. On cooling, bromine separated from the mixture although before adding to the mercury compound all the bromine had been in solution. The bromine was removed by extraction with chloroform. The aqueous solution was diluted to about 100 cc. and acidified with 5 cc. of concd. hydrochloric acid. The resultant crystalline precipitate was filtered and dried. It contained no mercury and melted at 186–188°. A mixed melting-point determination with 2-bromo-3-nitrobenzoic acid obtained by A. F. Holleman[3] by the nitration of *o*-bromobenzoic acid showed the identity of these materials.

By a similar process 2-iodo-3-nitrobenzoic acid, melting at 204–205.5°, was obtained.

Treatment with chlorine gave 2-chloro-3-nitrobenzoic acid melting at 180–182°. Holleman gives the melting point as 185°.[4]

Mercuration of 3-Bromophthalic Acid.—A solution of 10 g. of 3-bromophthalic acid (m. p. 186.5–189°) in 100 cc. of water containing 4 g. of anhydrous sodium carbonate was mixedwth a solution of 13 g. of mercuric acetate in 100 cc. of water and 5 cc. of glacial acetic acid The resulting precipitate was filtered, washed and dried. The precipitated mercuric salt was suspended in 200 cc. of water and heated under a reflux condenser for fifty-three hours. At that point the mixture was completely soluble in sodium hydroxide. The entire mixture was made alkaline with sodium hydroxide, filtered from a slight residue and acidified with acetic acid. The precipitate formed was always obtained in a gelatinous form which seemed impossible to purify. Boiling this material with concd. hydrochloric acid gave *m*-bromobenzoic acid melting at 150–154°. Addition of known *m*-bromobenzoic acid did not lower the melting point.

Mercuration of 3-Chlorophthalic Acid.—3-Chlorophthalic acid (m. p. 185–187°) was mercurated in a similar way. Treatment of the mercury compound with hydrochloric acid gave *m*-chlorobenzoic acid melting at 150.5–154°. Addition of known *m*-chlorobenzoic acid failed to lower the melting point.

Summary

1. 3-Nitro-, 3-bromo- and 3-chlorophthalic acids react with mercuric acetate on long refluxing to form carbon dioxide and products containing mercury in place of the 2-carboxyl.

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[3] Holleman and de Bruyn, *Rec. trav. chim.*, **20**, 211 (1901).

[4] Ref. 3, p. 209.

2. The mercury compound from 3-nitrophthalic acid is obtained in good yield and reacts with bromine and with iodine to give good yields of the otherwise difficultly obtainable 2-bromo-3-nitrobenzoic acid and 2-iodo-3-nitrobenzoic acid.

3. Anhydro-2-hydroxymercuri-3-nitrobenzoic acid can be refluxed with fuming nitric acid without breaking the C-Hg linkage. On the other hand a short heating with concd. hydrochloric acid removes the mercury completely from the organic molecule.

4. The results obtained with the 3-substituted phthalic acids show that the mercuration reaction consists in the replacement of the 2-carboxyl by mercury.

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[CONTRIBUTION FROM THE PLAUT LABORATORY OF LEHN AND FINK, INC.]

THE PREPARATION OF CERTAIN CHLORO AND BROMO DERIVATIVES OF 2,4-DIHYDROXYDIPHENYLMETHANE AND -ETHANE AND THEIR GERMICIDAL ACTION[1]

BY EMIL KLARMANN AND JOHN VON WOWERN

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Introduction

The introduction of aryl groups into the nucleus of resorcinol leads to compounds showing a very pronounced germicidal action.[2] It has been shown that of the three aryl groups, *viz.*, benzyl, phenylethyl and phenylpropyl, the introduction of the second produces the most active aryl derivative of resorcinol, the phenol coefficient of which was reported as being 41, against *B. typhosus.*[3]

It is well known that halogen substitution of phenol and its alkyl derivatives leads to compounds, the germicidal potency of which is very considerably greater than that of the unsubstituted compounds. While the germicidal action increases with the number of halogen atoms introduced (one molecule of pentabromophenol has the same effect upon *B. diphtheriae* as 500 molecules of phenol), the toxicity first drops but later rises again. Thus monohalogen phenol is less toxic than phenol, while the general toxicity of trihalogen phenol approximately equals that of phenol itself; tetra- and pentahalogen phenol derivatives are more toxic than phenol.[4]

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[1] Presented in part before the Division of Biological Chemistry at the meeting of the American Chemical Society in Swampscott, Massachusetts, September, 1928.

[2] E. Klarmann, THIS JOURNAL, **48**, 791 (1926).

[3] E. Klarmann, *ibid.*, **48**, 2358 (1926).

[4] R. Koch, *Mitt. Kais. Gesundheitsamt*, **1**, 234 (1881); H. Bechhold and P. Ehrlich, *Z. physiol. Chem.*, **47**, 173 (1906); K. Laubenheimer, "Phenol und seine Derivate als Desinfektionsmittel." Berlin-Wien, **1909.**