and it was then diluted with a small amount of water and cooled. The product which separated on being crystallized once from glacial acetic acid gave 2.4 g. (36%) of pure quinone in the form of long, pale yellow needles, m. p. 283–284°, dec. (unchanged on further crystallization). The quinone gives a vat test.

Anal. Calcd. for $C_{21}H_{18}O_4$: C, 75.44; H, 5.43. Found: C, 75.66, 75.67; H, 5.74, 5.78.

1',2',3',4' - Tetrahydro - 6 - methyl - 1,2 - benzanthracene-5-acetic Acid (V).—A mixture of 20 g. of zinc dust, 0.2 g. of copper sulfate, 100 cc. of concentrated ammonia solution, and 2.4 g. of the quinone IV was heated for forty-eight hours with the addition in portions of 500 cc. more ammonia solution. Some of the product precipitated on acidifying the filtered ammonia solution, but the bulk of it was recovered from the filter cake after leaching with dilute acid to remove the zinc. One crystallization from glacial acetic acid gave 1.7 g. (78%) of crude, gray product, m. p. 254–256°, dec. This was dissolved in 50 cc. of 10% sodium carbonate solution and saturated carbonate solution was added to the hot filtrate until the sodium salt of the acid began to crystallize. The salt separated on cooling in lustrous plates and on acidifying a solution of the compound in water the free acid separated in a colorless condition, m. p. 255–257°, dec., yield 1.55 g. After two crystallizations from alcohol the substance formed pale yellow needles, m. p. 267–269°, dec.

Anal. Calcd. for $C_{21}H_{20}O_2$: C, 82.55; H, 6.65. Found: C, 82.58; H, 6.65.

Treated with thionyl chloride in ether, the acid was converted into a black tar. Phosphorus pentachloride in ligroin gave what appeared to be a satisfactory acid chloride, but the product obtained on treating this in carbon bisulfide with stannic chloride and aluminum chloride contained more oxygen than required for a normal cyclization product and failed to yield a semicarbazone.

β-Phenylnaphthalene.—The sample used for spectrographic measurement was synthesized from β-bromonaphthalene (8 g.) and cyclohexanone (4.2 g.). The product from the Grignard reaction on distillation gave 5.8 g. (72%) of the unsaturated hydrocarbon as a light yellow oil, b. p. 212–215° (9 mm.). This was heated with 1.8 g. of sulfur at 240–260° for one hour, the product was distilled, and the solidified distillate crystallized from alcohol as colorless prisms, m. p. 100–101°; yield 1.9 g. (33%). After two more crystallizations from alcohol the substance melted constantly at 102.2–102.7°. Bamberger and Chattaway[11] give 102–102.5°.

Summary

The hexahydro derivative which Wieland and Dane obtained by reducing methylcholanthrene with sodium and amyl alcohol has been shown by oxidation to be the 1,2,3,4,11,14-hexahydride. Catalytic hydrogenation gives some of the same product along with the 6,7-dihydride, and the two reactions appear to be concurrent and independent. The sodium–alcohol reduction follows the same course as with simpler 1,2-benzanthracene derivatives, but in the catalytic process methylcholanthrene behaves differently from the other members of the series.

The structure of 6,7-dihydro-20-methylcholanthrene was established by comparison of the ultraviolet absorption spectrum with the spectra of compounds having the unsaturated absorbing centers of the various possible di- and tetrahydro derivatives of methylcholanthrene. The spectrographic measurements were made at the Biochemical Research Laboratories of the Franklin Institute.

(11) Bamberger and Chattaway, *Ber.*, **26**, 1745 (1893).

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The Phosphorus Analogs and Homologs of Choline and Betaine. Onium Compounds. XVII

BY R. R. RENSHAW AND R. A. BISHOP

The products here described were made a number of years ago and their pharmacological investigation was carried out by Reid Hunt.[1] Since it was shown that the phosphorus compounds produced qualitatively the same physiological action that analogous nitrogen compounds gave, it seemed clear that the onium element is not, *per se*, of primary significance in the physiological activity of these compounds. It was, therefore, postulated[2] that the onium element merely determines an effective geometrical structure which, in turn, makes possible some specific type of adsorption or desorption process.

Triethylphosphine, from which the triethyl analogs of choline and betaine derivatives were prepared, was readily obtained by the Grignard reaction as shown by Hibbert.[3] We were unable, however, under a great variety of experi-

(1) Hunt and Renshaw, *J. Pharmacol.*, **25**, 315 (1925); **29**, 17 (1926).

(2) Renshaw, *Science*, **62**, 384 (1925).

(3) Hibbert, *Ber.*, **39**, 160 (1906).

mental conditions to apply the Grignard reaction to the preparation of trimethylphosphine. While barely more than traces of phosphine were formed, we were able to isolate notable quantities of tetramethylphosphonium salts. We assume that this failure is due to an extraordinary ease of methylation of the alkyl phosphines. This checks with the results of Hofmann[4] (as well as our own),[5] who showed that when phosphonium iodide was treated with as little as a molar quantity of methyl alcohol neither primary nor secondary phosphine could be detected, though there were present phosphine and tetramethylphosphonium iodide.

Experimental Part

Hydroxyethyl-trimethylphosphonium Chloride.[6]—This phosphorus analog of choline was prepared as follows: to 12 g. of trimethylphosphine in a pressure bottle there was added an excess of chloroethyl alcohol (15 g.) dissolved in 20 cc. of absolute alcohol and the material heated for six to seven hours at 90–100°. The product was then diluted with alcohol and the "phospho choline" precipitated by ether. The product was purified by successive fractional precipitations of its alcohol solutions by ether. When the precipitation is carried on slowly the product separates out in beautiful long needle crystals, which are very hygroscopic and very soluble in water and alcohols, and substantially insoluble in benzene, ether, petroleum ether, and carbon disulfide.

Anal. Calcd. for $C_5H_{14}PCl$: Cl, 22.68. Found: Cl, 22.46, 22.65.

The Action of Alcoholic Potassium Hydroxide on Bromoethyl-trimethylphosphonium Bromide.—The process used, in an attempt to prepare the phosphorus analog of neurine, was the same as that found to be successful with the nitrogen compound. To 8.5 g. of bromoethyl-trimethylphosphonium bromide dissolved in absolute alcohol, there was added 34.24 cc. of absolute alcoholic potassium hydroxide containing one molecular equivalent of the base. Alkalinity, which persisted after shaking, was obtained when only 20 cc. of the alkali was added. The solution at the same time began to give off a strong odor of trimethylphosphine. After adding the theoretical quantity of alkali and filtering off the potassium bromide the mixture was warmed on the water-bath for an hour. There was a marked evolution of trimethylphosphine. The solution was cooled, filtered and precipitated with ether. The precipitate weighed 3 g. It was purified by three recrystallizations from alcohol and then analyzed. It appears to be hexamethylethenyldiphosphonium bromide, $[(CH_3)_3PCH_2CH_2P(CH_3)_3]Br_2$. The formation of this indicates that the "phospho neurine" first produced decomposes, particularly on heating, giving off trimethylphosphine, which then reacts readily in the alcohol solution with the bromine of the bromoethyl-trimethylphosphonium compound still present.

Anal. Calcd. for $C_8H_{22}P_2Br_2$: Br, 47.06. Found: Br, 46.90, 46.86.

Hydroxyethyl-triethylphosphonium Bromide.—Triethylphosphine was prepared in 70% yield by the Grignard[3] reaction. Equal molecular quantities of this product and bromoethyl alcohol were heated for twelve hours at 50° in a pressure bottle. The solid which formed was filtered, washed with ether, dried and purified by several fractional precipitations of its solution in absolute alcohol with absolute ether. So purified it forms long needle crystals, m. p. 223° (corr.).

Anal. Calcd. for $C_8H_{20}POBr$: Br, 32.87. Found: Br, 32.94, 32.87.

Acetoxyethyl-triethylphosphonium Bromide.—Molar quantities of triethylphosphine and β-bromoethyl acetate were warmed for ten hours at 40° when the reaction seemed to be complete. The very hygroscopic solid was purified with some difficulty by recrystallizing from absolute alcohol–ether mixture; m. p. 74.6° (corr.).

Anal. Calcd. for $C_{10}H_{22}PO_2Br$: Br, 28.03. Found: Br, 27.94, 28.00.

Carboethoxymethyl-triethylphosphonium Bromide.—Ethyl bromoacetate reacts vigorously with triethylphosphine at room temperature. This analog of a betaine ester was obtained in the form of plates from its solution in absolute alcohol–ether. It, like the ethylcholine analog, shows a marked tendency to precipitate from its solutions as an oil; m. p. 83.2° (corr.).

Anal. Calcd. for $C_{10}H_{22}PO_2Br$: Br, 28.03. Found: Br, 27.75, 27.93.

Hunt[1] has shown that the phosphorus analog of choline (trimethyl derivative) has a marked muscarine action which was markedly increased by acetylation.[7] The triethyl homolog of phosphocholine, acetylcholine and betaine ester, like the corresponding nitrogen compounds, showed none of the stimulating actions of acetylcholine, but, like the nitrogen analog, gave a marked paralyzing nicotine action.

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Summary

The preparation of the phosphocholine is described as well as its ethyl analog, the acetyl derivative of the latter and the ethyl ester of the triethylphosphonium betaine. Pharmacological activity of these, as compared with the corresponding nitrogen compounds, is reviewed briefly.

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(4) Hofmann, *Ber.*, **4**, 209 (1871).

(5) Renshaw and Bell, THIS JOURNAL, **43**, 917 (1921).

(6) The work on the trimethylphosphine derivatives was done by the senior author in 1918.

(7) Recently, Welch and Roepke [*J. Pharmacol.*, **55**, 118 (1935)] have made a more thorough investigation of the pharmacological activity of acetylphosphocholine.